

Characterization of pharmacotherapy for opportunistic infections and comorbidities among hospitalized patients with HIV/AIDS from 2018 to 2023

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ABSTRACT

Objective: To characterize the pharmacotherapy for opportunistic infections and comorbidities among hospitalized patients with HIV/AIDS at Hospital Universidad del Norte from 2018 to June 2023. **Materials and methods:** A descriptive, retrospective, cross-sectional study, focusing on the retrieval of clinical data from 2018 to June 2023 and using a non-experimental research approach. Data collection was conducted at Hospital Universidad del Norte among patients diagnosed with HIV/AIDS, which served as the target population. A convenience sample of 109 patients was selected based on predefined inclusion criteria, which required participants to be over 18 years of age and have a hospital stay longer than four days. Clinical data were collected from medical records and analyzed using IBM SPSS Statistics and Microsoft Excel. **Results:** The mean age of the patients was 43.6 years, with an average hospital stay of 14.9 days per patient. Fluconazole was the most commonly prescribed medication for the treatment of opportunistic infections, used by 58.5 % of the study population. For comorbidities, amlodipine was the most frequently prescribed medication, used by 23.1 % of the study population. The most prevalent opportunistic infections were oropharyngeal candidiasis (15.43 %), followed by *Pneumocystis jirovecii* pneumonia (PJP) (12.75 %), tuberculosis (11.40 %), and toxoplasmosis (10.73 %). The most common comorbidities were hypertension (28.94 %) and major depressive disorder (18.42 %). The economic impact of medication-related problems (MRPs) and negative medication-related outcomes (NMROs) amounted to associated costs of \$1,223,717 and \$5,008,521, respectively. **Conclusions:** The age group most susceptible to opportunistic infections was between 40 and 50 years, with males being the most affected. The majority of patients were at the AIDS stage of HIV infection, particularly those diagnosed based on medical history. Fluconazole stood out as the most commonly prescribed medication for treating opportunistic infections, followed by the combination of both trimethoprim + sulfamethoxazole and rifampicin + isoniazid + pyrazinamide + ethambutol. In the treatment of comorbidities, amlodipine was the most frequently prescribed medication, followed by losartan, mirtazapine, levetiracetam, and sertraline.

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INTRODUCTION

Human immunodeficiency virus (HIV) infection remains a major global public health challenge, affecting millions of people. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), by the end of 2022, an estimated 39 million people were living with HIV (range: 33.1-45.7 million). Since the beginning of the epidemic, 40.4 million deaths related to acquired immunodeficiency syndrome (AIDS) have been reported. Opportunistic infections (OIs) play a critical role in HIV-associated morbidity and mortality⁽¹⁻³⁾.

In Colombia, 12,919 new HIV infections were reported between 2021 and 2022, representing a 40.27 % increase compared with the previous period and underscoring HIV persistence as a public health concern. Regions such as Bogotá, Antioquia, and Valle del Cauca have shown a high concentration of cases and a rise in patients at the AIDS stage of HIV infection, highlighting the urgent need for effective prevention and management strategies^(4,5). OIs accounted for 33.3 % of hospitalizations, with tuberculosis, histoplasmosis, and cryptococcosis being the most frequent. Most patients presented with CD4 lymphocyte counts below 200 cells/mm³, reflecting inadequate disease management^(6,7).

In-hospital barriers faced by patients with HIV/AIDS include high costs, limited accessibility, and social stigmatization, which contribute to greater demand for health services and increase the economic burden for the State ⁽⁸⁾. This study aims to characterize the pharmacotherapy of opportunistic infections and comorbidities among hospitalized patients with HIV/AIDS at Hospital Universidad del Norte between 2018 and June 2023.

MATERIALS AND METHODS

Study design and population

A descriptive, retrospective, cross-sectional study was carried out focusing on the retrieval of clinical data from the medical records of patients with HIV/AIDS hospitalized between 2018 and June 2023. Data collection was conducted at Hospital Universidad del Norte, located in Soledad city, Atlántico department. A convenience sample of 109 patients was selected.

