

## Antimicrobial stewardship outcomes in a medium-sized Itajaí Valley hospital

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### Abstract

**Objectives:** Antimicrobial resistance is a major healthcare challenge, reducing treatment effectiveness and raising infection risks. Antimicrobial Stewardship Programs (ASP) aim to optimize medicine use and curb resistant strains. This study evaluates the impact of ASP implementation in a medium-sized teaching hospital in Southern Brazil by measuring changes in antimicrobial use with Defined Daily Dose (DDD) and Days of Therapy (DOT). **Methods:** This study retrospectively reviews electronic medical record data from September 2023 to September 2024 across three care areas: Intensive Care Unit (ICU), Medical Clinic, and Surgical Clinic. Data were compared between pre- and post-implementation periods of the ASP using the Mann–Whitney test. **Results:** Following ASP implementation, significant reductions were observed in the use of carbapenems, in the ICU (13.0%) and in the Surgical Clinic (68.5%), as well as fluoroquinolones in the ICU (41.4%). In contrast, penicillin combined with  $\beta$ -lactamase inhibitors increased substantially in the Medical Clinic (115.3%), suggesting a therapeutic shift toward safer agents. Fourth-generation cephalosporins and glycopeptides displayed localized increases consistent with rationalization of empirical and targeted therapy. For these agents, there was an 11.3% decrease in DDD within the ICU (11.3%), whereas there were increases in the Medical (18.7%) and Surgical Clinics (3.1%). **Conclusion:** The implementation of the ASP effectively modulated antimicrobial consumption, reducing the use of high-risk broad-spectrum agents while promoting rational alternatives. These findings demonstrate that ASPs can yield measurable benefits even in resource-limited hospital settings, reinforcing the need for continuous surveillance using DDD and DOT indicators to sustain progress against antimicrobial resistance.

**Keywords:** health services; antimicrobial stewardship; indicators of health services; drug resistance

## Resultados de um programa de gestão de antimicrobianos em um hospital de médio porte no Vale de Itajaí

### Resumo

**Objetivos:** A resistência antimicrobiana é um grande desafio na área da saúde, pois reduz a eficácia do tratamento e aumenta os riscos de infecção. Os programas de gerenciamento de antimicrobianos (PGA) visam otimizar o uso de medicamentos e conter as bactérias resistentes. Este estudo avalia o efeito da implementação de um PGA em um hospital de ensino de médio porte no sul do Brasil, analisando as mudanças no consumo de antimicrobianos por meio da dose diária definida (DDD) e dos dias de terapia (DOT). **Métodos:** Este estudo analisa retrospectivamente os dados dos prontuários eletrônicos de setembro de 2023 a setembro de 2024 em três áreas de assistência: Unidade de Terapia Intensiva (UTI), clínica médica e clínica cirúrgica. Os dados foram comparados entre os períodos pré e pós-implantação do PGA usando o teste de Mann-Whitney. **Resultados:** Após a implementação do PGA, observaram-se reduções significativas no uso de carbapenêmicos, na UTI (13,0%) e na clínica cirúrgica (68,5%), bem como de fluoroquinolonas na UTI (41,4%). Em contrapartida, as penicilinas combinadas com inibidores da  $\beta$ -lactamase aumentaram substancialmente na clínica médica (115,3%), sugerindo uma mudança terapêutica para agentes mais seguros. As cefalosporinas de quarta geração e os glicopeptídeos apresentaram aumentos localizados consistentes com a racionalização da terapia empírica e direcionada. Para esses agentes, houve uma redução de 11,3% na DDD na UTI (11,3%), enquanto houve aumentos na clínica médica (18,7%) e na Clínica Cirúrgica (3,1%). **Conclusão:** A implementação do PGA modulou efetivamente o consumo de antimicrobianos, reduzindo o uso de agentes de amplo espectro de alto risco e promovendo alternativas racionais. Esses achados demonstram que os



PGAs podem produzir benefícios mensuráveis mesmo em ambientes hospitalares com recursos limitados, reforçando a necessidade de vigilância contínua usando indicadores DDD e DOT para sustentar o progresso contra a resistência antimicrobiana.

