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An Analysis of the Accounting Costs Associated with 20-Month DR TB Regimens in Maputo City, Mozambique

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Abstract

Introduction: Socioeconomic and demographic conditions in a country can influence tuberculosis incidence and mortality, with nearly 95% of tuberculosis-related deaths occurring in poorer countries. Mozambique is among the 30 countries with the highest TB burden. **Objective:** The study aimed to estimate the average direct medical cost of treating drug-resistant tuberculosis in 19 health centers in Maputo City, Mozambique. **Methods:** A retrospective analysis of direct medical costs was conducted on patients aged 18 and older who completed 20-month drug-resistant tuberculosis treatment regimens in Maputo City in 2019. **Results:** This analysis covered 140 patients who completed a 20-month treatment regimen, with 64.3% (78) being male and 35.7% (62) female. Approximately 50% of the participants were aged between 29 and 47. The average direct medical cost of DRTB treatment was $4789.43, reaching up to $6568.00, with a standard deviation of $753.26, including clinical interventions and treatment. **Conclusion:** The direct medical costs for a basic treatment package for a patient with drug-resistant TB in Mozambique equal 36 minimum wages. Developing alternative and innovative funding mechanisms and identifying ways to mitigate costs through the use of generic medicines would be beneficial.

Keywords

Antitubercular Agents, Multidrug-Resistant, Healthcare Costs, Tuberculosis, Mozambique

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1. Introduction

Tuberculosis (TB) is one of deadliest infectious diseases in history. The World Health Organization reports that it not only devastates patients and their families but also negatively impacts a country's economy and social life [1] [2]. In 2021, approximately 10.6 million new TB cases were diagnosed, and 1.6 million people died from the disease [3].

TB mortality and incidence remain high due to increasing drug resistance. Antimicrobial resistance has made TB one of the leading causes of death [4]. Tuberculosis drug resistance includes resistance to effective first-line drugs (Rifampicin and Isoniazid), as well as fluoroquinolone resistance. Treating drug-resistant TB (DRTB) is more challenging because effective first-line drugs cannot be used [2]. Globally, DRTB has worsened treatment outcomes and accounted for 47% of national TB programs' budgets, significantly straining national health systems [5].

Mozambique is among the 30 high-burden countries that account for 90 percent of all tuberculosis (TB) cases worldwide. The World Health Organization (WHO) reports that Mozambique has a TB incidence rate of 361 per 100,000 people. In 2021, there were approximately 450,000 cases of drug-resistant TB (DRTB) globally, marking a 3.1% increase from the 437,000 cases reported in 2020. Mozambique's TB, TB/HIV, and DRTB burdens are among the highest globally, with 98,000 TB cases reported in 2021, including 3.7% DRTB cases [3]. The treatment success rate improved from 40% in 2017 to 72% in 2021, yet it still falls short of the WHO's 90% target [3] [6] [7].

New diagnostic platforms and treatment regimens have significantly advanced the detection and treatment of drug-resistant tuberculosis (DRTB) worldwide. Since 2013, Mozambique has employed molecular tests (Xpert® MTB/RIF) as the initial tests in its tuberculosis program. By 2018, there were 109 machines across the country. This expansion increased announcements of drug-resistant cases [8]. As of 2019, Mozambique implemented oral regimens for DRTB treatment to reduce adverse effects on patients and improve adherence to treatment [9].

Based on current guidelines, Mozambique recommends a 20-month oral regimen for drug-resistant tuberculosis (DR TB), consisting of a 6-month intensive phase and a 14-month maintenance phase. Patients are primarily treated in outpatient clinics. During the intensive phase, the regimen includes five oral medications: Linezolid (Lzd) for one month, and Bedaquiline (Bdq), Levofloxacin (Lfx), Clofazimine (Cfz), and Cicloserine (Cs) for six months. For the maintenance phase, patients continue with Levofloxacin (Lfx), Clofazimine (Cfz), and Cicloserine (Cs). Delamanid (DLM) may be added for patients meeting specific criteria, such as resistance to fluoroquinolones. To prevent neuropathy side effects from DR TB treatment, vitamin B6 (pyridoxine) is administered concurrently. Primary health care centers in Mozambique manage and report TB cases [10].

The WHO notes that these new TB treatment regimens are more expensive

than previous injectable ones [1]. To combat TB globally, an annual $13 billion is needed, yet only $5.4 billion was secured in 2021, a decrease from $6.0 billion in 2019 [3]. In 2020, Mozambique's national TB program received $26,225,047 in funding, with 12% from domestic sources and 88% from external sources such as the Global Fund and USAID. Over half of these funds were allocated to treatment [1] [9].

