

Direct Costs of the Treatment of Pulmonary Tuberculosis in Adherent and Non-Adherent Patients in a Public Hospital of the City of Buenos Aires

Costos directos del tratamiento de la tuberculosis pulmonar en pacientes adherentes y no adherentes en un hospital público de la Ciudad Autónoma de Buenos Aires

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ABSTRACT

Objective: To determine the direct costs of the treatment in three groups of patients with pulmonary tuberculosis (PTB): adherent outpatients (AOs), hospitalized-adherent (HA), and hospitalized non-adherent (HNA).

Methods: Three groups were considered: AOs, HA, and HNA patients. Direct costs were determined from the perspective of the funder, based on the cost modules provided by the Government of the City of Buenos Aires (GCBA) as of July 2022, with a peso/dollar exchange rate of 140. The cost of antituberculous drugs was provided by the Tuberculosis Program of the GCBA.

Results: Ten AOs were included, with a treatment duration of 24±2.52 weeks and 100 % adherence. The direct cost was US\$ 257.79 per patient (IQR [interquartile range]=191.6-328.55). Twenty HNA patients and ten HA patients were included, with no differences between the groups in age and gender. HNA patients showed the following characteristics: higher smoking load, homelessness, malnutrition, alcoholism, addictions, and HIV (all p<0.05). The duration of the first treatment was 5.5 weeks for HNA patients (IQR=3-8), and 24 weeks for HA patients. The duration of subsequent treatments for HNA patients ranged from 0.5 to 9 weeks. The final cost was US\$ 8,165.87 per patient (IQR=4,706.45-12,897.82) in the HNA group and US\$ 4,015.26 per patient (IQR=3,458.15-4,482.6) in the HA group (p<0.01).

Conclusion: The direct cost of treatment in AOs was US\$ 257 per patient. The direct cost of treatment withdrawal in HNA patients is twice the cost of HA patients (US\$ 8,165 vs. US\$ 4,015). The cost of treating AOs is fifteen times lower than the cost of hospitalizing them. This is the first study about direct costs on this topic to be conducted in our country. Programs to improve treatment adherence should be implemented to prevent high healthcare costs, drug resistance, and increased morbidity and mortality.

Key words: Pulmonary tuberculosis; Hospitalization; Treatment; Adherence; Withdrawal

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RESUMEN

Objetivo: Determinar costos directos del tratamiento en tres grupos de pacientes con tuberculosis pulmonar (TP): ambulatorios-adherentes (AA), hospitalizados adherentes (HA) y hospitalizados no adherentes (HNA).

Materiales y métodos: Se consideraron tres grupos: AA, HA y HNA. Se determinaron costos directos desde la perspectiva del financiador, según modulación del Gobierno de la Ciudad de Buenos Aires (GCBA) a julio 2022, cotización peso/dólar 140. El costo de las drogas antituberculosis fue provisto por el Programa de Tuberculosis del GCBA.

Resultados: Se incluyeron 10 pacientes AA, tiempo de tratamiento 24 ± 2.52 semanas, adherencia 100 %. El costo directo fue 257.79 dólares/paciente (RIQ=191.6-328.55). Se incluyeron 20 pacientes HNA y 10 HA, sin diferencias en edad y género entre ellos. Los HNA tenía mayor carga tabáquica, situación de calle, desnutrición, alcoholismo, adicciones y HIV (todos $p < 0.05$). El tiempo de primer tratamiento fue para HNA 5.5 semanas (RIQ=3-8) y 24 semanas para HA. La duración en HNA de siguientes tratamientos fue 0.5-9 semanas. El costo final fue 8165.87 dólares/paciente (RIQ=4706.45-12 897.82) en HNA y 4015.26 dólares (RIQ=3458.15-4482.6) en HA ($p < 0.01$).

Conclusión: El costo directo del tratamiento en AA fue 257 dólares/paciente. El costo directo del abandono del tratamiento de HNA es el doble que HA (8165 vs. 4015 dólares). El costo de tratar a AA es quince veces menor que internarlos. Es el primer estudio de costos directos en nuestro país sobre el tema. Se deben instrumentar programas de mejora de adherencia al tratamiento para evitar alto costo sanitario, drogo-resistencia y aumento de la morbi-mortalidad.