Variables and measurements

Patients over 18 years of age with HIV/AIDS who presented with opportunistic infections and/or comorbidities and who had a hospital stay longer than four days were selected. Patients who requested voluntary discharge were excluded. Variables extracted from the medical records included age, sex, health insurance scheme, place of origin, opportunistic infections, comorbidities, CD4 lymphocyte count, length of hospital stay, prescribed medications, and the pharmacological and economic impact of medication-related problems (MRPs) and negative medication-related outcomes (NMROs). Data on MRPs and NMROs were collected through a comprehensive review of medical records, including progress notes and paraclinical test results. The pharmacological impact was assessed based

on the occurrence of health problems, prolonged hospital stays, administration of inadequate doses, initiation of a new drug regimen, dosage or frequency adjustments, and discontinuation of previous drug regimens. This impact was further quantified in economic terms using tools such as the *Termómetro de Precios de Medicamentos* (Medicine Price Thermometer), which enabled calculation of the overall economic impact of MRPs and NMROs.

Statistical analysis

Data were analyzed using IBM SPSS Statistics 2016 and Microsoft Excel.

Ethical considerations

Approval was obtained from the Ethics Committee of both the Universidad del Atlántico School of Chemistry and Pharmacy and Hospital Universidad del Norte on November 10, 2023. Confidentiality of the medical records was maintained at all stages of the research, and patient privacy was ensured by coding identifying data.

RESULTS

The mean age of the patients was 43.6 years. The most common age group was 40-50 years, followed by 29-39, 51-61, 18-28, and 62-73 years. Most patients were male, and a large proportion were enrolled in the subsidized health insurance scheme. The majority resided in the Barranquilla metropolitan area, followed by Barranquilla city, rural areas, and other departments. More than 50 % of patients had a previous serological diagnosis. The mean CD4 lymphocyte count was 158.8 cells/mm³; the most frequent count was 0-200 cells/mm³, followed by 200-400 cells/mm³ and 400-1500 cells/mm³. The mean length of hospital stay was 14.92 days (Table 1).

Table 1. Sociodemographic and paraclinical characteristics of hospitalized patients with HIV/AIDS

Sociodemographic and paraclinical characteristics	N = 109 patients	%
Age (years)		
Mean	43.6	
40-50	34	31.19
29-39	28	25.68
51-61	22	20.18
18-28	14	12.84
62-73	11	10.09
Sex		
Male	80	73.39
Female	29	26.60
Health insurance scheme		
Subsidized	91	83.48

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Sociodemographic and paraclinical characteristics	N = 109 patients	%
Contributory	18	16.51
Place of residence		
Barranquilla metropolitan area	70	64.22
Barranquilla city	32	29.35
Rural areas	5	4.58
Other departments	2	1.83
Serological diagnosis		
Mean	158.8	
Previous diagnosis	79	72.47
Recent diagnosis	30	27.52
CD4 lymphocyte count (cells/mm³)		
0-200	69	63.30
Not reported	15	13.76
200-400	13	11.92
400-1500	12	11.00
Length of hospital stay (days)		
Mean	14.92	
Standard deviation	7.076	

Oropharyngeal candidiasis was the most frequent opportunistic infection, followed by *Pneumocystis jirovecii* pneumonia (PJP), tuberculosis, toxoplasmosis, and esophageal and

oral candidiasis. The most common comorbidities were hypertension, major depressive disorder, type 2 diabetes mellitus, and hypothyroidism (Table 2).