An analysis of the direct costs associated with drug-resistant tuberculosis (DRTB) treatment in low and middle-income countries (LMICs) for regimens lasting 18 - 24 months was conducted. Direct costs included drugs, hospital stays, outpatient clinic visits, laboratory tests, program supervision, and side effect management. The study found that DRTB treatment costs ranged from $2423 to $14,657 per patient, with an average cost of $13,259 per patient under the outpatient model [11]. A randomized controlled trial in Ethiopia and South Africa compared the costs of long-term (20 to 22 months) and short-term (9 to 11 months) DRTB treatment regimens. Using both bottom-up and top-down approaches to calculate health system costs, it was determined that the long regimen was significantly more expensive than the short regimen: $6096.6 versus $4552.3 in Ethiopia and $8340.7 versus $6618.0 in South Africa [12].

Low-resource countries like Mozambique struggle to access drug-resistant TB (DRTB) treatments due to high costs. Treatment for DRTB patients is significantly more expensive than for those with drug-sensitive TB [13] [14]. Mozambique's national TB program, Programa Nacional de Controlo da Tuberculose (PNCT), provides free screening, diagnosis, and treatment for TB. However, a resource-constrained health system such as Mozambique's could be further burdened by DRTB. To our knowledge, Mozambique does not collect data on the direct medical costs of DRTB treatment.

The Ministry of Health in Mozambique covers all direct costs (health staff salaries, medications, etc.) [15] [16] related to the treatment of DRTB (with the support of cooperation partners). The public health sector offers these services free of charge [10]. Activities related to the tuberculosis program are integrated with those of the national health system, and the direct costs for all programs are combined. Estimating non-medical costs of TB services, such as administrative expenses, physical facilities, and utilities, is often challenging. However, direct medical costs, including drugs, consultations, laboratory tests, and diagnostic devices, are easier to calculate. Thus, this study aims to estimate the average direct medical cost of TB treatment in 19 health centers in Maputo, Mozambique.

This study, focusing on an accounting cost analysis of drug-resistant tuberculosis (DRTB) treatment per patient, will help Mozambique's national TB program optimize the use of limited resources. Establishing the essential financial requirements for DRTB treatment, including medication, consultations, and diagnostics costs, is crucial for adequate funding. Understanding these accounting costs can lead to more efficient financial planning and optimization, ensuring consistent and reliable funding for drug-resistant TB programs. Additionally, knowledge of the accounting costs of DRTB treatment enables beneficiaries and

the public to understand how public funds are allocated in national TB programs.

2. Materials and Methods

2.1. Study Design

A retrospective cost analysis was conducted, including revision of records, which were collected from patients who completed the standard 20-month DRTB treatment regimen in 2019. Data collection took place between December 2022 and April 2023.

2.2. Study Site and Population

We conducted a study in all primary health centers in Maputo City, Mozambique, that had diagnosed and notified at least one DRTB case. We included records of adults who completed the standard 20-month DRTB treatment regimen between January 1, 2019, and December 31, 2019, in all 19 health centers.

We selected Maputo city's health centers because a) they reported the highest number of DRTB notifications in 2019, accounting for 20% of the country's total (see **Supplementary material 1**), b) Maputo has a superior record management system compared to other regions, and c) the health facilities in Maputo are closely located and easily accessible, which reduces the study's logistics costs. The study aimed to evaluate the direct medical costs associated with complete DRTB treatment, hence a representative sample for the entire country was not necessary.

Maputo, the capital and largest city of Mozambique, is situated in the southern part of the country. It is bordered by Maputo Bay to the east and Maputo Province to the south, comprising seven districts: Kampfumo, Nlhamankulu, KaMaxaquene, KaMavota, KaMubukwana, KaTembe, and KaNyaka. The city has a population density of 3245 inhabitants per square kilometer, with an estimated population of 1,112,607 [17].

The city hosts four general hospitals, one mental health hospital, 36 public health units, and 30 health clinics. In 2019, 19 clinics reported patients with DRTB (**Table 1**). Maputo employs 3210 medical professionals, including 720 doctors and 9 pulmonologists [9].

2.3. Participant Selection

The study did not aim to calculate the Ministry of Health's expenditure on DRTB treatment throughout the study period. Instead, it estimated the average direct medical costs of DRTB treatment per patient, following the standard recommended 20-month regimen. The analysis focused solely on patient records that adhered to the guidelines and completed both intensive and maintenance phases.

