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# Analysis of pharmaceutical interventions on avoidable costs with pharmacotherapy in a teaching hospital in Sergipe (Brazil) in the first months of Covid-19

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## Abstract

**Objectives:** To assess the impact of pharmaceutical interventions on avoidable costs with pharmacotherapy in a teaching hospital in the first months of Covid-19. **Methods:** A cross-sectional retrospective study, with a quantitative approach carried out in a teaching hospital. The evaluated data were obtained from the documentation of interventions carried out between April and October 2020 by the institution's clinical pharmacists. To calculate the estimated initial cost and the final cost of treatment, the value of the drug and the inputs used for administration were considered multiplied by the dosage (frequency and prescribed treatment time). In order to obtain the value saved for each intervention, the final discovered cost was subtracted from the estimated initial value of the treatment. **Results:** 167 pharmaceutical interventions were registered with cost reduction, generating savings corresponding to \$ 9.067,83. The units that most demanded pharmaceutical interventions were Intensive Care Units (ICU) general and Covid-19. Antimicrobials stood out with the largest number of interventions related to cost reduction and with the largest amount saved. As for the type of intervention related to cost reduction, the most frequent was dose reduction due to changes in renal function (49.48%). **Conclusion:** Pharmaceutical interventions act as a tool to promote the rational use of medicines for their clinical and economic benefits. This study allowed to demonstrate that the pharmaceutical service can collaborate to reduce unnecessary health expenses.

**Keywords:** economics pharmaceutical; pharmaceutical services; pharmacy service hospital.

## Análise das intervenções farmacêuticas associadas a custos evitáveis com a farmacoterapia em um hospital de ensino de Sergipe (Brasil) nos primeiros meses da Covid-19

## Resumo

**Objetivo:** avaliar a repercussão das intervenções farmacêuticas nos custos evitáveis com a farmacoterapia em um hospital de ensino nos primeiros meses da Covid-19. **Métodos:** Estudo transversal retrospectivo, com abordagem quantitativa realizado em um hospital de ensino. Os dados avaliados foram obtidos a partir da documentação das intervenções realizadas entre abril e outubro de 2020 pelos farmacêuticos clínicos da instituição. Para calcular o custo inicial estimado e o custo final do tratamento foram considerados o valor do medicamento e os insumos utilizados para a sua administração multiplicado pela posologia (frequência e tempo de tratamento prescrito). Para a obtenção do valor economizado a cada intervenção subtraiu-se do valor inicial estimado do tratamento o custo final obtido. **Resultados:** foram registradas 167 intervenções farmacêuticas com redução de custos, gerando uma economia correspondente a \$ 9.067,83. As unidades que mais demandaram intervenções farmacêuticas foram as Unidades de Terapia Intensiva (UTI) geral e Covid-19. Os antimicrobianos se destacaram com o maior número de intervenções relacionadas à redução de custo e com o maior montante economizado. Quanto ao tipo de intervenção relacionada à redução de custos, a mais frequente foi a redução de dose devido à alteração da função renal (49,48%). **Conclusão:** As intervenções farmacêuticas atuam como ferramenta para a promoção do uso racional de medicamentos pelos benefícios clínicos e econômicos. Este estudo permitiu demonstrar que o serviço farmacêutico, pode colaborar para a diminuição de gastos desnecessários na saúde.

**Palavras-chave:** economia farmacêutica; cuidados farmacêuticos; serviço de farmácia hospitalar.



## Introduction

In the last four decades, the growing health care expenses have raised concerns regarding better management of the resources destined for this purpose.<sup>1</sup> A relevant part of the costs has been attributed to unnecessary or avoidable expenses. The Organization for Economic Cooperation and Development (OECD) estimates that more than 10% of the hospital expenses is allocated to correcting preventable medical errors or infections acquired during hospitalization in several countries that make up the organization.<sup>2</sup>

In the current Brazilian context, research studies related to the optimization of resources and to the reduction of health costs are indispensable since, in addition to the health crisis caused by the COVID-19 pandemic, the country has faced a political-economic crisis that imposes budget cuts in the health area.<sup>3</sup>

Economic evaluations provide tools for rationalizing health care and are conceptualized as a comparative analysis of alternative actions in terms of costs and consequences. In the context of health technologies, evaluation of medications is considered one of the central axes of health economics, as it constitutes a category in which costs and results are better known.<sup>4</sup> Cost analysis is considered a fundamental stage to provide subsidies for the development of economic evaluations.<sup>5</sup>

