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## Assessment of Adherence to Clinical Protocols and Interface with Antimicrobial Stewardship Program

Avaliação da Adesão aos Protocolos Clínicos e a Interface com o *Antimicrobial Stewardship Program*

Evaluación de la adherencia a los protocolos clínicos y la interfaz con el *Antimicrobial Stewardship Program*

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### ABSTRACT

**Introduction:** Antimicrobial resistance is a global concern. Antimicrobial Stewardship Program interventions are necessary to guide the implementation of treatment protocols for major infectious syndromes. **Aim:** To evaluate the adherence rate to clinical protocols related to the prescription of antimicrobials in a teaching hospital in Rio Grande do Sul. **Outlining:** Retrospective cross-sectional study, conducted with secondary data from antimicrobial prescriptions of patients hospitalized in clinical units from July to December 2020. **Results:** 4028 antimicrobial prescriptions were evaluated, with 42.9% non-adherence to institutional clinical protocols, 39.3% with complete adherence and 17.8% with partial adherence. **Implications:** Knowing the adherence data to clinical protocols provides an opportunity to intervene in improvements in antimicrobial prescribing, verifying the need for permanent education for prescribers, medical students, and residents. This contributes to the promotion of rational use of antimicrobials and helps in the fight against antimicrobial resistance.

### DESCRIPTORS

Antimicrobial Agents; Drug Resistance, Microbial; Stewardship Program; Clinical Guidelines.

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## INTRODUCTION

Antimicrobial resistance is one of the biggest global concerns in public health currently, as antimicrobials are becoming less effective due to their widespread use.<sup>1</sup> About 40% of antimicrobial prescriptions in the hospital setting are inadequate or unnecessary, demonstrating that inappropriate prescription of this therapeutic class is a risk factor for lack of clinical response.<sup>2-3</sup> It is estimated that by 2050 there will be global increases of up to one trillion dollars in healthcare costs,<sup>4</sup> and that deaths due to antimicrobial resistance may surpass those related to cancer.<sup>5</sup>

Interventions by Antimicrobial Stewardship Programs (ASPs) are necessary and critical to minimize this global crisis.<sup>2</sup> ASP is a term defined by the Infectious Diseases Society of America (IDSA) as a set of coordinated interventions aimed at improving and measuring the use of antimicrobial agents through optimization of the ideal antimicrobial regimen.<sup>6</sup> Interventions should be prioritized through an interdisciplinary team that is trained and motivated, with a convergent language and institutional support, according to policies and objectives defined in accordance with patient safety standards.<sup>7-8</sup> The operational team should consist of an infectious disease physician, a clinical pharmacist with expertise in infectious diseases and antimicrobial use, an infection control nurse, and a clinical microbiologist.<sup>9</sup> The team leader is usually a pharmacist who assists in the development of clinical protocols, evaluates the need for maintenance of treatment, monitors, restricts and analyzes resistance patterns, and promotes education of the team on the judicious use of antibiotics.<sup>7</sup>

Clinical protocols for the use of antimicrobials are one of the central elements of Antimicrobial Stewardship Programs<sup>10</sup> and should be developed according to institutional clinical characteristics, epidemiological and microbiological profiles. Implementation is crucial to guide actions, both by technicians and managers, as they provide

information on the directed use of antimicrobials, guiding first-line choice for empirical treatment, as well as promoting rational and evidence-based prescription.<sup>11-12</sup> This study is unprecedented in the institution in which it was conducted and is justified as adherence allows for the standardization of practices and the improvement of process/result evaluation with increased quality and safety of care, as well as being a useful tool to measure morbidity and mortality, length of hospital stay and all related healthcare costs (direct and indirect).<sup>13</sup>

The objective of this study was to evaluate the adherence rate to clinical protocols for antimicrobials, analyze the prescription profile and compare adherence between private and non-private units, as well as prescriptions by resident and attending physicians.

## METHOD

The present study, a retrospective cross-sectional design, was conducted using secondary data from medical records of adult patients hospitalized in non-private and private clinical units of a teaching hospital in Rio Grande do Sul, which is the main health center in the Vale do Rio Pardo region, and a reference in high complexity cardiovascular, traumatology and orthopedics, ophthalmology, and high-risk pregnant women. During the study period, from July to December 2020, there were 4,079 hospitalized patients (680 patients per month), with 2,308 (385 patients per month) in the non-private ward and 1,771 (295 patients per month) in the two private units. This study was approved by the Research Ethics Committee of the University of Santa Cruz do Sul (CAAE No. 44063721.6.0000.5343).