2.3.1. Inclusion Criteria

A study team reviewed the clinical records of patients aged 18 and older who

Table 1. Health clinics that notified and registered DRTB cases in 2019.

District	Health clinic	# of DRTB cases notified	# of elegible for study	#excluded
Kamavota	CS 1 de Junho	6	4	2
Kamaxakene	CS 1 de Maio	25	20	5
Kamavota	CS Albazine	4	1	3
Kampfumo	CS Alto Maé	63	37	26
Kamubukwana	CS Bagamoio	26	0	26
Katembe	CS Catembe	3	1	2
Nlhamankulu	CS Chamanculo	14	6	8
Kamavota	CS Hulene	7	1	6
Kamubukwana	CS Inhagoia	3	0	3
Nlhamankulu	CS José Macamo	6	2	4
Kamubukwana	CS Magoanine	2	1	1
Kamubukwana	CS Magoanine Tendas	3	0	3
Kampfumo	CS Malhangalene	2	0	2
Kamavota	CS Mavalane	49	32	17
Kamavota	CS Pescadores	4	0	4
Kamaxakene	CS PolanaCaniço	18	15	3
Kamavota	CS Romão	3	0	3
Nlhamankulu	CS Xipamanine	30	18	12
Kamubukwana	CS Zimpeto	6	2	4
Total		**274**	**140**	**134**

completed DRTB treatment in 2019 and had a treatment outcome at the time of review.

2.3.2. Exclusion Criteria

We excluded patients who were still on treatment, died, or were lost to follow-up, received treatment in the private sector, were inpatients, lacked outcome evaluations, or had incomplete clinical records during the study period. This exclusion was due to the difficulties in quantifying costs. Additionally, the pediatric drug-resistant tuberculosis (DRTB) group was excluded because their treatment regimens involve different formulations and dosages, and the sample size at the selected sites was very small.

2.4. Sample Size

A total of 274 patients from 19 health facilities, registered in the Mozambique health information system (SIS-MA 2021), were included in the study. Given the relatively small population of DRTB patients, all participants meeting the inclu-

sion criteria were incorporated into the study. However, out of the 274 DRTB patients registered, 134 did not meet the inclusion criteria and were deemed ineligible. Consequently, only 140 patients were included and considered in the study sample (Table 1).

2.5. Operational Definitions

Direct medicalcosts include expenses for patient consultations, laboratory tests, medications, and X-ray services.

Direct nonmedicalcosts cover transportation, family care, and other expenses unrelated to medical care.

Direct costs cover both direct medical and non-medical expenses related to patient care.

Indirect costs include the patient's loss of productivity due to illness.

Total costs combine direct and indirect expenses involved in managing TB, including screening, diagnosis, treatment, and follow-up.

DRTB treatment is defined as a full 20-month treatment, which includes a six-month intensive phase and a fourteen-month maintenance phase.

The intensive phase of treatment, which is the initial six months aimed at reducing transmissibility, includes five oral medications, monthly sputum smears, full blood counts, and biochemistry tests. X-rays are performed as deemed necessary by the treating clinician.

A maintenance phase of treatment lasts 14 months, aiming for sterilization. This phase involves three oral medications, monthly clinic visits, monthly sputum smears for the first 12 months, and then every two months until treatment concludes. A complete blood count and biochemistry are conducted every two months. X-rays are performed as needed, at the treating clinician's discretion.

Cured: a complete treatment cycle, as recommended by program standards, with no evidence of failure and three or more consecutive negative cultures collected 30 days apart after the intensive phase.

Treatment completion: A complete treatment cycle, as per program standards, without evidence of failure but fewer than three consecutive negative cultures collected 30 days after intensive treatment.

2.6. Cost Ascertainment

The cost data were collected from the health system perspective, excluding direct non-medical and indirect costs. Direct medical costs included laboratory diagnostic tests for TB (GeneXpert, LPA), HIV tests, X-ray examinations, laboratory tests during diagnosis and treatment, clinic visits, and medication during intensive and maintenance phases.

Since there is no combined fixed-dose regimen for treating DRTB, the unit cost of each drug was calculated using the Global Fund price list. The cost of each medication (Table 2) was determined by multiplying the average number of pills for each medication by the price per pill, based on the average patient

Table 2. Cost of medicines in united states dollars ($).