A number of studies suggest that the role of the clinical pharmacist, in addition to promoting patient safety by reducing avoidable adverse drug events and prescription errors, generates savings for the health services related to cost reduction with treatment, optimizing resources.<sup>6-8</sup> Pharmaceutical interventions are all actions in which the pharmacist participates actively, such as in decision-making about the patients' therapy and also in the evaluation of the results obtained.<sup>9</sup> Cost reduction interventions comprise a small percentage of the clinical pharmacy interventions, but generate substantial savings.<sup>8</sup>

The implementation of studies focused on this theme is an important strategy for therapeutic rationalization.<sup>10</sup> A systematic review that evaluated the economic impact of pharmaceutical interventions in Brazil concluded that eight of the ten studies included showed that pharmaceutical interventions result in cost savings for the health services, in addition to providing improvements in clinical parameters related to the disease and pharmacotherapy. The review was conducted with studies published until November 2019, prior to the pandemic context, and most (90%) of the studies included were carried out in the South and Southeast regions.<sup>3</sup>

In view of the urgency to optimize health care expenses and the low availability of studies related to the theme in the country, this article aims at evaluating the effect of pharmaceutical interventions on costs considered avoidable with pharmacotherapy at a teaching hospital in Sergipe (Brazil) in the first months of COVID-19.

## Methods

This is a retrospective, descriptive and cross-sectional study with a quantitative approach carried out at a teaching hospital, which operates as a medium- and high-complexity hospital unit, currently with 142 beds, 24 of which are in Intensive Care Units (10 for general hospitalizations and 14 for COVID-19).<sup>11</sup>

The data evaluated were obtained from the documentation of interventions carried out between April and October 2020, by the institution's clinical pharmacists (n=11) and performed through the analysis of the prescription, pharmacotherapy monitoring, medication conciliation, stewardship of antimicrobials and/or discharge guidance. As for the economic impact, pharmaceutical interventions can generate increased costs by adding medications or replacing them with more expensive therapies. However, as the current study focuses on the pharmaceutical contribution to the health economy, the inclusion criteria were considered to be the interventions recorded during the study period that presented cost reductions, that is, pharmaceutical interventions related to the minimization of unnecessary health expenses. Interventions that were not recorded in full were excluded.

The study period coincides with the beginning of the antimicrobial stewardship program at the institution, which marked assiduity in recording the interventions performed by the unit's pharmacists, as well as their impacts on cost reduction and, consequently, the acquisition of a more robust database for conducting the study. Importantly, implementation of this program promoted proper use of antimicrobials, which predicted a reduction in costs related to this therapy. *Microsoft Office Excel* was used to record the interventions and to evaluate the data obtained.

The diverse information collected for the evaluation involved the clinical unit where the intervention was performed, the medication and the supplies involved (Supplementary Material 1), the type of intervention and the impact on cost reduction, which, when positive, was quantified considering the initial value of the treatment, the final cost after the intervention and, consequently, the economic difference generated.

To calculate the estimated cost prior to the pharmaceutical intervention and the actual final cost of the treatment, the following was considered: the value of the medication recorded in the last acquisition process in force at the time of the intervention, available in the Genus® program, used by the hospital for inventory management and distribution of drugs, and the inputs used for its administration, considering the need for reconstitution and dilution (Supplementary Material 1) when it came to injectable medications. These added up values were subsequently multiplied by the dosage (frequency and treatment time prescribed).

To size the amount saved in each intervention, the final cost obtained was subtracted from the estimated initial value of the treatment. The monetary values were expressed in US dollars, corrected by the IPCA variation corresponding to October 2021.

It is important to note that, in the cases of interventions related to interruption and replacement of the pharmacological therapy, the savings generated were calculated by subtracting the final cost after the pharmaceutical intervention from the total cost with the initially planned treatment, considering the number of inputs needed based on the treatment time. In this study, the monetary values related to the direct costs involved in pharmacotherapy were measured.

In relation to the ethical aspects, the current study did not need to be registered or analyzed by the Research Ethics Committee, as internal secondary data were used without the possibility of individual identification of patients.



## Results

During the study period, 1,522 pharmaceutical interventions were carried out; of these, 11.0% (n=167) were related to cost reduction, generating \$ 9,067.83 in savings, which estimates a 57.5% minimization of the initial estimated value of \$ 15,778.06. In the same period, the institution's expenditure on medications was \$ 260,311.97. The number of interventions performed per month, as well as the unnecessary costs and expenses related to them, are shown in Table 1.