Prescriptions containing antimicrobials were analyzed based on the standard justification, from the report of the MV2000 computerized system provided by the institution's IT service, in compliance with the Brazilian General Data Protection Law. The inclusion criteria were all antimicrobial prescriptions from private and non-private clinical units, containing

identifiable justifications parameterized by the Hospital Infection Control Commission in conjunction with the Clinical Pharmacy Team, evaluated according to the corresponding institutional protocols (Table 1). Excluded from the study were all antimicrobial prophylaxis regimens, prescriptions with justifications without standardized protocols (infections of the reproductive system, surgical site

infections, infections in the eyes, ears, nose, throat, and mouth), incomplete data, and inconsistencies from the spreadsheet provided by the IT department (medications that were not antimicrobials) or unidentified justifications. Prescriptions from emergency and intensive care units were not included in the study.

**Table 1** - Standard justifications associated with the treatment protocols used in the hospital institution where the study was conducted, and the respective recommended antimicrobials. Santa Cruz do Sul, RS, 2020.

STANDARD JUSTIFICATION	NAME OF THE TREATMENT PROTOCOL	RECOMMENDED ANTIMICROBIAL(S)
Infections of the gastrointestinal system	Intra Abdominal Infection	Ciprofloxacin + Metronidazole; Ampicillin + Sulbactam; Piperacillin + Tazobactam; Ceftriaxone + Metronidazole
	<i>Clostridium difficile</i> infection	Vancomycin; metronidazole
Central nervous system infections	Identification and Treatment of Meningitis	Ceftriaxone; Vancomycin; Ceftriaxone + Vancomycin; Ceftriaxone + Ampicillin; Ceftriaxone + Rifampicin; Ceftriaxone + Gentamicin; Ampicillin; Oxacillin; Ampicillin + Gentamicin; Cefepime; Ciprofloxacin; rifampicin
osteoarticular infections	Methicillin Resistant <i>Staphylococcus aureus</i> ;	Teicoplanin; Sulfamethoxazole+Trimethoprim; Clindamycin; Rifampicin; Doxycycline; Ciprofloxacin; Levofloxacin; norfloxacin
Infections of the cardiovascular system	Methicillin Resistant <i>Staphylococcus aureus</i> ;	Teicoplanin; Teicoplanin + Rifampicin / Gentamicin
Skin and subcutaneous tissue infections	Methicillin Resistant <i>Staphylococcus aureus</i> ;	Sulfamatoxazole+Trimethoprim; Doxycycline; Clindamycin; Teicoplanin
Respiratory system infections	Pneumonia Associated with Hospital Admission and Pneumonia Associated with Mechanical Ventilation	Cefepime; Teicoplanin; Piperacillin + Tazobactam
	Community Acquired Pneumonia	Amoxicillin + Clavulanate Levofloxin; Azithromycin
	Methicillin Resistant <i>Staphylococcus aureus</i> ;	Teicoplanin + Metronidazole
bloodstream infection	Central venous catheter-related bloodstream infection	Teicoplanin; Vancomycin; Cefepime; Beta-lactams; Meropenem; Polymyxin B
Urinary tract infection	Treatment for urinary tract infection	amikacin; cephalothin
clinical sepsis	Sepsis/septic shock in adults	Cefepime; Cefepime + Metronidazole Cefepime + Teicoplanin

Source: Direct search.

The collected data were organized (Microsoft Excel®) and exported to the Statistical Package for Social Sciences software (SPSS 23.0®, IBM, Armonk, NY, USA). Absolute and relative descriptive analyses were performed (frequency and percentage). Categorical variables were divided into: patient's admission number, hospital unit, type of doctor classified by name in the prescription (resident or attending physician), prescribed antimicrobials, and justifications. Clinical justifications (written in a free field) were adjusted to institutional standard justifications whenever possible. The treatment protocol was analyzed by a clinical pharmacist according to the justification selected by the physician, and adherence to the protocol was classified as: yes (prescription of the antimicrobial suggested in the protocol), no (did not prescribe the antimicrobial suggested in the protocol), or partial, meaning this classification was used in case of combination therapy, when one antimicrobial was in accordance and another was not.

## RESULTS

**Table 2** - Frequency of the most prescribed antimicrobials according to the standard justifications used by the prescribers. Santa Cruz do Sul, RS, 2020.

Justification	Antimicrobials (%)	Total (%)
Infection of the Gastrointestinal System	Ampicillin+sulbactam (25%) Ciprofloxacin/Metronidazole (19.1%) Ceftriaxone/Metronidazole (14.1%)	1058 (26.3)
Infections of the Skin and Subcutaneous Cell Tissue	Ciprofloxacin/Clindamycin (18.8%) Sulfamethoxazole + trimethoprim (11.8%) Piperacillin + tazobactam (10.5%)	948 (23.5)
Urinary tract infection	Ceftriaxone (31.5%) Ciprofloxacin (13.9%) Sulfamethoxazole + trimethoprim (9.7%)	693 (17.2)
Respiratory System Infections	Piperacillin + tazobactam (23.1%) Ceftriaxone (13.5%) Amoxicillin + clavulanate (12%)	635 (15.8)
Osteoarticular Infections	Ciprofloxacin (14.1%) Cephalothin/Gentamicin (11.3%) Cephalothin (10.3%)	319 (7.9)
clinical sepsis	Ceftriaxone (32.7%) Cefepime (19.7%) Piperacillin + tazobactam (13.6%)	162 (4.0)
Central Nervous System Infections	Ceftriaxone (41.7%) Clindamycin (37.0%) Crystalline benzylpenicillin (17.8%)	84 (2.1)
Bloodstream Infection	Vancomycin (35.8%) Meropenem (33.3%) Teicoplanin (7.4%)	81 (2.0)