Nr.	Drugs	abbreviation	Quantity in bottle	Price per bottle ($)	Unit price ($)	Average pills per day	Average pills per month	Monthly cost ($)
1	Bedaquiline, 100 mg	BDQ	188	334.77	1.78	2	60	106.84
2	Clofazimine, 100 mg [Capsule(s)]	CFZ	100	79.56	0.80	1	30	23.87
3	Cycloserine, 250 mg	Cs	100	25.01	0.25	3	90	22.51
4	Delamanid, 50 mg	DLM	672	1673.85	2.49	1	30	74.73
5	Ethambutol, 400 mg	E-400	672	27.47	0.04	3	90	3.68
6	Ethionamide, 250 mg	Eto-250	100	9.02	0.09	3	90	8.12
7	Isoniazid, 300 mg	H-300	672	13.03	0.02	5	150	2.91
8	Levofloxacin, 250 mg	Lfx-250	100	2.92	0.03	3	90	2.63
9	Linezolid, 600 mg	Lzd-600	100	21.07	0.21	1	30	6.32
10	Moxifloxacin, 400 mg	Mfx-400	100	15.75	0.16	1	30	4.73
11	Pyrazinamide, 400 mg	Z-400	672	13.78	0.02	5	150	3.08
12	Prothionamide, 250 mg	Pto-250	100	9.83	0.10	3	90	8.84
13	Pyridoxine, 50 mg	Pyr(B6)	50	0.65	0.01	1	30	0.39

Source: Global fund catalogue (2023).

weight outlined by the National TB Control Programme [10]. The conversion rate to US dollars was set at 1$ = 65 Meticais, according to the Bank of Mozambique's rate at the time of the study. (source: Bank of Mozambique).

A pattern emerged in the clinical diary's record of medical interventions during the review of clinical records. The diary indicated that medical consultations, sputum smears, blood counts, biochemistry, radiography, GeneXpert tests, and HIV serology were the most frequent interventions.

Table 3 illustrates the frequency of medical interventions performed and medications prescribed during the two phases of DRTB treatment.

The costs of the interventions mentioned above are presented in Table 4.

Unit costs were derived by visiting three private health units in Maputo and obtaining the costs for each intervention, followed by calculating the average cost. Unlike the public sector, which aggregates costs for all diseases, private health units provide clearly defined costs for each intervention. This approach enabled the estimation of the cost of similar interventions in the public sector.

2.7. Data Management and Analysis

The collection of data was done using a dedicated check-list for the clinical record revision (**Supplementary Material 2**).

Data from clinical records were entered into an Excel spreadsheet using a checklist and analyzed with IBM® SPSS Statistics 20.0. Descriptive statistics (frequencies) were generated for the sociodemographic and clinical variables of

Table 3. Frequency of medical interventions and medical prescriptions per treatment phase.

Items	N	Mean*	Mode*	Minimum	Maximum	Standard deviation
Medical consultation	140	19.21	22	15	24	2.57
Sputum smear	140	18.53	19	13	24	2.33
Full Blood count	140	18.46	19	13	24	2.33
Radiography (Chest X-ray)	140	0.83	1	0	1	0.38
GeneXpert	140	0.96	1	0	1	0.19
HIV serology	140	0.19	0	0	1	0.40
Biochemistry	140	18.44	19	13	24	2.32
Line Probe Assay (LPA)	140	1.34	1	1	2	0.48
Duration (months) of phase 1 (intensive) (only medications included)	140	11.09	11	7	18	1.568
Duration (months) of phase 2 (Maintenance) (only medications included)	140	8.21	8	5	13	1.721

*refers to the average number of months of treatment estimated in the study sample. The mode refers to the most prevalent trend (which is most repeated) of months of treatment (it is the most common to be observed at an individual level in the sample).

Table 4. Costs of medical interventions/patient in United States Dollars ($).

Items	Unit cost ($)	Mean ($)	Minimum value ($)	Maximum value ($)	Standard deviation ($)
Medical consultation	26.15	559.80	438.46	701.54	74.45
Sputum smear	7.31	135.40	95.00	175.38	17.05
Full blood count	10.26	198.77	140.00	258.46	25.13
Radiography	28.00	23.20	-	28.00	10.59
GeneXpert	193.68	186.76	-	193.68	36.07
HIV serology	10.88	2.38	-	12.32	4.88
Biochemistry	46.57	926.22	653.13	1,205.78	116.74
LPA (Line Probe Assay)	3.23	4.55	3.38	6.77	1.61

the study participants. Measures of central tendency (means) were calculated for medical consultations, clinical analyses, diagnostic tests, and treatment costs. Additionally, the most frequently performed laboratory tests (mode) and treatment lines were analyzed. Using the standard deviation, we estimated the dispersion trend of treatment costs, indicating the degree of variation from the mean, along with the minimum and maximum estimates, to better understand the dispersion trend of treatment costs.