During the study period, the units that most demanded pharmaceutical interventions were the General and COVID-19 Intensive Care Units (ICUs), respectively with 23.8% (n=40) and 33.9% (n=57) of the interventions.

The value of the savings generated with the interventions performed in the General and COVID-18 ICUs is shown in Table 1. It is important to highlight that the COVID-19 ICU operated between May and September 2020 with 14 beds and that, after being closed, there was an increase in the number of beds available in the General ICU due to the high demand in this unit, from 5 to 10. In the same period, the clinical pharmacists resumed the pharmacotherapy monitoring activities of the hospitalized patients, which led to an increase in interventions related to cost reduction in this unit.

Due to the pandemic, during the study period, admissions to the other wards of the unit (Medical Clinic, Pediatrics, Pneumology, and Infectology) were minimized and elective surgeries were

suspended, which also justifies the reduction in the flow of patients in the institution and, consequently, the number of interventions related to cost reduction.

Antimicrobials, including antibiotics, antifungals and antivirals, stood out as the therapeutic class with the highest number of pharmaceutical interventions related to cost reduction (n=97), which reflects the highest percentage of these interventions (58.1%) and the amount saved (93.4%), corresponding to \$ 8,470.85. In the same period, the expenditure related to antimicrobial drugs at the institution was \$ 70,297.43 (Table 1); nearly 50% of the antimicrobial interventions related to cost reduction were associated with three medications: meropenem trihydrate, 25.5% (n=25); teicoplanin, 14.3% (n=14); and vancomycin hydrochloride, 13.3% (n=13).

As for the types of intervention related to antimicrobial cost reduction, dose reduction due to altered renal function (49.5%) and drug suspension/replacement (43.3%) were the most frequent. Among the main reasons for treatment suspension were unnecessary prolongation of pharmacotherapy (n=18) and divergence of indication between the prescription and clinical protocols and the scientific literature (n=18). This category also includes the intervention that individually conferred the greatest monetary reduction, which occurred from the replacement of liposomal amphotericin B for the conventional presentation, resulting in \$ 3,367.70 in savings, which represents 39.7% of the total amount saved.

**Table 1.** Interventions performed and savings generated (Sergipe – From April to October 2020).

Information	All	April	May	June	July	August	September	October	Mean	Standard deviation
<b>Global of interventions</b>										
Interventions n (%)	<b>167</b>	22 (13.1)	26 (15.6)	39 (23.4)	21 (12.6)	22 (13.1)	14 (8.4)	23 (13.8)	23.9	7.6
Predicted initial cost (US\$ <sup>1</sup> )	<b>15,778.06</b>	432.82	221.54	4,733.19	3,605.88	2,230.85	3,828.34	725.44	254.0	1,836.5
Final cost of the intervention (US\$ <sup>1</sup> )	<b>6,710.23</b>	185.93	119.18	3,380.38	2,304.14	390.96	223.98	105.66	958.6	1,327.1
Savings (US\$ <sup>1</sup> )	<b>9,067.83</b>	246.89	102.36	1,352.81	1,301.74	1,839.89	3,604.36	619.78	1,295.4	1,197.9
Proportion (%)	<b>57.5</b>	57.0	46.2	28.6	36.1	82.5	94.1	85.4	61.4	26.0
<b>Total cost related to medications<sup>2</sup> (US\$<sup>1</sup>)</b>	<b>260,311.97</b>	25,263.10	22,501.81	39,287.79	41,215.30	54,133.59	28,841.83	50,228.55	37,353.1	12,282.7
<b>Intensive Care Units</b>										
<b>General ICU</b>										
Interventions n (%)	<b>40</b>	3 (7.5)	1 (2.5)	3 (7.5)	9 (22.5)	3 (7.5)	3 (7.5)	18 (45.0)	5.7	6.0
Savings (US\$ <sup>1</sup> )	<b>1,253.55</b>	81.15	17.53	207.81	620.97	111.78	35.99	178.32	179.1	206.9
<b>COVID-19 ICU</b>										
Interventions n (%)	<b>57</b>	-	11 (19.3)	25 (43.8)	7 (12.3)	11 (19.3)	3 (5.3)	-	11.4	8.3
Savings (US\$ <sup>1</sup> )	<b>1,905.63</b>	-	32.57	776.81	70.34	989.73	36.18	-	381.1	464.8
<b>Type of medication</b>										
<b>All</b>										
Interventions n (%)	<b>167</b>	22 (13.1)	26 (15.6)	39 (23.4)	21 (12.6)	22 (13.1)	14 (8.4)	23 (13.8)	23.9	7.6
Savings (US\$ <sup>1</sup> )	<b>9,067.77</b>	246.88	102.35	1,352.80	1,301.73	1,839.89	3,604.35	619.77	1,295.4	1,197.9
<b>Antimicrobials</b>										
Interventions n (%)	<b>97 (58.1)</b>	11 (11.3)	9 (9.3)	30 (30.9)	16 (16.5)	12 (12.4)	6 (6.2)	13 (13.4)	13.9	7.8
Savings (US\$ <sup>1</sup> )	<b>8,470.85</b>	207.37	70.51	1,239.91	1,281.44	1,747.59	3,542.18	381.85	1,198.2	1,320.4
Proportion (%)	<b>93.4</b>	84.0	68.9	91.7	98.4	95.0	98.3	61.6	85.4	14.8
<b>Total cost related to antimicrobials (US\$<sup>1</sup>)</b>	<b>70,297.43</b>	4,872.29	5,335.57	13,864.81	8,554.84	16,118.01	10,594.82	11,216.38	10,870.1	3,950.6