**Palavras-chave:** serviços de saúde; gestão de antimicrobianos; indicadores de serviços; resistência microbiana a medicamentos

## Introduction

Antimicrobial resistance poses a major threat to public health globally.<sup>1</sup> The widespread and often improper use of antimicrobials has led to the rise of multidrug-resistant strains, reducing the effectiveness of treatments and increasing illness and death rates across clinical settings.<sup>2</sup> In response, healthcare institutions have adopted antimicrobial stewardship programs (ASP) to optimize antimicrobial use and preserve the effectiveness of essential therapies. Such programs aim to improve clinical outcomes, reduce antimicrobial resistance, and decrease healthcare costs by promoting appropriate antimicrobial prescribing practices.<sup>3</sup> The implementation of ASP in healthcare facilities is critical for mitigating the threat of antimicrobial resistance and improving patient outcomes.<sup>4</sup> This involves strategies that include constant prescription review, professional education, and implementation of protocols to promote rational medication use.<sup>5,6</sup>

In Brazil, the appropriate use of antimicrobials faces significant challenges, particularly in medium-sized and large hospitals, where the complexity of patient cases and the high demand for intensive treatments can contribute to the excessive use of broad-spectrum agents.<sup>7</sup> Consequently, it is crucial to systematically evaluate the impact of interventions, such as the implementation of ASPs, to validate the effectiveness of the adopted strategies and guide future actions. In hospital settings this is usually achieved by using two standardized indicators: defined daily dose (DDD) and days of therapy (DOT). These indicators enable the measurement of antimicrobial consumption. DDD represents the assumed average maintenance dose per day for a drug used for its main indication in adults, calculated by dividing the total amount of drug consumed (in grams) by the WHO-assigned standard daily dose. DOT, in contrast, quantifies the number of days a patient receives a specific antimicrobial, regardless of dose, and is obtained by summing all days of exposure to each agent and standardizing per 1,000 patient-days.<sup>8</sup>

The aim of this study was to investigate the potential reduction in antimicrobial consumption, based on DDD and DOT indicators, in a medium-sized philanthropic hospital located in Southern Brazil, following the implementation of a structured ASP. Furthermore, the study focused on determining the variations in the consumption profile across different care areas, enabling a better understanding of the unique challenges and characteristics presented by each sector.

## Population And Antimicrobial Selection

This quasi-experimental before-and-after design study was conducted using data extracted from the electronic medical records of a medium-sized hospital in Southern Brazil. The institution is recognized for providing highly complex care and counts with a 20-bed intensive care unit (ICU) for adult patients. In addition, it serves as a teaching and multi-professional residency center in the fields of Medicine, Nursing, Nutrition, Psychology, and Physical Therapy.

The study included adult patients, aged 18 years and older, admitted to the ICU, medical and surgical clinics, who received antimicrobials classified according to the AWaRe classification, as well as the antifungal micafungin, between the period from September 2023 to September 2025.

**Table 1.** Subgroups of antimicrobials listed according to the Anatomical Therapeutic Chemical (ATC) and AWaRe classification (WHO, 2023).

Subgroup	ATC	Antimicrobial	AWaRe
J01CR- Penicillin combinations with beta-lactamase inhibitors	J01CR05	Piperacillin + enzyme inhibitor	Watch
	J01CR01	Ampicilin + enzyme inhibitor	Watch
J01DD- 3 <sup>rd</sup> generation Cephalosporins	J01DD52	Ceftazidime + Avibactam	Reserve
	J01DD04	Ceftriaxone	Watch
J01DE- 4 <sup>th</sup> generation Cephalosporins	J01DE01	Cefepime	Watch
J01DH – Carbapenems	J01DH03	Ertapenem	Watch
	J01DH02	Meropenem	Watch
J01MA – Fluoroquinolones	J01MA12	Levofloxacin	Watch
	J01MA02	Ciprofloxacin	Watch
J01XA – Glycopeptides	J01XA01	Vancomycin	Watch
Subgroup	ATC	Antifungal	AWaRe
J02A- Antimycotics for systemic use	J02AX05	Micafungin	*

\*Micafungin is not classified within AWaRe because it is an antimycotic.