2.8. Ethics Statement

The principles of the Declaration of Helsinki, along with Good Clinical Practice

(GCP) guidelines and national regulations, were adhered to during this study. The Institutional Ethics Committee (CIBS) in Beira approved the protocol and informed consent documents on 8 December 2022 (Reference number 069/CIBS-Sofala/2022). Additionally, approval was secured from the Ministry of Health and the Maputo Municipality's Department of Health and Social Action. Data was pseudonymized, and no patient identifiers were included in the analysis to ensure confidentiality. For this retrospective review of patient records, a waiver for informed consent was granted. However, for the broader project analyzing the cost of DRTB treatment on patients, informed consent was obtained from all adult patients, as approved by Beira's Institutional Ethics Committee (CIBS) on 8 December 2022 (Reference number 069/CIBS-Sofala/2022).

3. Results

3.1. Sociodemographic and Clinical Profile of Patients Undergoing DRTB Treatment in Health Units in the City of Maputo

Approximately 64.3% of the 140 cases that completed treatment were male, and 35.7% were female. The majority of cases (n = 112) were cured, while the remainder completed treatment. KaMavota district had the highest number of patients (25.7%), followed by Kampfumo district (23.6%), and KaTembe had the fewest (2.1%). Among the revised records, 27.1% did not have an identified profession, followed by domestic workers at 21.4% and traders at 12.1% (See Table 5).

3.2. Treatment Regimens and Associated Costs

During the review of clinical records, it was noted that while a standard treatment regimen is recommended for each phase, variations may occur in practice based on the patient's clinical and laboratory characteristics. Table 6 below displays the different treatment variations encountered, the number of patients on each treatment, and the cost of the medications for one month, calculated using the National TB Control Programme's unit cost of acquiring medicines.

During the intensive phase of DRTB treatment, health professionals opt first for the CS-LFX-LZD-BDQ-CFZ regimen (51 patients) valued at $159.05. This is followed by the BDQ-DLM-LZD-CFZ-CS-B6 regimen (48 patients) estimated at $269.85, and the BDQ-LZD-LFX-CS CFZ-B6 regimen (41 patients) valued at $186.50.

During the maintenance phase, the most used regimens are LFX-CFZ-CS (51 patients) valued at $56.36, LZD-CFZ-CS (48 patients) valued at $60.60, LFX-CS-CFZ-B6 (41 patients) valued at $56.81.

3.3. Medical Interventions and Associated Costs

GeneXpert has the highest cost per patient among medical interventions, with a unit cost of $193.68. Following this are biochemistry exams, a combination of several tests, with a unit cost of $46.57. Among the interventions, Line Probe Assays (LPAs) have the lowest unit cost at $3.23 per patient.

Table 5. Sociodemographic profile of patients treated for DR-TB in 2019.

Variables	Categories	Frequency	%
Sex	Female	62	35.7
	Male	78	64.3
Age (Mean 42)	18 - 27	20	14.3
	28 - 37	36	25.7
	38 - 47	39	27.9
	48 - 57	25	17.9
	58 - 67	16	11.4
	68 - 77	2	1.4
	78+	2	1.4
Residence	Kamavota	36	25.7
	Kamaxaquene	10	7.1
	Kamfumo	33	23.6
	Kamubukwana	28	20.0
	Katembe	3	2.1
	Nlhamankulu	30	21.4
Outcomes	Cure	112	80
	Treatment completion	28	20
Occupation	Others	15	10.8
	Retired	5	3.6
	Tradesman	17	12.1
	Domestic worker	30	21.4
	Student	6	4.3
	Security guard	6	4.3
	Miner	3	2.1
	Bricklayer	7	5.0
	Police	4	2.9
	Prisoner	2	1.4
	Teacher	7	5.0
	No information	38	27.1

Table 6. Cost of the most used treatment lines in United States Dollars ($).

Phase 1/Intensive*	Unit cost (1 month)	Nr of Patients
BDQ-LZD-LFX-CS CFZ-B6	$186.50	41
CS-LFX-LZD-BDQ-CFZ	$159.05	51
BDQ-DLM-LZD-CFZ-CS-B6	$269.85	48
Total		**140**

Continued

Phase 2/Maintenance*	Unit cost (1 month)	Nr of Patients
LFX-CS-CFZ-B6	$56.81	41
LFX-CFZ-CS	$56.36	51
LZD -CFZ –CS	$60.60	48
Total		**140**

*Bedaquiline (BDQ), Linezolid (LZD), Levofloxacin (LFX), Cycloserine (Cs), Clofazimine (CFZ), Vitamin B6/pyridoxine (B6), Delamanid (DLM).