Table 2. Clinical characteristics of hospitalized patients with HIV/AIDS

Clinical characteristics	n	%
Opportunistic infections (N = 149)		
Oropharyngeal candidiasis	23	15.43
PJP	19	12.75
Tuberculosis	17	11.40
Toxoplasmosis	16	10.73
Esophageal candidiasis	13	8.72
Oral candidiasis	13	8.72
Cryptococcal meningitis	11	7.38
Neurosyphilis	8	5.36
Syphilis	5	3.35
Late latent syphilis	5	3.35

Clinical characteristics	<i>n</i>	%
Herpes simplex	4	2.68
Esophagitis	3	2.01
Herpes zoster	3	2.01
Histoplasmosis	3	2.01
Giardiasis	2	1.34
Amebiasis	1	0.67
Bacteremia	1	0.67
Diarrheal infection	1	0.67
Progressive multifocal leukoencephalopathy	1	0.67
Comorbidities (N = 38)		
Hypertension	11	28.94
Major depressive disorder	7	18.42
Type 2 diabetes mellitus	3	7.89
Hypothyroidism	3	7.89
Kidney disease	2	5.26
Major depressive episode	2	5.26
Mixed anxiety-depressive disorder	2	5.26
Epilepsy	2	5.26
Refractory epilepsy	1	2.63
Adjustment disorder with depressive symptoms	1	2.63
Focal status epilepticus	1	2.63
Symptomatic epilepsy	1	2.63
Structural epilepsy	1	2.63
Severe pulmonary hypertension	1	2.63
Chronic lung disease	1	2.63

For the treatment of opportunistic infections, fluconazole stood out as the most commonly prescribed medication, followed by the combination of both trimethoprim + sulfamethoxazole and rifampicin + isoniazid + pyrazinamide + ethambutol, and nystatin. Other medications used included liposomal

amphotericin B, penicillin G benzathine, flucytosine, penicillin G sodium, acyclovir, metronidazole, valacyclovir, itraconazole, nitazoxanide, pyrimethamine, ceftriaxone, oxacillin, vancomycin, dolutegravir, and emtricitabine + tenofovir disoproxil (Figure 1).

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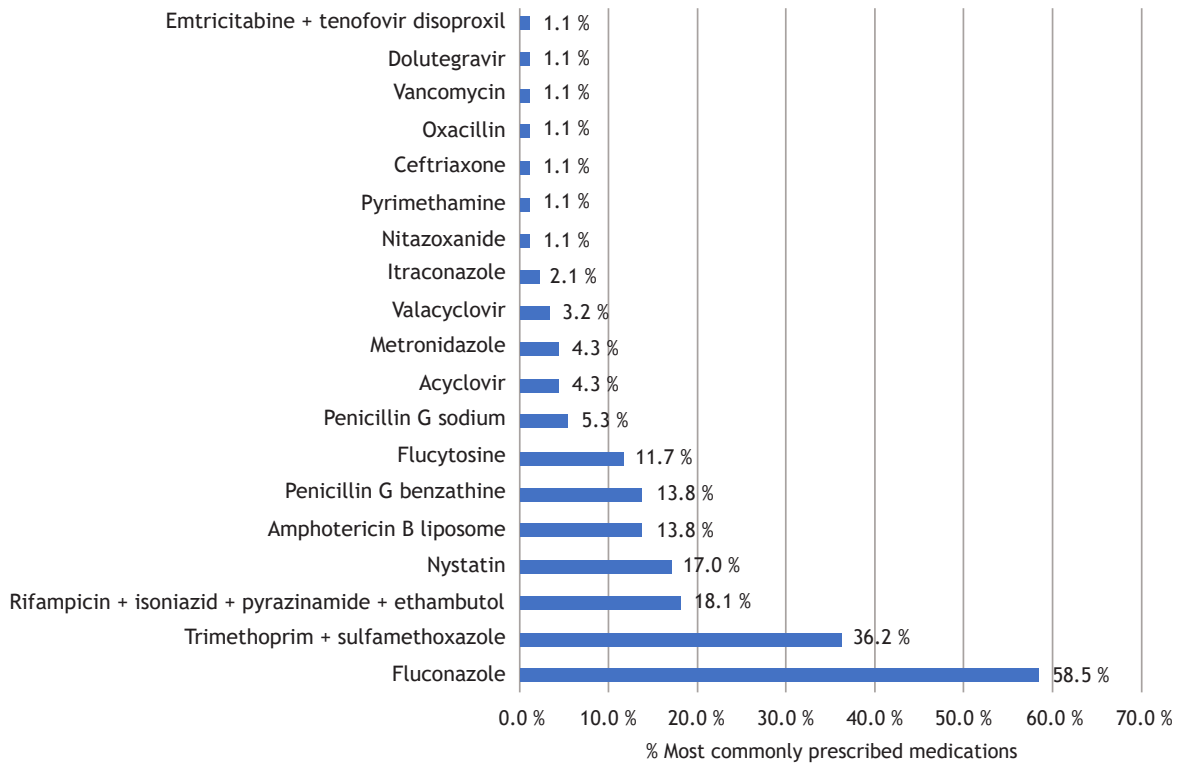