Palabras clave: Tuberculosis pulmonar; Hospitalización; Tratamiento; Adherencia; Abandono

INTRODUCTION

Tuberculosis (TB) remains an unresolved global health problem, particularly affecting poor, developing countries; and it can be associated with other comorbidities or not. There is a significant percentage of underdiagnosis and treatment withdrawal due to a lack of education and socioeconomic factors.¹

The World Health Organization (WHO) report of 2022 revealed that 6.4 million people contracted TB in 2021, a figure that underestimates the true impact of the disease due to underreporting linked to the pandemic.² It is estimated that there were 1.4 million deaths in individuals without human immunodeficiency virus (HIV) infection and 187,000 deaths among people with HIV.²

In 2021, the Ministry of Health of Argentina reported 12,569 TB cases, representing a TB notification rate of 27.4/100,000 inhabitants (13.5 % higher than in 2020 and slightly lower than in 2019 at 28.2, used as a reference so as not to consider the pandemic effect). The cases were concentrated

at 59.8 % in individuals aged 15 to 44, with a mortality rate of 1.49/100,000: 6 % higher than in 2018 (26.2/100,000).³ The Autonomous City of Buenos Aires (CABA) together with the province of Buenos Aires had the highest number of cases, with 65.67 % of the country's reported cases (39.8 and 39.7 per 100,000 inhabitants, respectively).³

Withdrawal of antituberculous treatment is a significant obstacle to disease control. The consequences of non-adherence to treatment include the continuation of the disease transmission chain, the development of bacterial resistance mechanisms, a subsequent increase in morbidity and mortality, and an escalation of treatment costs with an impact on healthcare services. Various studies have investigated the cost of TB treatment, both direct and indirect, in many countries worldwide, but to our knowledge, there are no such investigations in our country.⁴⁻¹⁶

The expenditure on TB treatment is half the cost of human immunodeficiency virus treatment and less than a tenth of the cost of COVID-19 treatment. This spending has been decreasing

year by year, despite tuberculosis being the infectious disease with the highest mortality until the year 2020.¹⁷

The objective of this study is to determine the direct costs, from the perspective of the funder of the treatment of patients with pulmonary TB, including adherent outpatients (AOs) and hospitalized individuals, comparing adherent (HA) with non-adherent (HNA) patients. This research is conducted within the setting of a multispecialty public hospital in CABA.

MATERIALS AND METHODS

The medical records of patients diagnosed with pulmonary TB upon admission to our hospital between the years 2017 and 2021 were retrospectively evaluated. Direct costs were determined from the perspective of the funder, taking into account medication costs and the hospitalization cost modules of the Government of the City of Buenos Aires (GCBA) as of July 2022, at an exchange rate of 140 pesos/dollar (Banco Nación Rep. Argentina). Argentina). The cost of antituberculous drugs was provided by the TB Program of the Ministry of Health of the GCBA. The cost of drugs outside the cost modules was determined using the pharmaceutical manual Kairos of July 2022 and the diagnostic studies of nomenclature guidelines of the GCBA.

Three groups of patients were considered for cost analysis: adherent outpatients (AOs), hospitalized-adherent (HA), and hospitalized non-adherent (HNA). To select the patient profile to be included in the AOs group, a sample

was taken representing in its demographic, clinical, and social characteristics the profile of the entire database of patients treated on an outpatient basis in our Unit. A number of hospitalized patients were included for the analysis in a 2:1 ratio for the HNA:HA groups. A patient was considered non-adherent if they discontinued the anti-tuberculous treatment for more than 4 weeks and without any medical supervision.¹ For hospitalized patients who were non-adherent from the second admission onwards, sputum GeneXpert and solid culture tests were requested for each admission. Central (median) and dispersion (IQR 25-75 %) measures were used for quantitative variables, and percentages were used for categorical variables. For the comparison between subgroups HNA and HA of categorical variables, the Fisher's test was used. The statistical package of the Biostat program was used.

RESULTS

The demographic characteristics of the 3 groups are detailed in Table 1.