Table 7 shows the total direct medical costs incurred in diagnosing and treating DRTB per patient.

Every drug prescribed during the intensive and maintenance phases of treatment was calculated based on its unit cost per pill. In the intensive phase, the average unit cost was $2276.74 per patient for medications, with a maximum of $4047.76 per patient. In the maintenance phase, the average unit cost was approximately $475.61 per patient for medications, with a maximum of $732.66 per patient.

When considering the sum of clinical interventions and treatment, the average direct medical cost for a complete DRTB treatment per patient is $4789.43, with a maximum value of $6568.00 per patient and a standard deviation of $753.26.

The total costs incurred by the national health system for the 140 patients included in the study are presented in Table 8, which sums up the costs of all 140 patients for each intervention.

The Mozambique national health system spent $670778.45 on direct medical costs for 140 patients, as defined in this study. Over the 20-month treatment period, HIV serology tests were the least expensive, while biochemistry tests were the most costly and performed more frequently.

4. Discussion

Based on an analysis of 140 records, the intensive phase treatment cost per patient was estimated at $2276.74, totaling $318743.60 for all 140 patients undergoing DRTB treatment. This cost represents 50% of all direct medical costs associated with DRTB treatment in the study.

In the study, the total cost of medical interventions and medications for DRTB treatment was approximately $4789.43 per patient. This amount equates to 35.55 months of minimum wages, given that Mozambique's minimum wage for public servants is $134.74 per month [18]. Approximately $670778.45 was covered by state funds, equivalent to 4978.32 months of minimum wages in Mozambique.

In Mozambique, the Global Fund is the primary financier of tuberculosis (TB) programs, disbursing $167,437,586 in 2019 to fight HIV/AIDS, TB/HIV co-infection, TB, and malaria. Of this, only 5.4% ($9,092,885) was allocated to TB,

Table 7. Total direct medical costs incurred in diagnosing and treating DRTB per patient.

Items	Mean ($)	Minimum value ($)	Maximum value ($)	Standard deviation ($)
Intensive phase (only medications included)	2276.74	1272.38	4047.76	633.92
Maintenance phase (only medications included)	475.61	281.79	732.66	99.09
Diagnostics + consultation costs	2037.08	1523.65	2569.60	227.67
Total cost of all interventions (medications, diagnostics and consultations)	**4789.43**	**3452.73**	**6568.00**	**753.26**

Table 8. Summary of the cumulative direct costs of the interventions and treatment for the 140 patients.

Items	N	Total price ($)
Medical consultation	140	78630.77
Sputum smear	140	18956.15
Full blood count	140	27827.69
Radiography	140	3248.00
GeneXpert	140	26146.38
HIV serology	140	332.72
Biochemistry	140	129671.43
Line Probe Assay (LPA)	140	636.31
Intensive phase (only medications included)	140	318743.60
Maintenance phase (only medications included)	140	66585.40
Total costs (interventions and treatment)	140	**670778.45**

while 57.8% ($96,786,444) and 35.8% ($50,895,945) were dedicated to HIV and malaria, respectively [19]. In the same year, Mozambique reported 1398 cases of DRTB [9]. Considering the direct medical costs per patient, a significant portion of the TB budget, over 50%, would be required to cover basic treatment costs for DRTB, leaving minimal funds for other critical activities such as patient support, prevention, and community engagement, essential for TB control.

These findings align with Lange *et al.* (2014), who argue that the high cost of DRTB treatment can be prohibitive for some national TB programs. They suggest that, in theory, the costs of treating DRTB cases could surpass the total healthcare budgets of developing countries [20]. It is crucial to explore innovative financing methods for DRTB treatment, including alternative funding sources and increasing access to generic medicines. Cost reduction could be achieved through strategies such as early detection and diagnosis in the community, ensuring patient and healthcare provider adherence to treatment protocols, and advocating for lower prices for DRTB medications in resource-limited settings.

In resource-limited settings, challenges such as limited access to affordable diagnostics and drugs, insufficient healthcare infrastructure and expertise, and restricted resources for patient monitoring and support exacerbate the costs of treating drug-resistant tuberculosis (DRTB). These challenges hinder effective treatment and prevention, leading to increased transmission and poorer health outcomes for affected individuals and communities [21] [22]. Therefore, it is crucial to emphasize the importance of strengthening health systems and building capacity in these settings to effectively address DRTB treatment costs. Investing in training healthcare workers, improving laboratory infrastructure, and implementing robust surveillance systems can enhance the ability to diagnose, treat, and prevent DRTB more efficiently and sustainably. Applying such holistic approaches is essential to improving health outcomes for individuals and communities affected by DRTB. Future research could explore the cost-effectiveness of various financing strategies for DRTB treatment, such as social health insurance schemes or public-private partnerships.