Figure 1. Most commonly prescribed medications for managing opportunistic infections among hospitalized patients with HIV/AIDS

For the management of comorbidities, the most frequently prescribed medication was amlodipine, followed by losartan, mirtazapine, and levetiracetam. Other medications included sertraline, metoprolol, levothyroxine, insulin glulisine

and glargine, clonidine, prazosin, sildenafil, escitalopram, phenytoin, atorvastatin, bosentan, captopril, furosemide, hydrochlorothiazide, quetiapine, olanzapine, lorazepam, fluoxetine, valproic acid, and ipratropium bromide (Figure 2).

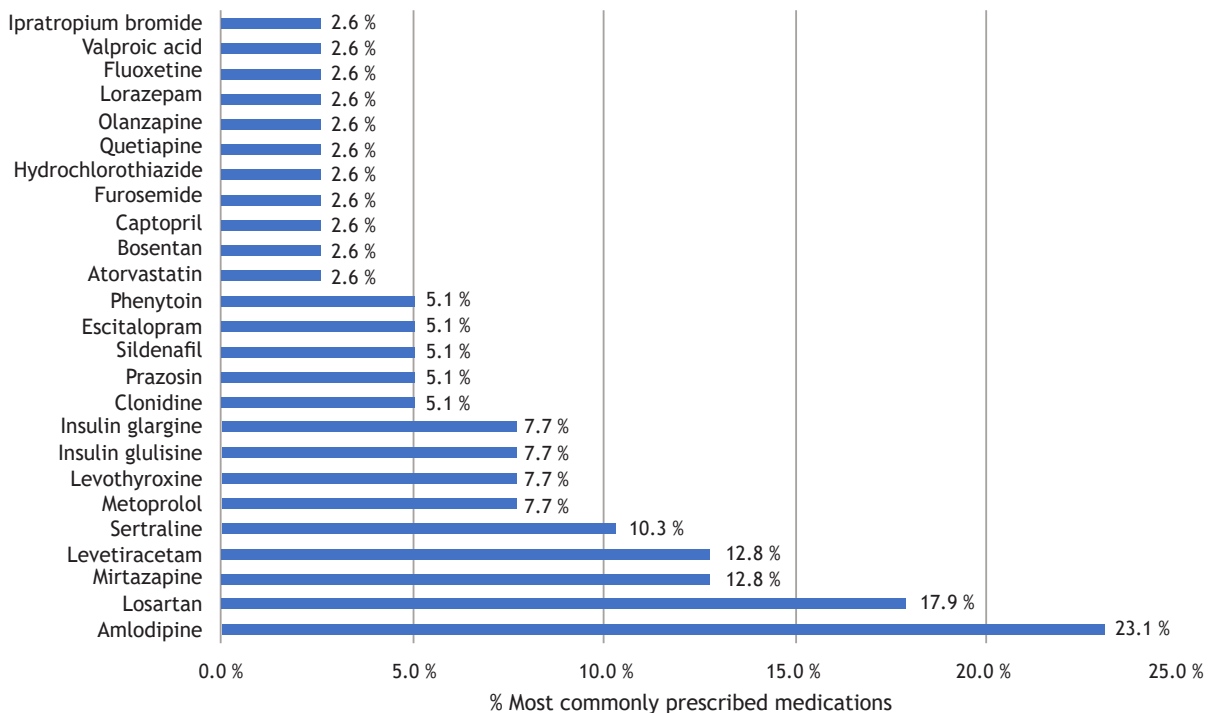


Figure 2. Most commonly prescribed medications for managing comorbidities among hospitalized patients with HIV/AIDS

A total of 273 MRPs were identified, with a mean of 2.5 MRPs per patient. In addition, 24 NMROs were reported, with a mean of 0.22 per patient (Table 3).

Table 3. Data on MRPs and NMROs among hospitalized patients with HIV/AIDS

MRPs (N = 109 patients)	
Total	273
Mean	2.5
Most frequently used	88.00 %
NMROs (N = 109 patients)	
Total	24
Mean	0.22
Most frequently used	24.00 %

Regarding MRPs, the most frequent pharmacological impact was “administration of inadequate doses,” followed by “suboptimal therapy,” “dose modification,” and “initiation of a new drug regimen.” Economically, the greatest cost, totaling

\$1,174,765, was attributed to “administration of inadequate doses.” In contrast, “initiation of a new drug regimen” accounted for \$48,952. Overall, MRPs generated a total cost of \$1,223,717 (Table 4).

Table 4. Pharmacological and economic impact of MRPs among hospitalized patients with HIV/AIDS

MRP type	Pharmacological impact	Count	% within MRP type	MRP cost	% within MRP cost
Personal characteristics	Administration of inadequate doses	19	76.00	\$1,174,765	95.99
Contraindication					
Inadequate dosage/regimen and/or indication	Suboptimal therapy	4	16.00		
Prescription errors					
Nonadherence	Dose modification	1	4.00		
Interactions					