<sup>1</sup>US\$ – American dollars corrected by the IPCA variation corresponding to October 2021. <sup>2</sup>Total cost related to the medications requested to the Hospital Pharmacy sector in the study period. <sup>3</sup>Cost related to the antimicrobials requested to the Hospital Pharmacy sector in the study period.

## Discussion

Cost is a study element of pharmacoeconomics, which involves all relevant resources in application of the therapy, and is characterized by its complexity as it encompasses measurable elements (direct costs), both quantitatively and qualitatively, but which in the health area is not always palpable; we classify these as indirect costs.<sup>12</sup> Economic evaluations are based on opportunity cost and, as resources are scarce, this means that the decision to allocate resources to a certain technology or program will imply non-application of this resource in other activities, so that its cost is not only portrayed by the resources spent on that technology, but also in the value of what is not being provided (DRUMMOND *et al.*, 2015).<sup>5</sup>

It is important to highlight that the monetary data obtained in this study may be underestimated due to the limitations of not counting materials such as macrodrop and infusion pump equipment, connections, central and peripheral catheters, dressings and other supplies related to drug administration due to the difficulty measuring their exchange rates, given that this is a retrospective study. As a weakness, the absence of documentation of the interventions performed can also be cited, such as those related to volume reduction in the infusion of vasoactive and sedative drugs – a common practice in intensive care units; this is largely due to the registration framework of the pharmaceutical interventions related to cost reduction, a practice adopted from April 2020 that has been improved in subsequent months; this was also the month of the beginning of the Stewardship program of antimicrobials aimed at promoting proper use of this class and, consequently, at reducing the unnecessary costs related to this therapy.

The units with the highest number of interventions related to cost reduction in the study correspond to the ICUs, due to the study period occurring concurrently with the new Coronavirus pandemic. On average, 20% of the patients diagnosed with COVID-19 develop more severe forms requiring hospitalization, with 5%-12% of them requiring ICU admission due to respiratory failure, kidney damage, and/or shock.<sup>13</sup> The clinical management of patients diagnosed with COVID-19 who develop the severe form of the disease and require intensive care is complex.<sup>14</sup>

Complementarily, in the study guided by Teich *et al.* conducted in 2020, 84.7% of the patients received intravenous antibiotic therapy, invasive mechanical ventilation was required in 65% of them, 58.3% were diagnosed with pneumonia, followed by acute kidney injury (9.7%) and acute respiratory distress syndrome (8.3%), considering only the patients who required intensive care, the mean length of stay in the ICU was from 15 to 25 days.<sup>15</sup> Respiratory tract infections, most commonly pneumonia, usually associated with mechanical ventilation; urinary tract infection, often associated with catheters; and bloodstream infection, usually associated with the use of an intravascular device, are responsible for more than 60% of the healthcare-associated infections.<sup>16</sup>

Given the above, the complexity of the patients admitted to this type of unit, the invasive devices involved, and the need for prolonged hospitalization in the management of the usual clinical conditions are understood, which can predispose to the need for antimicrobial use. In a different period, Ricieri *et al.*, with the objective of evaluating pharmaceutical interventions with economic impact, showed that the class of antimicrobials represented an expressive percentage of 87.8% in cost reduction in a total period of 14 months. If compared to other therapeutic classes, in addition to representing a high consumption, antimicrobials generate a relevant financial impact among the hospital expenses.<sup>17</sup>