Cost of adherent outpatient group

10 patients were included. The average treatment duration was 24 weeks, with 100 % adherence to the treatment regimen of 2 months of isoniazid-ri-fampicin-pyrazinamide-ethambutol and 4 months of isoniazid-rifampicin (2HRZE/4HR). The median total direct costs per patient were US\$ 257.79 (IQR= 191.6-328.55).

TABLE 1. Demographic characteristics

	Adherent outpatients Median (IQR)	Hospitalization-adherent patients Median (IQR)	Hospitalization non-adherent patients Median (IQR)
No. of patients	10	10	23
Age	33.5 (22.25-48.75)	31.5 (21.5-35.5)	40 (28-48.5)*
Masculine gender, %	50#	80	82.6
Smoking			
At present, %	20	10	39%
Formerly, %	---	20	17.4%
No, %	80	70	43.7%
No. of packs-years	5 (5-5)	12 (6.5-12)	25 (13-30)#
Homelessness, %	10	---	26%*
Malnutrition, %	10	----	34.7%
Unemployment, %	---	20	43.4%
HIV, %	---	10	47.8%
Alcoholism, %	---	---	60.8%#
Addictions, %	10	10	56.5%

*p<0.05, # p<0.01

Cost of hospitalized-adherent group

10 patients were included. One patient died. One patient was found to have rifampicin resistance during follow-up. The average treatment duration was 24 weeks, with 100 % adherence to the 2HRZE/4HR treatment regimen. The total direct cost per patient was US\$4,015.26 (IQR= 3,458.15- 4,482.6).

Cost of hospitalized non-adherent group

20 patients were included. The first treatment began with HRZE, and those who could move on to the second phase were treated with HR. The duration of the first treatment was 6 weeks (IQR=3-9). The duration of the second to the sixth treatment ranged from 0.5 to 9 weeks. Fourteen patients underwent two treatments (duration of 8 weeks, IQR=4.5-12); eight patients underwent three treatments (duration of 6 weeks, IQR=5-12); two patients underwent four treatments (duration of 4 weeks), and one patient underwent six treatments (0.5 week). In 100 % of treatment withdrawal cases, the patient left the hospital voluntarily. Only one patient died (human immunodeficiency virus-HIV) one year after the second hospitalization due to an undiagnosed space-occupying mass. The number of visits to the emergency room, the inpatient ward, and the Intensive Care Unit are detailed in Table 2. The total direct cost per patient was US\$8,165.87 (IQR=4,706.45-12 897.82).

Comparison between hospitalized-adherent and non-adherent groups

Table 1 shows the demographic variables of both groups. There were differences in age between the groups (older age in the HNA group, $p<0.05$). Regarding the gender, there was a predominance

of males among hospitalized patients ($p<0.05$). In the HNA group, there were more patients with smoking load, homelessness ($p<0.05$), unemployment, malnutrition, alcoholism, drug addiction, and reactive HIV serology (for the rest $p<0.01$). There were no differences during the first hospitalization between both groups (HA: 21.5 vs. HNA: 19 days).

When comparing the final cost per patient of both hospitalized patient groups, a significant difference was observed ($p<0.01$). Comparing the direct non-modular costs of both hospitalized patient groups, a significant difference was observed (33 % for the HNA group vs. 8.29 % for the HA group, $p<0.05$).

DISCUSSION

The direct cost of complying with pulmonary TB outpatient treatment in a public hospital of the city of Buenos Aires is US\$257 per patient. The patient profile could be representative of those treated in the public healthcare system. The direct cost of treatment withdrawal per hospitalized patient who began treatment for pulmonary TB is twice the cost of patients who complete the treatment (US\$8,165 vs. US\$ 4,015). In the HNA group, there were more patients with smoking load, homelessness, unemployment, malnutrition, alcoholism, drug addiction, and reactive HIV serology ($p<0.05$). The cost of treating outpatients is fifteen times lower than the cost of hospitalizing them.