Adverse effects					
Undertreated health problem	Initiation of a new drug regimen	1	4.00	\$48,952	4.01
Other					
Total		25	100.00	\$1,223,717	100.00

With respect to NMROs, in the necessity dimension the most frequent pharmacological impacts were “initiation of a new drug regimen” and “hypertensive crisis.” In the effectiveness dimension, “initiation of a new drug regimen” was the most common impact. In the safety dimension, the most frequent impacts were “initiation of a new drug regimen”

and “discontinuation of previous drug regimens.” From an economic perspective, the safety dimension accounted for the highest cost at \$2,951,097 (58.93 %), followed by the necessity dimension at \$2,019,213 (40.31 %) and the effectiveness dimension at \$38,211 (0.76 %). In total, NMROs generated a cost of \$5,008,521 (Table 5).

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Table 5. Pharmacological and economic impact of NMROs among hospitalized patients with HIV/AIDS

NMRO type	Pharmacological impact	Count	% within NMRO type	NMRO cost	% within NMRO cost
Necessity	Initiation of a new drug regimen	3	5.35	\$2,019,213	40.31
	Hypertensive crisis	3	5.35		
	Increased hospital stay	1	1.78		
	Discontinuation of previous drug regimens	1	1.78		
	Decrease in platelet volume	1	1.78		
	Administration of inadequate doses	1	1.78		
Effectiveness	Increased blood pressure	1	1.78	\$38,211	0.76
	Initiation of a new drug regimen	2	3.57		
	Dose modification	1	1.78		
	Initiation of a new drug regimen	13	23.21		
	Discontinuation of previous drug regimens	5	8.92		
	Acute kidney injury	4	7.14		
Safety	Dose modification	3	5.35	\$2,951,097	58.93
	Referral to specialist	3	5.35		
	Generalized rash	3	5.35		
	Increased hospital stay	2	3.57		
	Increased blood pressure	2	3.57		
	Cellular damage	1	1.78		
	Increased transaminases	1	1.78		
	Increased creatinine level	1	1.78		
	Bradycardia	1	1.78		
	Decreased blood pressure	1	1.78		
	Hyperkalemia	1	1.78		
	Hypertensive crisis	1	1.78		
	Total	56	100.00	\$5,008,521	100.00