This study was approved by the Human Research Ethics Committee of the Federal University of Santa Catarina (Protocol Number 6.818.378). As it was a retrospective study based on data from electronic medical records, there was no need for direct data collection from patients.

## Methods

The data were extracted from the electronic medical records registered in the Tasy system, complemented by the monitoring spreadsheets developed by the ASP Group. This group is responsible for the periodic review of antimicrobial prescriptions, using an institutional protocol that includes the evaluation of results from cultures, antibiograms, patient weight, and renal clearance, performed between 48 and 72 hours after the initiation of therapy.

Additionally, the ASP group held interdisciplinary meetings and used a standardized checklist to ensure that the ASP interventions were carried out in an aligned and consistent manner, promoting a critical review of prescriptions and targeted therapeutic adjustments. This process allowed for a comprehensive and systematic approach to antimicrobial management, supporting the optimization of prescribing practices and patient outcomes.

The study used DDD and DOT indicators as they provide complementary perspectives on antimicrobial consumption: DDD reflects standardized drug volume, while DOT captures actual exposure duration. Using both metrics strengthens interpretation, particularly in ICUs, where adjustments can distort DDD values. DOT mitigates these distortions, but does not account for dose intensity. Their combined use offers a more accurate and balanced assessment of antimicrobial consumption patterns and ASP impact in critically ill populations.

The data assessed the monthly average antimicrobial use across the different care units over defined pre-implementation (September 1<sup>st</sup>, 2023, to August 31<sup>st</sup>, 2024) and post-implementation (September 1<sup>st</sup>, 2024 to August 31<sup>st</sup>, 2025) periods, with no transition or washout phase between them. The dataset was structured to allow direct comparison between these intervals, enabling the identification of significant trends and variations in antimicrobial use.

Statistical analysis was conducted with GraphPad Prism for Windows software, version 8.0. Descriptive statistics were used to characterize the data, followed by the application of the Mann-Whitney test to compare independent groups. As a non-parametric test, it provides a robust approach for detecting differences in non-normally distributed datasets, making it appropriate for the structure and distribution of the variables analyzed. The absence of time-series analyses is as a limitation of the study. P values smaller than 0.05 were considered statistically significant.

## Results

The establishment of ASP has been extensively recognized as an effective strategy to optimize antimicrobial use and combat bacterial resistance in various international contexts. Studies have shown significant reductions in both prescription rates and consumption of these drugs, reflecting improvements in clinical and economic outcomes for health systems.<sup>9</sup> Recent efforts led by the ASP Brazil (ASP-BR) group, in collaboration with the Brazilian Health Regulatory Agency (ANVISA), the Ministry of Health, the University of Santa Cruz do Sul, and the Brazilian Association of Infection Control and Hospital Epidemiology Professionals, have sought to understand and expand the implementation of ASPs in Brazilian hospitals.

A multicenter study conducted by ASP-BR between July and August 2019 evaluated ASP in Brazilian hospitals with adult ICUs. Among the 954 participating hospitals, approximately half (47.5%) had an ASP implemented: the majority at basic (32.2%) or intermediate (43.1%) levels, with only a few classified as advanced (23.6%)<sup>10</sup>. Similar results have already been identified in other countries, pointing to a lack of human and technological resources as barriers to the effectiveness of ASP.<sup>11</sup> A new assessment conducted between October 2022 and January 2023 revealed progress, with an increase (36.8%) in intermediate and advanced levels and improvements in the education dimension, although support from senior management declined slightly.<sup>6</sup>

This study evaluated the impact of implementing an ASP in a medium-sized hospital in Southern Brazil through an integrated analysis of DDD and DOT. These indicators allow for a quantitative assessment of standardized antimicrobial consumption (DDD/1,000 patient-days) and the duration of therapeutic exposure (DOT/1,000 patient-days) and are recommended for the longitudinal monitoring of antimicrobial use in different hospital settings. The results are summarized in Tables 2 and 3 and graphically represented in Figure 1.