6651 prescriptions containing antimicrobials were selected for the study. Of these, 2623 were excluded (1134 prescriptions with prophylactic antimicrobial therapy, 173 due to justifications without a protocol option, 1316 due to incomplete data, non-conformities from the report provided by the IT department (medications that did not fit the study) or unidentifiable justifications). The total number of evaluated prescriptions was 4028 (60.6%).

Considering all the prescriptions analyzed, resident physicians supervised by the preceptor physician were responsible for 2,179 (54.1%) prescriptions, while the assistant clinical staff were responsible for 1,849 (45.9%). Doctors made 2,199 prescriptions with a non-standardized justification entered into the system (54.6%), while in 1,829 (45.4%) they prescribed with the standard justification offered by the institution. The most commonly used justification was "gastrointestinal system infections," present in 1,058 prescriptions (26.3%), as can be seen in Table 2. A total of 2,739 (68%) prescriptions were made in the non-private inpatient unit of the institution, while in private units there were 1,289 (32%).

Infections of the Cardiovascular System	Ceftriaxone/Gentamicin (33.3%) Piperacillin + tazobactam (22.9%) Meropenem (16.7%)	48 (1.2)
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Source: Direct search.

Regarding the frequency of prescribed antimicrobials, ciprofloxacin was used in 755 (14.9%) prescriptions, followed by ceftriaxone in 748 (14.7%) and metronidazole in 637 (12.5%). The Beta-lactam class was present in 2,201 prescriptions (43.2%),

represented by Cephalosporins in 1,042 (20.4%), Penicillins in 1,002 (19.7%), and Carbapenems in 157 (3.1%). In Table 3, it is possible to verify all the prescribed antimicrobials, organized according to the therapeutic class.

**Table 3** - Frequency of prescribed antimicrobials according to the therapeutic class. Santa Cruz do Sul, RS, 2020.

Therapeutic class	antimicrobials	Frequency (%)	Total (%)
Cephalosporins (Beta-lactams)	Ceftriaxone	748 (14.7)	1,042 (20.4)
	Cefepime	154 (3.0)	
	cephalothin	82 (1.6)	
	cephalexin	38 (0.7)	
	cefazolin	20 (0.4)	
Penicillins (Beta-lactams)	Piperacillin + Tazobactam	417 (8.2)	1,002 (19.7)
	Ampicillin + Sulbactam	388 (7.6)	
	Amoxicillin + Clavulanate	106 (2.1)	
	amoxicillin	46 (0.9)	
	ampicillin	25 (0.5)	
	Crystalline Benzylpenicillin oxacillin	15 (0.3) 5 (0.1)	
Fluoroquinolones	Ciprofloxacin	755 (14.9)	948 (18.7)
	Levofloxacin	176 (3.5)	
	norfloxacin	17 (0.3)	
Nitroimidazoles	metronidazole	637 (12.5)	637 (12.5)
Lincosamides	Clindamycin	423 (8.3)	423 (8.3)
Sulfonamides	Sulfamethoxazole + Trimethoprim	227 (4.5)	227 (4.5)
Aminoglycosides	gentamicin	101 (2.0)	197 (3.9)
	amikacin	96 (1.9)	
Glycopeptides	Vancomycin	127 (2.5)	175 (3.4)
	Teicoplanin	48 (0.9)	
Carbapenems (Beta-lactams)	meropenem	157 (3.1)	157 (3.1)
Macrolides	Azithromycin	128 (2.5)	128 (2.5)
nitrofurans	Nitrofurantoin	52 (1.0)	52 (1.0)
Polypeptides	Polymyxin B	47 (0.9)	47 (0.9)
	<b>TOTAL*</b>	5,080 (100)	5,080 (100)

\*Number of times the antimicrobial was prescribed (including combined therapies).

Source: Direct search

Monotherapy was frequent in 2,965 (73.6%) prescriptions, while in 1,059 (26.3%) patients used combination therapy with two antimicrobials. Only 4 patients (0.1%) used three antimicrobials concomitantly.

Regarding adherence to protocols, it was found that in 1,729 (42.9%) there was no adherence to clinical protocols, 1,583 (39.3%) showed total adherence, and 716 (17.8%) partial adherence. The attending physicians (hospital medical staff) did not adhere to protocols in 39.6% of their prescriptions, while residents supervised by preceptors did not adhere in 45.9%.