5. Limitations

While this study represents an important initial step in generating cost evidence for DRTB treatment in Mozambique, it has limitations. The study is constrained by the absence of comprehensive cost data for all components of DR-TB treatment, leading to potential underestimation or overestimation of direct medical costs. Moreover, it only accounts for direct healthcare expenditures, omitting indirect costs such as productivity losses and patient transportation expenses, thus rendering the economic burden assessment of DR-TB incomplete.

The severity of illness, presence of comorbidities, and response to treatment vary among patient populations. Our study did not account for this heterogeneity, limiting our understanding of cost variation. We only captured direct medical costs during a specific period, without considering long-term costs associated with relapses, treatment failures, or post-treatment monitoring. Since healthcare infrastructure, drug pricing, and patient demographics vary by region, our results cannot be generalized to other countries or regions. Additionally, our cost estimations may be affected by inflation over the year 2019, which was not considered in our analysis.

6. Conclusion

In Mozambique, the direct medical cost of a basic drug-resistant tuberculosis (DRTB) treatment package per patient is equivalent to about 36 months of minimum wages, significantly burdening the limited available tuberculosis resources. It is crucial to identify alternative and innovative funding sources for DRTB treatment and reduce costs by increasing access to generic medicines.

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Availability of Data and Materials

All datasets and materials of the study are available from corresponding author upon reasonable request.

Authors Contribution

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All authors read and approved the final version of the manuscript.

Conflicts of Interest

The authors have no conflict of interest to declare.

References

[1] WHO (2021) Global Tuberculosis Report 2020. World Health Organization, Geneva. https://www.who.int/publications/i/item/9789240013131

[2] Bu, Q., Qiang, R., Fang, L., Peng, X., Zhang, H. and Cheng, H. (2023) Global Trends in the Incidence Rates of MDR and XDR Tuberculosis: Findings from the Global Burden of Disease Study 2019. *Frontiers in Pharmacology*, **14**, Article 1156249. https://www.frontiersin.org/articles/10.3389/fphar.2023.1156249 https://doi.org/10.3389/fphar.2023.1156249

[3] WHO (2023) Global Tuberculosis Report 2022. World Health Organization, Geneva. https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022

[4] Monedero-Recuero, I., Gegia, M., Wares, D.F., Chadha, S.S. and Mirzayev, F. (2021) Situational Analysis of 10 Countries with a High Burden of Drug-Resistant Tuberculosis 2 Years Post-UNHLM Declaration: Progress and Setbacks in a Changing Landscape. *International Journal of Infectious Diseases*, **108**, 557-567. https://doi.org/10.1016/j.ijid.2021.06.022

[5] Ou, Z.J., Yu, D.F., Liang, Y.H., He, W.Q., Li, Y.Z., Meng, Y.X., *et al.* (2021) Trends in Burden of Multidrug-Resistant Tuberculosis in Countries, Regions, and Worldwide from 1990 to 2017: Results from the Global Burden of Disease Study. *Infectious Diseases of Poverty*, **10**, Article No. 24. https://doi.org/10.1186/s40249-021-00803-w

[6] Programa Nacional de Controle da Tuberculose (2021) Relatório de desempenho do PNCT 2017. Misau.

[7] Programa Nacional de Controle da Tuberculose (2021) Relatório de desempenho do PNCT 2021. Misau.

[8] Mutemba, C.M., Schindele, A., Munyangaju, I., Ramanlal, N., Manhiça, I., José, B., *et al.* (2023) Contribution of Xpert® MTB/RIF to Pediatric TB Diagnosis in Mozambique. *International Journal of Tuberculosis and Lung Disease*, **27**, 419-421. https://doi.org/10.5588/ijtld.22.0479

[9] Programa Nacional de Controle da Tuberculose (2021) Relatório Anual do Programa 2019. Misau.

[10] Programa Nacional de Controle da Tuberculose (2023) Manual de Manejo Clínico e Programático da Tuberculose Multirresistente. Misau.