The DDD analysis showed an overall decrease in antimicrobial consumption in the ICU, from 606.3 to 537.8 DDD/1,000 bed-days (-11.3%), a trend similar to that recorded in the surgical clinic (+3.1%) and contrasting with the increase observed in the Medical Clinic (+18.7%). Noteworthy were the reductions in carbapenems (-13.0% in the ICU, and -68.5% in the surgical clinic), third-generation cephalosporins (-15.5% in the ICU), and fluoroquinolones (-41.4% in the ICU, and -37.6% in the Surgical Clinic). These findings are consistent with the findings in other countries, such as Argentina, Chile, Canada, China, Uruguay, and Spain, where the adoption of national control policies has resulted in significant declines in antimicrobial consumption in hospitalized patients.<sup>12-15</sup>

Complementarily, DOT analysis revealed a similar pattern. There was an overall decrease in antimicrobial consumption of 4.9% (from 583.8 to 555.2 DOT/1,000 patient-days) in the ICU, while in the Surgical and Medical Clinics there were increases of 21.0% and 23.9%, respectively. The most significant reductions occurred in the use of carbapenems, with decreases of 5.9% in the ICU, 16.0% in the medical clinic, and 68.2% in the surgical clinic. These results indicate strategic therapeutic substitutions for narrower spectrum antimicrobials, such as penicillins with beta-lactamase inhibitors, that had their consumption increased by 115.3% in the medical clinic (DOT), highlighting the implementation of de-escalation strategies, as recommended in good ASP practices.<sup>16</sup>

The consumption of fluoroquinolones, traditionally associated with resistance selection and adverse events, reduced in the ICU when considering both DDD (-41.4%) and DOT (-33.0%) indicators. These results are comparable to those reported in Canadian and Ecuadorian studies, which relate this trend to the implementation of more restrictive strategies and therapeutic audits.<sup>13,17-19</sup>

Conversely, there was a significant rise in the use of glycopeptides in the Surgical Clinic (675.2% in DDD and 586.9% in DOT) that differs from previous Latin American studies showing reductions in this group after the implementation of ASP.<sup>12,20</sup> However, this is not related to ASP not fulfilling its function in the present study. What happened was that, at first, glycopeptide consumption at the investigated hospital was limited, reflecting a care profile less focused on highly complex procedures and with less demand for coverage against resistant pathogens. However, following approval to perform orthopedic surgeries, there was a turning point in the care profile, especially in the surgical clinic.

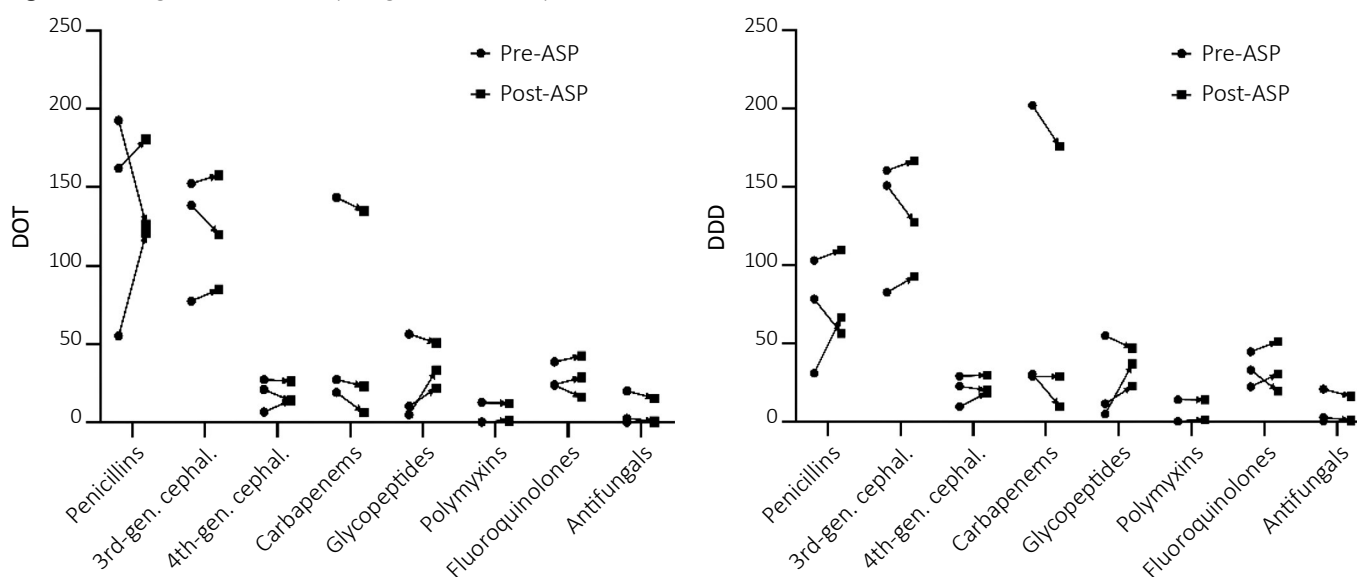
The expansion of orthopedic procedures brought with it an increase in the number of hospitalized patients with complex postoperative conditions, who were more susceptible to serious infections, such as osteomyelitis and joint prosthesis infections. In these clinical circumstances, the use of broad-spectrum antimicrobials becomes important, with glycopeptides frequently chosen for their effectiveness against multidrug-resistant microorganisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA).<sup>21</sup>