DISCUSSION

The mean age of the patients was 43.6 years, with the 40-50 and 29-39 age groups being the most affected by opportunistic infections. This finding is consistent with Guzmán ⁽⁹⁾, who reported in 2022 that 29.4 % of patients were aged 35-44 years and 29.1 % were aged 25-34 years. Similarly, Figueroa-Agudelo et al. ⁽¹⁰⁾ documented in 2018 a mean age of 41 years, slightly lower than in the present study but in line with the overall trend.

By contrast, Mitiku et al. ⁽¹¹⁾ in 2015 and León-Pinzón et al. ⁽¹²⁾ in 2021 reported mean ages of 34 and 38 years, respectively, reflecting variations in the age distribution of patients with opportunistic infections.

Regarding sex distribution, 73.4 % of patients in this study were male, consistent with Figueroa-Agudelo et al. ⁽¹⁰⁾, who

reported 81.1% in 2018. Pang et al. ⁽¹³⁾ observed an even higher proportion (90.4 %) in 2018, while Rubaihayo et al. ⁽¹⁴⁾ reported a lower figure (64 %) in 2016. Overall, these findings indicate a greater prevalence of opportunistic infections among men, though with differences across studies.

The higher prevalence of opportunistic infections in men compared with women may be attributable to several factors, particularly the stigma surrounding HIV. Men, associating their diagnosis with perceived weakness, may delay or avoid seeking medical care, including diagnostic testing and treatment. Greig et al. ⁽¹⁵⁾ support this explanation, noting that prevailing social constructs of masculinity discourage men from accessing health services because doing so may be perceived as a sign of vulnerability.

In terms of serological diagnosis, most patients in this study were at the AIDS stage of HIV infection: 27.52 % were recently diagnosed, whereas 72.47 % had a previous diagnosis. Persistence at this stage may be linked to lack of knowledge of the disease, education level, socioeconomic status, geographic remoteness from healthcare centers, and the stigma associated with HIV. Vargas and Boza ⁽¹⁶⁾ confirm these associations, highlighting that lack of knowledge of the disease contributes to progression to AIDS. These findings underscore the importance of implementing educational and awareness programs to improve early detection and management, while also addressing socioeconomic and cultural barriers to diagnosis and follow-up.

The most common opportunistic infections in this study were oropharyngeal candidiasis, PJP, tuberculosis, and cerebral toxoplasmosis. These results are in line with Díaz Hernández et al. ^(7,17), who reported in 2019 oral candidiasis (38.5 %), pulmonary tuberculosis (37.6 %), cerebral toxoplasmosis (22.2 %), and pneumonia (18.8 %). Similarly, Montúfar Andrade et al. ⁽⁵⁾ documented in 2016 prevalences of 33 % for tuberculosis, 17 % for histoplasmosis, and 9.7 % for cryptococcosis. More recently, Meng et al. ⁽¹⁸⁾ found in 2023 pneumonia (39.8 %), tuberculosis (35.3 %), and candidiasis (28.8 %) as the most frequent infections among hospitalized patients with HIV. In addition, Gonzales Barreto ⁽¹⁹⁾ reported in 2020 that the most common infection was candidiasis (31.1 %), followed by tuberculosis (24.6 %), toxoplasmosis (24 %), histoplasmosis (17.4 %), and PJP (13.8 %).