The WHO “End TB” strategy for the year 2025 includes reducing the incidence rate by 50 % in the 2015-2025 decade, reducing mortality by 75 %,

TABLE 2. Description of baseline data of analyzed patients

	Hospitalized-adherent median days (IQR)		Hospitalized non-adherent	
	Emergency room	Ward	median days (IQR)	Ward
First hospitalization	--	19.5 (16.5-21.75)	2 (2-2)	22 (12.5-42)
Second hospitalization			2 (2-2)	25 (19.5-45.5)
Third hospitalization			2 (1.5-2.5)	21 (2-35)
Fourth hospitalization*			0	3
Fifth hospitalization*			3	4
Sixth hospitalization*			1	3

*Only one patient

and bringing the percentage of patients with catastrophic costs to 0.² As of 2021, these three indicators were at 10 %, 5.9 %, and 48 %, respectively, far from the target to be achieved.² Moreover, an important related issue is the worryingly low rate of treatment adherence. The WHO defined adherence in 2003 as “the degree to which a patient’s behavior, in terms of medicine-taking, following a diet, or making lifestyle changes, corresponds with the recommendations of the healthcare provider.”¹⁸ There are tools for the assessment of adherence, such as the Morinsky Green questionnaire.¹⁹ Factors related to the adherence to anti-tuberculous treatment are detailed in Table 3.²⁰⁻²⁵ Among those factors associated with the patient, young men in economically active ages are less adherent than women. This has been observed in various studies, including our study. Single men are more likely to withdraw treatment compared to married individuals, probably due to lack of family support. The low socioeconomic status and unemployment lead to precarious living conditions, as shown in our study. Also, low schooling rates are associated with lower treatment adherence. In some studies, non-compliance was five times greater in illiterate patients compared to those with primary or secondary education.²⁰ Our study includes other factors that are related to higher withdrawal rates: homelessness, lack of housing, alcoholism, and addiction to illicit drugs.²¹⁻²⁴ Also the number and type of comorbidities, such as HIV, psychiatric disorders, physical impairment, etc. The migration of individuals from one coun-

try to another after starting treatment also make compliance difficult. In Argentina, Herrero et al conducted a study in the Buenos Aires Metropolitan Area on 123 TB patients (38 non-adherent and 85 adherent) to identify factors associated with non-adherence.²⁵ They determined that the factors mostly associated with non-adherence were: male gender (Odds Ratio, OR=2.8), patients attending a hospital (OR=3.4), and those facing difficulties due to transportation costs (OR=2.5).²⁵ In the 2022 Tuberculosis Epidemiological Bulletin of Argentina, out of 12,569 cases reported in 2021, 31 % lacked treatment evaluation records, which may imply possible treatment withdrawal in many of those cases.³ Among the factors associated with the treatment, prolonged duration is one of the main patient complaints. Patients also complain about the number of drugs. The number of tablets affects adherence, and this factor worsens if the patient has other comorbidities requiring additional concomitant medications (e.g., antiretrovirals). Finally, adverse events such as diarrhea, vomiting, allergic reactions, liver disease, ototoxicity, etc.²⁰ Among the factors associated with health services, organization is crucial, with health staff training, including specialized doctors being essential for the implementation of an adequate TB program. Also, the distance from the patient’s home to the health center is an important factor that should be considered: greater distance usually correlates with lower adherence, as confirmed by various studies.^{20,25} Lastly, the healthcare provider-patient relationship is crucial, both with the doctor and

TABLE 3. Factors affecting adherence

<p>A) Associated with the patient</p> <ul style="list-style-type: none"> Age and gender Marital status Low socioeconomic stratum and unemployment Poor educational level Homelessness Alcohol and illicit drug consumption Comorbidities Migrations Distance to the healthcare center
<p>B) Associated with the treatment</p> <ul style="list-style-type: none"> Prolonged duration Number of drugs Adverse effects
<p>C) Associated with healthcare services</p> <ul style="list-style-type: none"> Organization of healthcare services Patient attendance from their home to the healthcare center Patient-healthcare staff relationship

the person administering the medication, to ensure the patient feels supported.