[11] Fitzpatrick, C. and Floyd, K. (2012) A Systematic Review of the Cost and Cost Effectiveness of Treatment for Multidrug-Resistant Tuberculosis. *PharmacoEconomics*, **30**, 63-80. https://doi.org/10.2165/11595340-000000000-00000

[12] Madan, J.J., Rosu, L., Tefera, M.G., Van Rensburg, C., Evans, D., Langley, I., *et al.* (2020) Economic Evaluation of Short Treatment for Multidrug-Resistant Tuberculosis, Ethiopia and South Africa: The STREAM Trial. *Bull World Health Organ*, **98**, 306-314. https://doi.org/10.2471/BLT.19.243584

[13] Hwang, T.J. and Keshavjee, S. (2014) Global Financing and Long-Term Technical Assistance for Multidrug-Resistant Tuberculosis: Scaling up Access to Treatment. *PLOS MEDICINE*, **11**, e1001738. https://doi.org/10.1371/journal.pmed.1001738

[14] Alemayehu, S., Yigezu, A., Hailemariam, D. and Hailu, A. (2020) Cost-Effectiveness of Treating Multidrug-Resistant Tuberculosis in Treatment Initiative Centers and Treatment Follow-Up Centers in Ethiopia. *PLOS ONE*, **15**, e0235820. https://doi.org/10.1371/journal.pone.0235820

[15] Fautrel, B., Boonen, A., Wit, M, De Grimm, S., Joore, M. and Guillemin, F. (2020) Cost Assessment of Health Interventions and Diseases. *RMD Open*, **6**, e001287. https://doi.org/10.1136/rmdopen-2020-001287

[16] Meltzer, M.I. (2001) Introduction to Health Economics for Physicians. *The Lancet*, **358**, 993-998. https://doi.org/10.1016/S0140-6736(01)06107-4

[17] INE (2023) Estatisticas dos Distritos da Cidade de Maputo—2017-2021. Instituto Nacional de Estatistica, Maputo. https://www.ine.gov.mz/web/guest/d/estatisticas-dos-distritos-da-cidade-de-maputo-2017-2021

[18] Lisboa, O. (2023) Civil Service Minimum Wage Doubles in Mozambique. Radio France Internationale (RFI), Mozambique.

[19] The Global Fund (2023) The Global Fund | Data Explorer—Datasets: Mozambique. https://data.theglobalfund.org/location/moz/disbursements/time-cycle

[20] Lange, C., Abubakar, I., Alffenaar, J.W.C., Bothamley, G., Caminero, J.A., Carvalho, A.C.C., *et al.* (2014) Management of Patients with Multidrug-Resistant/Extensively Drug-Resistant Tuberculosis in Europe: A TBNET Consensus Statement. *European Respiratory Journal*, **44**, 23-63. https://doi.org/10.1183/09031936.00188313

[21] Oga-Omenka, C., Tseja-Akinrin, A., Sen, P., Mac-Seing, M., Agbaje, A., Menzies, D. and Zarowsky, C. (2020) Factors Influencing Diagnosis and Treatment Initiation for Multidrug-Resistant/Rifampicin-Resistant Tuberculosis in Six Sub-Saharan African Countries: A Mixed-Methods Systematic Review. *BMJ Glob Health*, **5**, e002280. https://doi.org/10.1136/bmjgh-2019-002280

[22] Endo, Y., Jaramillo, J. and Yadav, R.P.H. (2022) Patient- and Health-System-Related Barriers to Treatment Adherence for Patients with Drug-Resistant Tuberculosis in the Philippines: A Mixed-Methods Study. *Tuberculosis Research and Treatment*, **2022**, Article ID: 6466960. https://doi.org/10.1155/2022/6466960

Supplementary Material 1

Table S1. DRTB cases notified per province in Mozambique (2019).

Province	Total cases notified
Cabo Delgado	41
Gaza	186
Inhambane	61
Manica	82
Maputo Cidade	274
Maputo Provincia	173
Nampula	168
Niassa	29
Sofala	120
Tete	100
Zambezia	164
Total	1398

Supplementary Material 2

Patient Clinical Record Data Collection Instrument

I) Identification

Health Facility: _____

Sex F ( ) M ( ) Age:_____ (in years)

Occupation: _____

Residential address: _____

II) Follow-up at the Health Unit

Expense items	Quantity	Unit cost	Total cost
Medical consultations			
Smear microscopy			
Full blood count			
Chest X-ray			
GeneXpert			
HIV serology			
Biochemistry			
LPA			

III) Case Closure

Medication	Treatment regimen	Duration	Date
Phase 1			
Phase 2			
Change of regimen			

( ) Cure ( ) Treatment completion ( ) Date: _____

Researcher: _____