**Table 2.** Average DDD per period and percentage difference between periods

Antimicrobial	Pre-ASP			Post-ASP			P value		
	ICU	Medical	Surgical	ICU	Medical	Surgical	ICU	Medical	Surgical
Penicillins	102.80	30.82	78.23	109.40 (6.4%)	66.35 (115.3%)	56.14 (-28.2%)	0.4776	0.0056*	0.1005
3 <sup>rd</sup> -generation Cephalosporins	150.60	160.20	82.32	127.30 (-15.5%)	166.60 (4.0%)	92.42 (12.3%)	0.2913	0.7987	0.6297
4 <sup>th</sup> -generation Cephalosporins / Advanced	28.91	22.44	9.39	29.55 (2.2%)	19.86 (-11.5%)	18.44 (96.3%)	0.9323	0.8116	0.2774
Carbapenems	201.80	28.67	30.24	175.60 (-13.0%)	28.88 (0.7%)	9.52 (-68.5%)	0.2913	0.8559	0.5136
Glycopeptides	54.78	11.29	4.74	46.71 (-14.7%)	22.48 (99.1%)	36.73 (675.2%)	0.7125	0.0907	0.0879◆
Polymyxins	13.89	0.1750	--	13.87 (-0.1%)	1.093 (+524.6)	--	0.9285	0.4783	--
Fluoroquinolones	32.81	44.50	22.10	19.23 (-41.4%)	51.13 (14.9%)	30.40 (37.6%)	0.2411	0.3777	0.2913
Antifungals	20.66	2.55	--	16.09 (-22.1%)	0.75 (-70.4%)	--	0.2633	0.3416	--
TOTAL	606.3	301.9	236.8	537.8 (-11.3%)	358.5 (+18.7%)	244.8 (+3.1%)	0.0887◆	0.0684◆	0.9323

Source: The author. \*: Significant P values, less than 0.05. ◆: P values between 0.06 and 0.09 indicate a trend. Mann-Whitney test performed.

**Figure 1.** Average DOT and DDD by drug class between periods.



Source: The author. Legend: 3rd-gen. cephal.: 3<sup>rd</sup>-generation cephalosporins; 4th-gen. cephal.: 4<sup>th</sup>-generation cephalosporins / Advanced.

The need of empirical therapy for surgical infections was attributed as the main reason for the increase in consumption of glycopeptides, especially in a scenario of increased major surgeries. This scenario, although predictable in institutions that expand their scope of complexity, highlights the importance of continuous monitoring of consumption patterns and local microbiological surveillance.