Liposomal amphotericin B was the antimicrobial that individually resulted in the greatest savings in this research; the same result was found in the study directed by Arantes *et al.* in 2020, whose intervention was related to the prescribed treatment time.<sup>6</sup> Medications consume a considerable portion of a country's resources, exerting a strong impact on total healthcare expenses.<sup>18</sup> Acquisition of medications requires expenses and, if these are not well-assisted by efficient and effective pharmaceutical assistance, probable losses will be inevitable, with an increase in expenses and implications on access.<sup>19</sup> There is a positive financial return of nine to thirteen times when the pharmacist works in the ICU.<sup>20</sup>

As for the types of interventions related to cost reduction, in the study by Maciel *et al.*, the most prevalent corresponded to drug suspension (58.5%) and dose reduction (32.6%),<sup>21</sup> similarly to the results portrayed in this article. In the study conducted by Lanes *et al.*, it was noticed that most of the adjustments made were related to changes in vancomycin serum level. Therapeutic monitoring from the measurement of vancomycin serum concentration is of utmost importance both to ensure effectiveness of the treatment and to reduce the occurrence of adverse events, being a strategic parameter for dose adjustment, in addition to reflecting in direct impacts on the costs related to the antibiotic therapy. With the insertion of the pharmacist in the multiprofessional team, errors related to vancomycin use and monitoring can be minimized.<sup>22</sup> In the unit where this study was conducted, this monitoring does not occur due to the absence of technologies that make it possible.

The installation of acute kidney injury in critically-ill patients is multifactorial; however, it is important that it is monitored, always correlating to the clinical conditions, laboratory tests and pharmacological therapy, mainly those with potential for kidney injury such as antibiotics, establishing preventive actions to minimize or identify them early in time, thus minimizing the negative outcomes.<sup>23</sup>

The pharmacokinetics of critically-ill patients can be significantly altered due to several factors, such as altered renal clearance, with the results of a study conducted in 2020 showing that this change occurred in 20% of the patients involved in the study. For these patients, several antimicrobials were prescribed that required dose adjustments, which reinforces the need to evaluate this variable to intervene when necessary.<sup>24</sup>

Kidney failure reduces plasma clearance of the drugs, whose elimination mechanisms depend on the kidneys' functional integrity. In this situation, some antibiotics with nephrotoxic effects may accumulate in the body if administered at their usual doses; therefore, it is necessary to adjust the dose according to the patient's renal function after the initial loading dose.<sup>25</sup> In general, a review published by Martins *et al.* in 2009 elucidated that pharmaceutical care is a practice capable of promoting rational use of medications, enabling greater therapeutic control of the disease, minimizing the occurrence of drug-related problems and reducing costs, avoiding waste of financial resources in the treatment.<sup>26</sup>

A limitation to be noted is the fact that the information was obtained from the institution's database, which can contain biases. An important initial reduction of the clinical pharmacists' face-to-face activities in the care units, with regard to the caution required by the COVID-19 health emergency, interfered both with closer communication with other members of the health care team and patients, and with confirming the acceptability of some interventions, impacting registration.





The direct costs of some medical supplies were not calculated, nor were the indirect costs related to clinical outcomes such as hospitalization time and prevention of adverse events, for example, or time saved by the health professional devoted to care. Even so, the results show that the role of the clinical pharmacist can provide rationalization of the resources invested in health and, as a result, generate savings related to unnecessary expenses in terms of medications.

## Conclusion

From the recording of pharmaceutical interventions it became possible to measure the direct reduction of costs with the use of drugs, and those elucidated in this study represented a relevant economic impact, showing that the pharmaceutical service, in addition to contributing to optimization of the use of medications, can favor the reduction of unnecessary expenses in health. The pharmaceutical interventions that contributed the most to cost reduction were those performed in intensive care units and those related to antimicrobials, which signals the possibility of greater collaboration of the clinical pharmacist for performance in ICUs and the Antimicrobial Stewardship program.

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## Collaborators

All the authors (LMA; LCO; GCC; MIAM) took part in the stages corresponding to elaboration of the project and relevant critical review of the intellectual content, with LCO and SMS also contributing to the design, data analysis and interpretation, and writing of the article.

## Conflict of interest statement

The authors declare that there is no conflict of interest in relation to this article.

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