Comparing the prescriptions performed according to the hospital units, 2,744 prescriptions

were made in the non-private unit. Of these, 1,223 (44.5%) did not adhere to the protocol and 1,031 (37.5%) did adhere. Partial adherence was observed in 490 (17.8%). In the private hospital units, a total of 1,284 prescriptions were analyzed, and in 552 (43%) the antimicrobial was in accordance with the protocol analyzed, non-adherence occurred in 506 (39.4%), and partial adherence in 226 (17.6%).

It was observed that "Clostridium difficile infection" and "hospital-acquired pneumonia associated with mechanical ventilation" achieved 100% adherence to the protocol. Non-adherence was mostly observed in "urinary tract infection" (93.6%) and in "sepsis/septic shock in adults," where non-adherence was observed in 77.8% of

prescriptions. Table 4 shows all the protocols analyzed versus adherence, but in 4% of the prescriptions, it was not possible to identify which

protocol the prescribed antimicrobial was related to because they could fit into more than one option. In these cases, there was no adherence to any protocol.

**Table 4 - Adherence to evaluated clinical protocols. Santa Cruz do Sul, RS, 2020.**

Protocol	Total Adherence	Partial Adhesion	non-adherence	Total
Pneumonia Associated with Hospital Admission and Associated with Mechanical Ventilation	163 (100%)	0	0	163 (4%)
<i>Clostridium difficile</i> infection	67 (100%)	0	0	67 (1.7%)
Central Catheter Related Bloodstream Infection	73 (90.1%)	0	8 (9.9%)	81 (2%)
Intra Abdominal Infection	686 (69.2%)	233 (23.5%)	72 (7.3%)	991 (24.6%)
Identification and Treatment of Meningitis	52 (61.9%)	1 (1.2%)	31 (36.9%)	84 (2.1%)
Community Acquired Pneumonia	152 (49.7%)	154 (50.3%)	0	306 (7.6%)
Methicillin Resistant <i>Staphylococcus Aureus</i> (MRSA)	314 (23.8%)	324 (24.5%)	682 (51.7%)	1320 (32.8%)
Sepsis/septic shock in adults	32 (19.7%)	4 (2.5%)	126 (77.8%)	162 (4%)
Treatment for urinary tract infection	44 (6.3%)	0	649 (93.6%)	693 (17.2%)
No possibility to specify	0	0	161 (4%)	161 (4%)
<b>TOTAL</b>				<b>4,028 (100%)</b>

Source: Direct search.

## DISCUSSION

The need for improvement in mechanisms to control the use of antimicrobials, through programs such as the Antimicrobial Stewardship Program, is one of the key strategies to address the problem of microbial resistance.<sup>13</sup> Adopting clinical protocols, which are one of the central elements developed by this program, allows for better evaluation of processes and outcomes, thereby increasing the quality and safety of care, and are essential for defining responsible use in the local context.<sup>10</sup>

In the present study, non-adherence to protocols was found in 42.9% of the total prescriptions evaluated. Wathne et al.<sup>14</sup> analyzed 1756 prescriptions and found non-adherence in 38%, while the Danish study by Hagen et al.<sup>15</sup> found non-adherence in 47%, similar to the present study. Other studies in this area also show that non-adherence to clinical practice guidelines or protocols is common.<sup>16-17</sup> We assume that some practices could explain this significant result, such as inappropriate initiation of antibiotics and absence of antibiotic prescription reevaluation. In contrast, the English study by Phillips et al.<sup>18</sup> found high adherence to protocols (82.6%). In our study, we depended on the justification for the analysis at the time of prescription, and if the incorrect filling out of this

was done, it may have negatively influenced adherence results. The treatment recommended in practice may also sometimes be modified because guidelines or protocols are general and may not apply based on circumstances.

Regarding adherence to specific protocols, Hagen et al.<sup>15</sup> found non-adherence to the urinary tract infection treatment protocol in 62.5% of prescriptions, while in this study, non-adherence was much higher (93.6%). In the study by Ferreira et al.<sup>19</sup>, adherence to the sepsis treatment protocol was relatively low, with it being absent in 62.4% of prescriptions, similar to the results found in this research, where 77.8% of prescriptions did not adhere to the sepsis/septic shock protocol. Haydar et al.<sup>20</sup> evaluated 112 prescriptions of patients diagnosed with bacterial meningitis, and 68.7% were incompatible with the protocols, different from this study where we observed non-adherence in 36.9%.

In the Japanese study by Sakamoto et al.<sup>21</sup>, prescriptions of patients with community-acquired pneumonia (CAP) were evaluated, and it was observed that only 22.5% were in agreement with the protocols. In this study, adherence was found in 49.7%, and partial adherence in 50.3%, with no prescription in total disagreement. In the Canadian study by Pflanzner et al.<sup>22</sup>, 55% of prescriptions were



aligned with the protocols for CAP, 55% for mechanically ventilated pneumonia, and 25% for aspiration pneumonia. In contrast to this study, 100% adherence was found to the hospital-acquired pneumonia and mechanical ventilation protocol, thus highlighting that patients in the study's hospital units maintained treatment according to the protocol initiated in the intensive care unit (ICU), thus verifying good communication between teams regarding care transition.