The consumption of antifungal agents also showed consistent decreases in the three units studied, particularly in the medical clinic (-70.4% in DDD and -68.8% in DOT) and ICU (-22.1% in both indicators). These reductions may be related to greater rigor in the

clinical and laboratory criteria for initiating antifungal therapy, as described in Spanish studies, which demonstrate the effectiveness of rapid diagnosis and early reassessment strategies in limiting unjustified empirical use.<sup>20,22</sup>

Fourth-generation cephalosporins showed a heterogeneous profile: an increase of 96.3% (DDD) and 113.7% (DOT) in the surgical clinic, but a reduction of 11.5% (DDD) and 35.1% (DOT) in the medical clinic. These variations suggest a potential replacement of carbapenems with intermediate-spectrum agents in intra-abdominal or respiratory infections, a practice already described in the literature as a way to preserve last-line antimicrobials.<sup>16</sup>

**Table 3.** Average DOT per period and percentage difference between periods

Antimicrobial	Pre-ASP			Post-ASP			P value		
	ICU	Medical	Surgical	ICU	Medical	Surgical	ICU	Medical	Surgical
Penicillins	162.00	55.07	192.70	180.60 (11.5%)	120.40 (118.6%)	126.50 (-34.4%)	0.3474	0.0045*	0.0519◆
3 <sup>rd</sup> -generation Cephalosporins	138.40	152.40	77.28	119.90 (-13.4%)	157.70 (3.5%)	84.79 (9.7%)	0.2657	0.7987	0.5137
4 <sup>th</sup> -generation Cephalosporins / Advanced	27.24	20.90	6.61	26.19 (-3.9%)	13.57 (-35.1%)	14.12 (113.7%)	0.8874	0.3551	0.3958
Carbapenems	143.40	27.34	19.02	134.90 (-5.9%)	22.97 (-16.0%)	96.05 (-68.2%)	0.3186	0.6011	0.5136
Glycopeptides	56.34	10.28	4.86	50.57 (-10.2%)	21.78 (111.9%)	33.35 (586.9%)	0.8428	0.0963◆	0.0879◆
Polymyxins	12.65	0.13	0.00	12.00 (-5.1%)	0.80 (506.9%)	1.38 (-)	0.8816	0.4783	--
Fluoroquinolones	23.73	38.56	24.02	15.91 (-33.0%)	42.43 (10.0%)	28.60 (19.1%)	0.2652	0.5899	0.7125
Antifungals	20.08	2.42	--	15.27 (-24.0%)	0.755 (-68.8%)	--	0.2167	0.3416	--
TOTAL	583.80	307.10	314.40	555.2 (-4.9%)	380.4 (+23.9%)	380.4 (+21.0%)	0.4428	0.0332*	0.0597◆

Source: The author. \*: Significant P values, less than 0.05. ◆: P values between 0.06 and 0.09 indicate a trend. Mann-Whitney test performed.

Although there was an overall decrease in consumption, the ICU maintained the highest absolute values for DDD and DOT compared to the other units. This pattern is consistent with the greater clinical severity of patients, frequent use of more invasive devices, and the increased risk of nosocomial infections, which are widely recognized in international studies.<sup>13,23</sup> This finding reinforces the need for specific strategies for ICUs, such as daily prescription reviews, de-escalation protocols, and therapeutic audits with a multidisciplinary approach. In fact, successful experiences indicate that a robust ASP in ICUs can reduce mortality, length of stay, and the incidence of infections caused by multidrug-resistant microorganisms.<sup>24</sup>

It is important to point out that this study has several key limitations. First, its single-center design limits generalizability, as antimicrobial use and hospital structures can differ significantly elsewhere; results may mainly reflect local conditions. Second, without a control group, observed changes in antimicrobial use cannot be linked solely to ASP interventions, since other factors may have influenced outcomes. Third, lacking time-series analyses further restricts trend and causality assessment. These constraints underscore the need for multicenter, controlled studies to provide stronger evidence for ASP effectiveness. With this study we demonstrated that implementing an ASP strategy can promote meaningful changes in antimicrobial consumption patterns, including substantial reductions in reserve agents and increased rational use of targeted antimicrobials.

These findings corroborate international evidence and underscore that ASPs are not only effective, but also scalable and feasible in medium-sized and resource-limited hospitals. By showing measurable improvements in antimicrobial use within a setting with constrained infrastructure and staffing, this work highlights the strategic value of ASP as an essential tool for patient safety and the sustainability of anti-infective therapies.

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#### Conflict Of Interest

None to declare.

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