The consequences of non-adherence to treatment can be evaluated from both the patient's and the society's standpoint. For the patient, it can lead to the worsening of the TB clinically, potentially resulting in death, or the development of antibiotic resistance, thus causing personal and social consequences. Consequently, future treatments will not yield the expected response. Multidrug-resistant TB (MDR-TB) is a growing global problem related to non-adherence, among other factors.¹⁻³ Social consequences are related to the emergence of MDR-TB but also to the economic consequences of increased consumption of health resources.²⁶⁻²⁷ Economic consequences can be analyzed from the perspective of the funder, the patient, or the society as a whole. This includes direct costs (medical: expenses for the maintenance of health centers and equipment amortization, healthcare team fees, diagnostic tests, and treatments; non-medical: transportation, meals) and indirect costs (loss of business days, decreased productivity, and economic loss due to premature death). However, we should also highlight the fact that when comparisons between studies are attempted, costs depend on the healthcare structure, which is inherent to

each country, and financing system. Therefore, it's not advisable to make such comparisons (Table 4).

In reviews regarding the economic consequences of TB treatment, 71 studies were identified for drug-susceptible TB, 10 for MDR-TB, and nine for both.²⁶⁻²⁷ These studies were conducted in 50 and 16 countries, respectively. They were conducted from the perspective of the funder (31 %), the patient (26 %), and both (43 %).²⁶ From the funder's perspective, the cost of drug-susceptible TB was US\$14,659 in high-income countries, US\$840 in middle-income countries, US\$273 in low to middle-income countries, and US\$258 in low-income countries.²⁶⁻²⁷ The treatment cost for MDR-TB was US\$83,365, US\$5,284, US\$6,313, and US\$1,218, respectively.²⁶⁻²⁷ From the patient's perspective in drug-susceptible TB, an additional cost of 3 % was observed in high-income countries, 72 % in middle-income countries, 60 % in low-to-middle-income countries, and 31 % in low-income countries.²⁶⁻²⁷ When combining all the costs, productivity loss was 16 %, 2 %, 40 %, and 38 %, respectively.²⁷

In a study by the WHO's Global TB Program, Tanimura et al determined an average cost of US\$847 per patient (20 % direct medical costs, 20 % direct non-medical costs, and 60 % indirect costs [income loss]), 50 % before TB treatment.²⁸

TABLE 4. Total cost structure for the management of tuberculosis

DIRECT COSTS*
HEALTHCARE-RELATED (funder's perspective) <ul style="list-style-type: none"> • Healthcare visits • Medication • Hospitalizations • Diagnostic tests and material for tuberculosis control • Medical transportation
NON-HEALTHCARE RELATED (patient's perspective) <ul style="list-style-type: none"> • Professional care • Formal personal care • Informal personal care • Non-healthcare related transportation
FOR THE PATIENT (patient's perspective) <ul style="list-style-type: none"> • Medication copayments • Private health insurance • Transportation • Materials • Private medical consultations • Private diagnostic tests or copayments
INDIRECT COSTS* (patient's perspective) <ul style="list-style-type: none"> • Premature death • Temporal or permanent disability • School absenteeism • Work absenteeism

*All costs should be measured from the societal perspective

Among developed countries, there are few studies evaluating the cost impact on the healthcare system.^{4-10,29} Chan et al in Australia determined a treatment cost of 11,538 Australian dollars for ten patients with drug-susceptible pulmonary TB.⁴ Only one patient with MDR-TB was included in the cost comparison analysis (258,089 Australian dollars, that is to say, twenty-two times more).⁴ Breaking down the costs, diagnosis accounted for 12 %, hospitalization 43 %, outpatient consultations 5 %, medication 7 %, and community programs and other costs 26 %. Oh et al reviewed eighteen studies on costs in the United States, finding an average direct cost per patient of US\$34,600 for drug-susceptible TB and US\$110,900 for MDR-TB (three times more).⁵ Breaking down the costs, outpatient consultations were US\$4,300 per patient, laboratory tests averaged US\$1,500 per patient, and antibiotics were \$800 per patient (2 % for drug-susceptible TB patients and 27 % for MDR-TB patients).⁵ The cost of hospitalized TB in the United States was US\$34,512, and for outpatient care, US\$3,296.⁶⁻⁷ The indirect costs due to productivity loss during hospitalization were US\$404 and US\$403 per patient, respectively, for the outpatient period.⁷ Grosse et al estimated the social indirect cost of premature death to be US\$574,751 per patient at the age of 65.⁸ Marks et al estimated the costs for MDR-TB and extensively drug-resistant TB⁹ in the United States. The outpatient cost was US\$83,909 and US\$221,916 per patient in 2020, respectively. For hospitalized patients, it was US\$98,278 and US\$345,792 per patient in 2020, respectively. Productivity loss was estimated at US\$165,137 per patient in 2020 for MDR-TB patients. For extensively drug-resistant TB patients, productivity loss was US\$161,331 per patient in 2020. The cost of premature death at the age of 55 was calculated at US\$1,031,513 per patient in 2020.⁹ In Europe, Diel et al reviewed TB management costs in the 27 countries of the European Community.¹⁰ Taking into account direct and indirect costs, the total cost was €10,282 for drug-susceptible TB, €57,213 for MDR-TB and €170,744 for extensively drug-resistant TB.¹⁰ Law et al developed a Markov theoretical model for cost-effectiveness to evaluate four different treatment regimens for MDR-TB with varying prevalence percentages.²⁹ Reinforced retreatment regimens were the most cost-effective schemes. However, the initial empirical regimen for MDR-