This study showed that the majority of antimicrobials were prescribed for the treatment of gastrointestinal infections, skin and subcutaneous tissue infections, urinary tract infections, and respiratory infections, respectively (Table 1). The large number of prescriptions for gastrointestinal tract infections may be justified because the institution has a general surgery residency program, where several surgical procedures are performed in the abdominal area and may require the use of antimicrobials. In addition, the data collection period for this research included winter months, which may have influenced the number of prescriptions for respiratory infections. In a study conducted in a hospital in Spain<sup>23</sup>, the results for the main infection sites were primarily for lower and upper respiratory tract (37.9%); for the urinary tract (27.2%) and skin and soft tissue infections (15.4%). The Spanish study<sup>3</sup> differs considerably from the present study regarding gastrointestinal infections, where only 1.6% were for this site of infection. In Dantas et al<sup>12</sup>, study, the main indications for antimicrobial use were respiratory infections in 33.2% (91), followed by urinary tract infections in 12.4% (34) and abdominal infections in 10.6% (29). Dylis et al<sup>16</sup> found that antimicrobials were prescribed in 25% for pneumonia and 47% for urinary tract infections. Urinary tract and respiratory tract infections were evident in all studies cited, including the present study.

Monotherapy was frequent in 2,965 (73.6%) prescriptions, a positive result because according to ASP recommendations and also from a

pharmacoeconomic point of view, monotherapy is always considered the best option when compared to combination therapy with two or more antimicrobials.<sup>23</sup> According to the results of Ripa<sup>24</sup> study, no difference in mortality was observed between patients who received monotherapy or combination therapy, and dual antimicrobial therapy showed benefit only in infections caused by *P. aeruginosa* and in neutropenic patients.

The beta-lactam class was the most used, with the cephalosporin class being evident in this study, with five representative antimicrobials prescribed, and ceftriaxone being one of the most prescribed in the study. Cephalosporins are frequently prescribed in hospitalization. Their broad spectrum of action allows for varied use in most medical specialties and they are active against many multi-resistant bacteria.<sup>25</sup> Regarding the frequency of antimicrobial prescription, ceftriaxone appeared in the second position, corroborating the findings of the study conducted by O'Neil et al.<sup>26</sup>, in which ceftriaxone was responsible for almost one-third (30.6%) of all prescribed antibiotics. In Yunquera-Romero et al<sup>3</sup> study, the antimicrobials with the highest prevalence were amoxicillin+clavulanate (36.7%), fosfomicin tromethamine (9%), and ciprofloxacin (8.9%). These results differ from the present study, where the prevalence of prescribed antimicrobials was ciprofloxacin, ceftriaxone, and metronidazole.

Ciprofloxacin, a member of the fluoroquinolone class, was the most prescribed antibiotic because it is considered first-line treatment for a wide range of bacterial infections, including respiratory, gastrointestinal, and urinary tract infections. It has a broad spectrum of activity and is generally the most widely used in its class, despite showing high levels of antimicrobial resistance to several pathogens due to its widespread use.<sup>27</sup> Metronidazole was also commonly prescribed, ranking third, mainly due to its use in gastrointestinal infections (the most common justification in this

study) and its recommendations in protocols for "intra-abdominal infection," "Clostridium difficile infection," "sepsis/septic shock" with abdominal focus, and "methicillin-resistant Staphylococcus aureus (MRSA)" in cases of complicated community-acquired pneumonia (CAP).

It is believed that the similar prominence of the antibiotic's ciprofloxacin (755) and ceftriaxone (748) in the number of prescriptions in this study occurred because both are commonly used and indicated for empirical use in various types of infection, and ceftriaxone also has the advantage of not requiring dose adjustment for renal function. Another factor is that both are recommended in various institution protocols, such as "intra-abdominal infection" in combination with metronidazole and in the "infection and treatment of meningitis" protocol. Quinolones are recommended for osteoarticular infections in the "methicillin-resistant Staphylococcus aureus (MRSA)" protocol.

Differences in both the site of infection and frequency of use of antimicrobials occur because there are epidemiological and microbiological differences that define the profile of each institution and are adapted according to the needs. It is important to note that the use of certain antimicrobials is related to the clinical specialties of the hospital, the type of infection, and the institution's antimicrobial use policy. Since the institution is a reference in high cardiovascular complexity, we observed that the index of infection treatment for this site was low, which is considered a positive point, as it appears that the use of antimicrobials was more for prophylaxis than treatment.