With respect to comorbidities, hypertension and major depressive disorder were the most prevalent, followed by type 2 diabetes mellitus and hypothyroidism. These findings are partially consistent with those of Gallant et al. ⁽²⁰⁾, who identified in 2017 hypertension, hyperlipidemia, and endocrine disorders as the most common comorbidities. Similarly, García Gonzalo et al. ⁽²¹⁾ reported hepatitis C virus (HCV) infection (51.3 %), dyslipidemia (37.9 %), diabetes (21.9 %), and hypertension (21.9 %) as the most frequent. Martínez-Iglesias et al. ⁽²²⁾ further supported these trends in 2019, noting prevalences of 15 % for dyslipidemia, 6 % for hypertension, and 6 % for diabetes mellitus.

The presence of mental and behavioral disorders among patients in this study may have been exacerbated by the lack

of a strong support network, low education levels, or unstable financial situations. This is supported by Wolff et al. ⁽²³⁾ and coincides with the findings of Salazar et al. ⁽²⁴⁾, who noted that this type of comorbidity is related to a decrease in CD4 lymphocyte counts and poor adherence to antiretroviral treatment. This, in turn, contributes to increased viral load and a higher risk of mortality among patients with HIV. In addition, the stigma associated with the infection not only imposes a significant mental burden but can also trigger other comorbidities. These findings underscore the importance of addressing both the direct medical complications of HIV and the psychosocial factors that affect disease progression and patients' quality of life.

For the treatment of opportunistic infections, fluconazole stood out as the most commonly prescribed medication (58.5 %), followed by the combination of both trimethoprim + sulfamethoxazole (36.2 %) and rifampicin + isoniazid + pyrazinamide + ethambutol (18.1%). These results align with research conducted by Velasco and Torralba ⁽²⁵⁾, the Pan American Health Organization (PAHO) ⁽²⁶⁾, León-Bratti ⁽²⁷⁾, and Vásquez de Azócar et al. ⁽²⁸⁾, which highlight the relevance of these therapies in the management of opportunistic infections and provide a solid basis for clinical decision-making.

A total of 273 MRPs were identified in this study, with prescription errors being the most frequent (78.3 %), followed by MRPs related to inadequate dosage, regimen, and/or duration (8.1 %). "Administration of inadequate doses" stood out as the most frequent and costly pharmacological impact, generating a total of \$1,223,717 (USD 298.97). These findings contrast with those of Alomi et al. ⁽²⁹⁾, who reported higher costs associated with adverse drug reactions of \$3,837,837 (USD 3,525.42) and treatment nonadherence of \$10,182,885 (USD 2,594.26). Similarly, Freitas et al. ⁽³⁰⁾ noted that 39.3 % of the expenditure was allocated to patients who experienced adverse reactions, at a cost of \$108,185,259 (USD 27,562), 36.9 % to treatment nonadherence at a cost of \$101,457,535 (USD 25,848), and 16.9 % to the treatment of comorbidities resulting from incorrect medication doses at a cost of \$46,544,547 (USD 11,858).

In the analysis of costs associated with NMROs, safety costs represented the largest share, reaching \$2,951,097 (USD 762.84), equivalent to 59 %. Necessity costs amounted to \$2,019,213 (USD 521.72), accounting for 40.3 %, and effectiveness costs amounted to \$38,211 (USD 9.76), representing 0.7 %. The total cost generated by NMROs was \$5,008,521 (USD 1,294.13). These results partially coincide with those of Serrano Caviedes et al. ⁽³¹⁾, who found that NMROs focused mainly on safety (49.2 %), followed by effectiveness (36.1 %) and necessity (14.7 %), with a total cost of \$808,582 (USD 206.01). Pérez Menéndez-Conde et al. ⁽³²⁾ also reported a total cost of \$1,008,766 (USD 257), in line with these findings.

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review. ATBF provided scientific advice and took part in the manuscript review.

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