TB, despite being more expensive, results in lower mortality compared to the traditional scheme, with an average cost of US\$4,650 per patient per every day with good-quality of life obtained.²⁹ In most middle-income countries, this is below the per capita income, which is the usual threshold taken as the incremental cost-effectiveness ratio (ICER).²⁹

Among the developing countries, there are two Latin American studies.¹¹⁻¹² Steffen et al from Brazil described the cost of directly observed therapy (DOT) versus self-administered treatment in 218 patients with pulmonary TB from the patient's and the healthcare system perspectives.¹¹ The cost during the pre-diagnostic phase was higher for the self-administered treatment, whereas during the treatment phase, it was higher for the DOT. The cost of complete self-administered treatment was US\$194 for the patient and US\$189 for the funder. For DOT, it was US\$336 and US\$726 respectively, nearly twice the cost of self-administered treatment, with completion rates of 79 % and 71 % respectively.¹¹ In Ecuador, Rouzier et al reported from a group of 104 patients with susceptible TB a total cost of US\$960 per patient from the patient's perspective, and for 14 patients with MDR-TB, the cost was US\$6,880 per patient (six times higher).¹² This represents 31 % and 223 % of Ecuador's average per capita income. In patients with MDR-TB, the cost was higher due to loss of income.¹² Among Asian countries, Chandra et al reviewed 13 studies on TB treatment costs in India.¹³ The cost from the patient's perspective was US\$235, with 45.5 % being direct costs in the public system. Only one study in the private system for drug-resistant TB determined a total direct cost of US\$7,778.¹³ In Indonesia, McAllister et al determined the treatment cost from the patient's perspective in 106 TB patients. The average cost was US\$243.66 per patient.¹⁴ In 2011, Long et al conducted a systematic analysis of the direct cost of antituberculous treatment in relation to adherence in China.¹⁵ While basic diagnosis (X-ray and bacilloscopy) and antibiotic treatment are free, a high percentage of withdrawal (73 %) was observed associated with the transportation and medical fees that patients have to pay. In the Chinese review, the outpatient cost from the patient's perspective ranged from US\$149 to US\$724, representing between 42 % and 119 % of household income and considered one of the main factors. It should be noted that

one-third of the world's MDR-TB patients are from China, and this can explain the high withdrawal rate, among other factors.¹⁵ More recently, in 2020, Xu et al reported a study on 326 TB patients, with 21.4 % below the poverty line.¹⁶ The total treatment cost per patient was US\$1,185.5 (88 % direct costs). Of this total, 37 % occurred before TB care. Factors associated with higher costs were elderly age, being divorced or living alone, residing in rural areas, greater poverty, and incomplete primary education.