The majority of the prescriptions evaluated in this study were from the non-private unit, as well as the majority of them were prescribed by resident doctors, since this unit has a medical residency program and most of the institution's beds are from the non-private wing (Unified Health System - SUS), since the hospital where the study was conducted is

philanthropic and serves up to 70% SUS. Resident doctors, always supervised by attending physicians, showed a higher rate of "non-adherence" than attendings in their prescriptions. In addition, when we compared the hospital units, we found higher adherence in the private units than in the non-private ones. This may be explained because the resident is still in a learning phase, so the attending clinical staff ended up adhering more to the protocols, either totally and/or partially. Out of the total number of prescriptions analyzed, the non-use of standard justifications by doctors may have occurred because they may not have been aware of this option that the system provides, and also because of annual changes that occur in the system, and there is no continuing education for doctors in this regard.

One of the main limitations of this study is that the evaluation of protocols was done through a secondary database, based solely on the antimicrobials prescribed according to their justification, without evaluating other specific data from patients' medical records, such as laboratory tests. The study design allows us to analyze, according to the medical prescription, whether the selection of the antimicrobial was correct.

## CONCLUSION

This study is an unprecedented research with a significant sample size, providing an overview of the prescriptions and use of antimicrobials at the study site, serving as an important tool for diagnosing the conditions in which they are being used. There was a significant number of prescriptions that did not adhere to clinical protocols at the institution, and understanding this data allows for interventions to improve antimicrobial prescriptions, contributing to the promotion of rational antimicrobial use and aiding in the fight against antimicrobial resistance. Disseminating these protocols, assessing the need for ongoing education for prescribers, as well as interaction between executing professionals and managers, and periodic monitoring of adherence to



treatment protocols are essential for the success of the Antimicrobial Stewardship Program.

## RESUMO

**Introdução:** A resistência antimicrobiana é uma preocupação global. As intervenções do *Antimicrobial Stewardship Program* são necessárias para orientar a implementação de protocolos de tratamentos direcionados às principais síndromes infecciosas. **Objetivo:** avaliar a taxa de adesão aos protocolos clínicos relacionados à prescrição de antimicrobianos em um hospital de ensino no Rio Grande do Sul. **Delineamento:** Estudo transversal retrospectivo, realizado com dados secundários das prescrições médicas de antimicrobianos de pacientes internados em unidades clínicas de julho a dezembro de 2020. **Resultados:** Foram avaliadas 4028 prescrições de antimicrobianos com 42,9% de não adesão aos protocolos clínicos institucionais, 39,3% com adesão completa e 17,8% com adesão parcial. **Implicações:** Conhecer os dados de adesão aos protocolos clínicos oferece a oportunidade de intervir em melhorias nas prescrições de antimicrobianos, verificando a necessidade de educação permanente para os prescritores, estudantes de medicina e residentes médicos. Isso contribui para a promoção do uso racional de antimicrobianos e auxilia no combate à resistência antimicrobiana.

## DESCRITORES

Agentes antimicrobianos; Resistência Microbiana a Medicamentos; Programa de Mayordomía; Pautas clínicas.

## RESUMEN

**Introducción:** La resistencia a los antimicrobianos es una preocupación mundial. Se necesitan intervenciones del *Antimicrobial Stewardship Program* para guiar la implementación de protocolos de tratamiento dirigidos a los principales síndromes infecciosos. El objetivo fue evaluar la tasa de adhesión a los protocolos clínicos relacionados con la prescripción de antimicrobianos en un hospital escuela de Rio Grande do Sul. **Delineación:** Estudio transversal retrospectivo, realizado con datos secundarios de prescripciones médicas de antimicrobianos de pacientes hospitalizados en unidades clínicas de julio a diciembre de 2020. **Resultados:** Se evaluaron 4028 prescripciones de antimicrobianos con un 42,9% de no adherencia a los protocolos clínicos institucionales, 39,3% con adherencia total y 17,8% con adherencia parcial. **Implicaciones:** Conocer los datos sobre la adherencia a los protocolos clínicos ofrece la oportunidad de intervenir en la mejora de las prescripciones de antimicrobianos, verificando la necesidad de educación permanente para prescritores, estudiantes de medicina y médicos residentes. Esto contribuye a la promoción del uso racional de los antimicrobianos y ayuda a combatir la resistencia a los antimicrobianos.

## DESCRIPTORES

Agentes antimicrobianos; Farmacorresistencia Microbiana; Programa de Mayordomía; Pautas clínicas.