The WHO defines catastrophic costs for TB as the direct and indirect costs of treatment that exceed 20 % of a person's annual economic income. In a systematic analysis, 29 studies were selected out of 5,114 studies.³⁰ The average proportion of catastrophic costs was 43 %. The major predictors of high catastrophic cost were country variables, MDR-TB, and HIV. Catastrophic costs were lower in active case-finding strategies (12 %) compared to passive waiting strategies (30 %).³⁰ In a study by the TB Program of the WHO, Tanimura et al determined that catastrophic costs accounted for 58 % of individual annual income, especially among the poorest people with MDR-TB.²⁸ Guidoni et al evaluated the cost of 350 TB patients prospectively in five Brazilian cities.³¹ Unfavorable outcomes were associated with catastrophic costs (OR=2.53, 95 %CI=1.13-5.67) and divorce (OR=5.29, 95 %CI=1.3-20.05).³¹ In India, Chandra et al conducted a review of 13 studies on costs and determined that catastrophic cost ranged from 7 to 32.4 % in patients with drug-susceptible TB and 68 % in drug-resistant TB patients.¹³ In Indonesia, McAllister et al found that 26.5 % of patients exceeded 20 % of their annual income.¹⁴

Few studies were found combining analyses and relating the implications of poor adherence to TB treatment with the impact on healthcare costs. For purposes of comparing costs, Kwon et al reported on 3,799 TB patients, 2,662 adherent and 1,137 non-adherents.³² Five years later, the costs for adherent patients were US\$2,270, and US\$2,694 for non-adherent patients. The monthly cost was 11 % lower for adherent patients, and the total cost for non-adherent patients was two and a half times higher.³² Chimeh et al conducted a systematic analysis between 2009 and 2019 where they compared the costs of TB management with non-adherence.³³ Out of 14 studies, 8 focused on non-adherence and death, 2 on treatment failure,

1 on treatment success, 1 on treatment successes and failures, and 2 on costs. Most studies were retrospective or case-control studies.³³ The results showed that non-adherence was associated with higher mortality, treatment failure, lower cure rates, and a significant negative economic impact.³³

In 2011, Long et al conducted a systematic analysis of the direct cost of antituberculous treatment in relation to adherence in China. Despite the fact that antibiotic treatment is free, a high percentage of withdrawal (73 %) was observed, which was associated with the amount of money the patient has to pay, for example in transportation and medical fees.¹⁵ In our study, the direct cost of treating outpatients is fifteen times lower than hospitalizing them, and the cost of withdrawing treatment in the case of a hospitalized patient with pulmonary TB is twice the cost of an adherent patient (US\$8,165 vs. US\$ 4,015 per patient, respectively).¹⁵ Factors associated with non-adherence included higher smoking load, homelessness, malnutrition, unemployment, alcoholism, substance abuse, and reactive HIV serology.¹⁵

Among the limitations of this study, it can be said that data collection from medical records was retrospective. Another limitation is that extrapolating its conclusions to other healthcare systems in our country or other regions (external validity) is not advisable due to the previously mentioned differing cost structures. Another limitation is that indirect costs were not evaluated (which are presumed to be higher than direct costs based on previously reviewed literature); and costs were not determined from other perspectives (for example, patient or societal perspectives). While costs were initially calculated in pesos, the currency instability and devaluation experienced by our country in recent times led us to report the results in dollars (taking into account the exchange rate of the beginning of the study).

Also, the fact that there is a small number of patients in the study is a limitation, thus, conclusions drawn from the statistical significance found should be evaluated with discretion.

Finally, another limitation would be that the cost modules used by the GCBA did not allow breaking down the internal cost structure to determine which variables have been considered and to what extent.

In conclusion, the direct cost of complying with outpatient treatment of pulmonary TB in a public hospital of the city of Buenos Aires is US\$257 per

patient. The patient profile could be representative of those treated in the public healthcare system. This is the first study in our country related to the direct costs of outpatient treatment of pulmonary TB in adherent patients. The cost of treating outpatients is fifteen times lower than the cost of hospitalizing them. The direct cost of treatment withdrawal per hospitalized patient who begins treatment for pulmonary TB is twice the cost of patients who complete the treatment (US\$8,165 vs. US\$ 4,015). In the HNA group, there were more patients with smoking load, homelessness, unemployment, malnutrition, alcoholism, drug addiction, and statistically significant reactive HIV serology. It is essential to achieve treatment adherence in order to cure TB and avoid drug resistance problems due to its social and health impact and increased morbidity and mortality. Interventions should be implemented to improve adherence, such as providing economic incentives to patients and educating them on their disease. Healthcare personnel, on the other hand, should prioritize the care of TB patients, minimize waiting times, and improve their relationship with the patient.

Conflict of interest

Authors have no conflict of interest to declare.

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