## REFERENCES

1. Agência Nacional de Vigilância Sanitária. Plano Nacional para a Prevenção e o Controle da Resistência Microbiana nos Serviços de Saúde. Brasília: ANVISA [Internet]; 2017; 1-81. Available from: <http://portal.anvisa.gov.br/documents/33852/271855/Plano+Nacional+para+a+Prevenção+e+o+Controle+da+Resistência+Microbiana+nos+Serviços+de+Saúde/9d9f63f3-592b-4fe1-8ff2-e035fcc0f31d>
2. Al Rahmany D, Albeloushi A, Alreesi I, Alzaabi A, Alreesi M, Pontiggia L, et al. Exploring bacterial resistance in Northern Oman, a foundation for implementing evidence-based antimicrobial stewardship program. *Int J Infect Dis* [Internet]. 2019 [cited 2022 Oct 8]; 83:77-82. Available from: <https://doi.org/10.1016/j.ijid.2019.04.004>
3. Yunquera-Romero L, Márquez-Gómez I, Henares-López A, Morales-Lara MJ, Gallego Fernández C, Asensi-Díez R. Adecuación de las prescripciones antimicrobianas realizadas en el área de urgencias de un hospital de tercer nivel. *Rev Española Quimioter* [Internet]. 2018 [cited 2022 Oct 8]; 31(3):209-16. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29771104>
4. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: A systematic review. *Antimicrob Resist Infect Control* [Internet]. 2019 [cited 2022 Oct 8]; 8(1):1-13. Available from: <https://doi.org/10.1186/s13756-019-0471-0>
5. European Commission. Antimicrobial Resistance. European Commission - EC. 2017. Available from: [https://ec.europa.eu/health/amr/antimicrobial-resistance\\_en](https://ec.europa.eu/health/amr/antimicrobial-resistance_en)
6. Infectious Diseases Society of America. Handbook on clinical practice guideline development. IDSA. 2015. Available from: [http://www.idsociety.org/uploadedFiles/IDSA/GuidelinesPatient\\_Care/IDSA\\_Practice\\_Guidelines/IDSA%20Handbook%20on%20CPG%20Development%2010.15.pdf](http://www.idsociety.org/uploadedFiles/IDSA/GuidelinesPatient_Care/IDSA_Practice_Guidelines/IDSA%20Handbook%20on%20CPG%20Development%2010.15.pdf)
7. Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs. Atlanta: CDC; 2014. Available from: <http://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf>
8. Nathwani, D; Sneddon, J. Practical Guide to Antimicrobial Stewardship in Hospitals. BiomérieuxR. Available from: [http://bsac.org.uk/wpcontent/uploads/2013/07/Stewardship-Booklet-Practical-Guide-toAntimicrobial-Stewardship-in-Hospital\\_s.pdf](http://bsac.org.uk/wpcontent/uploads/2013/07/Stewardship-Booklet-Practical-Guide-toAntimicrobial-Stewardship-in-Hospital_s.pdf)

9. Agência Nacional de Vigilância Sanitária. Diretriz Nacional para Elaboração de Programa de Gerenciamento do Uso de Antimicrobianos em Serviços de Saúde. Brasília: ANVISA; 2017. Available from: <http://antigo.anvisa.gov.br/documents/33852/271855/Diretriz+Nacional+para+Elabora%C3%A7%C3%A3o+de+Programa+de+Gerenciamento+do+Uso+de+Antimicrobianos+em+Servi%C3%A7os+de+Sa%C3%BAde/667979c2-7edc-411b-a7e0-49a6448880d4?version=1.0>
10. Pulcini C, Binda F, Lamkang AS, Trett A, Charani E, Goff DA, et al. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. *Clin Microbiol Infect* [Internet]. 2019 [cited 2022 Oct 8]; 25(1):20-5. Available from: <https://doi.org/10.1016/j.cmi.2018.03.033>
11. Infectious Diseases Society of America. Combating antimicrobial resistance: policy recommendations to save lives. IDSA Policy Paper; 2011.
12. Dantas J, Porto S, Neto P, Macêdo Lima M, Fraga Lobo I. Avaliação da prescrição de antimicrobianos de uso restrito em um hospital universitário. *J Infect Control*. [Internet]. 2015 [cited 2022 Oct 8]; 4(2):39-48. Available from: <https://jic-abih.com.br/index.php/jic/article/view/82>
13. Barlam TF, Cosgrove SE, Abbo LM, Macdougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* [Internet]. 2016 [cited 2022 Oct 8]; 62(10):e51-77. Available from: <http://dx.doi.org/10.1093/cid/ciw118>
14. Wathne JS, Harthug S, Kleppe LKS, Blix HS, Nilsen RM, Charani E, et al. The association between adherence to national antibiotic guidelines and mortality, readmission and length of stay in hospital inpatients: Results from a Norwegian multicentre, observational cohort study. *Antimicrob Resist Infect Control* [Internet]. 2019 [cited 2022 Oct 8]; 8(1):1-10. Available from: <http://dx.doi.org/10.1186/s13756-019-0515-5>
15. Hagen TL, Hertz MA, Uhrin GB, Dalager-Pedersen M, Schønheyder HC, Nielsen H. Adherence to local antimicrobial guidelines for initial treatment of community-acquired infections. *Dan Med J* [Internet]. 2017 [cited 2022 Oct 8]; 64(6):A5381. Available from: <https://pubmed.ncbi.nlm.nih.gov/28566116/>
16. Dylis A, Boureau AS, Coutant A, Batard E, Javaudin F, Berrut G, et al. Antibiotics prescription and guidelines adherence in elderly: Impact of the comorbidities. *BMC Geriatr* [Internet]. 2019 [cited 2022 Oct 8]; 19(1):1-6. Available from: <https://doi.org/10.1186/s12877-019-1265-1>
17. Ament SM, de Groot JJ, Maessen JM, Dirksen CD, van der Weijden T, Kleijnen J. Sustainability of professionals' adherence to clinical practice guidelines in medical care: a systematic review. *BMJ Open* [Internet]. 2015 [cited 2022 Oct 8]; 5(12):e008073. Available from: <https://doi.org/10.1136/bmjopen-2015-008073>
18. Phillips CJ, Gilchrist M, Cooke FJ, Franklin BD, Enoch DA, Murphy ME, Santos R, Brannigan ET, Holmes AH. Adherence to antibiotic guidelines and reported penicillin allergy: pooled cohort data on prescribing and allergy documentation from two English National Health Service (NHS) trusts. *BMJ Open* [Internet]. 2019 [cited 2022 Oct 8]; 9(2):e026624. doi: 10.1136 . Available from: <https://doi.org/10.1136/bmjopen-2018-026624>
19. Ferreira IER, Magalhães MKS, Albuquerque VC, Marques RB. Avaliação da adesão aos protocolos de sepse em um hospital de ensino do Piauí. *R. Interd* [Internet]. 2019 [cited 2022 Oct 8]; 12(4):20-31. Available from: <https://dialnet.unirioja.es/servlet/articulo?codigo=7962771>
20. Haydar SM, Hallit SR, Hallit RR, Salameh PR, Faddoul LJ, Chahine BA, Malaeb DN. Adherence to international guidelines for the treatment of meningitis infections in Lebanon. *Saudi Med J* [Internet]. 2019 [cited 2022 Oct 8]; 40(3):260-265. Available from: <http://dx.doi.org/10.15537/smj.2019.3.23965>
21. Sakamoto Y, Yamauchi Y, Yasunaga H, Takeshima H, Hasegawa W, Jo T, et al. Guidelines-concordant empiric antimicrobial therapy and mortality in patients with severe community-acquired pneumonia requiring mechanical ventilation. *Respir Investig* [Internet]. 2017 [cited 2022 Oct 8]; 55(1):39-44. Available from: <http://dx.doi.org/10.1016/j.resinv.2016.08.006>
22. Pflanzner S, Phillips C, Mailman J, Vanstone JR. AMS in the ICU: empiric therapy and adherence to guidelines for pneumonia. *BMJ Open Qual* [Internet]. 2019 [cited 2022 Oct 8]; 8(2):e000554. Available from: <http://dx.doi.org/10.1136/bmjopen-2018-000554>
23. Cunha CB, Cunha BA. Antimicrobial Therapy for Legionnaire's Disease: Antibiotic Stewardship Implications. *Infect Dis Clin North Am* [Internet]. 2017 [cited 2022 Oct 8]; 31(1):179-191. Available from: <http://dx.doi.org/10.1016/j.idc.2016.10.013>
24. Ripa M, Rodríguez-Núñez O, Cardozo C, Naharro-Abellán A, Almela M, Marco F, et al. Influence of empirical double-active combination antimicrobial therapy compared with active monotherapy on mortality in patients with septic shock: a propensity score-adjusted and matched analysis. *J Antimicrob Chemother* [Internet]. 2017 [cited 2022 Oct 8]; 12:3443-3452. Available from: <http://dx.doi.org/10.1093/jac/dkx315>
25. Jordan E, Voide C, Petignat PA, Gobin N. Céfalosporines: quelques considérations en pratique Clinique [Cephalosporins in clinical practice]. *Rev Med Suisse* [Internet]. 2020 [cited 2022 Oct 8]; 16(710):1906-1911. Available from: <https://pubmed.ncbi.nlm.nih.gov/33058575/>
26. O'Neal F, Kramer J, Cooper M, Septimus E, Sharma S, Burgess LH. Analysis of antibiotic use in a large network of emergency departments. *Am J Heal Pharm* [Internet]. 2019 [cited 2022 Oct 8]; 76(21):1753-61. Available from: <https://doi.org/10.1093/ajhp/zxz193>

27. Zlamal J E, Lehyn S A, Iyer M, Elane M L, Wong N A, Wamsley J W. Shared and Unique Evolutionary Trajectories to Ciprofloxacin Resistance in Gram-Negative Bacterial Pathogens. *mBio* [Internet]. 2021 [cited 2022 Oct 8]; 12:e00987-21. Available from: <http://dx.doi.org/10.1128/mBio.00987-21>

#### COLLABORATIONS

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Original database of the author.

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#### CONFLICTS OF INTEREST

There are no conflicts of interest to declare.