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Understanding treatment initiation pathways and associated costs among people with pulmonary tuberculosis in a peri-urban area of Mozambique: a cross-sectional study

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Abstract

Background People with tuberculosis (TB) may seek care from healthcare providers without designated TB diagnosis and treatment services. This can lead to missed or delayed diagnosis and erroneous treatment for other diseases before being correctly diagnosed with TB. Such delays can contribute to increased out-of-pocket expenditures and lost income. We described TB treatment initiation pathways, including the type and number of pre-treatment healthcare providers visited, the time to TB treatment initiation, and the associated costs, among adults with pulmonary TB in Maputo, Mozambique.

Methods We conducted a cross-sectional survey from December 2017 to January 2020 among adults (≥ 18 years) with pulmonary TB initiating TB treatment in health facilities with TB services in Maputo city and Maputo province, Mozambique. We used a locally adapted version of the World Health Organization's TB Patient Cost Survey tools to collect health and socioeconomic data including symptoms, type and number of pre-treatment healthcare providers visited, and out-of-pocket costs and lost income. Logistic regression models were used to evaluate the associations of health and socioeconomic variables with the number of pre-treatment healthcare providers visited.

Results Of 416 enrolled participants, 268 (64.4%) were male. Median age was 34.0 (IQR: 27.0–42.0) years, and 172/416 (41.4%) were breadwinners. Nearly two-thirds (61.5%, 256/416) visited two or more healthcare providers before TB treatment initiation. The mean times to first healthcare provider visits and initiation of TB treatment were 1.5 weeks (SD = 4.9) and 7.7 weeks (SD = 5.5), respectively. The mean cost of care-seeking was equivalent to 53.7% (95%CI = 38.8–68.5%) of the monthly household income and increased with additional visits to healthcare providers. Longer duration of TB symptoms prior to TB treatment initiation (aOR 6.0 [95%CI = 3.6–9.9], $p < 0.001$) and being in the least poor quintile of households (aOR 2.6 [95%CI = 1.3–5.5], $p = 0.011$) were associated with visiting two or more pre-treatment healthcare providers.

Conclusions Most people with TB symptoms sought care within two weeks but TB treatment initiation was delayed to nearly two months after symptoms onset. This suggests that delays in TB treatment initiation may be attributable

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to health system factors rather than the care-seeking behaviour of people with TB in Maputo, Mozambique. Additionally, there was a substantial financial burden of care-seeking exacerbated by additional healthcare provider visits. Evidence on interventions to address delays in diagnosis and treatment, and their associated health and socioeconomic impacts in Mozambique is urgently needed.

Keywords Tuberculosis, Pathways to care, Delay to treatment initiation, Mozambique

Introduction

Pathways to tuberculosis (TB) treatment initiation are often complex, requiring significant financial resources and time from individuals, households and healthcare systems [1–3]. Many high-burden TB countries have limited TB diagnostic capacity, which results in missed or misdiagnosed people and inefficiencies in the diagnostic pathway [4]. Consequently, people with TB often experience a delay in TB treatment initiation, which has been demonstrated to contribute to worse TB treatment and socioeconomic outcomes and increases in the likelihood of onward TB transmission [1, 5–8].

According to the international standards for TB care, individuals who present to healthcare providers with a cough lasting more than two weeks should be tested for TB [9, 10]. However, of the 10.8 million estimated people with TB worldwide in 2023 only 75.9% were detected and notified by national TB programs (NTP). In Mozambique, 95.4% of the estimated 117,000 people with TB were detected and notified to the NTP [11, 12], which although higher than the global average, still represents a substantial gap in case detection and notification. There are three main groups of people with TB who are missed: i) individuals who have not sought care due to multifaceted barriers, including financial (i.e. costs and catastrophic costs), social (i.e. stigma and discrimination) or geographical (i.e. distance to healthcare provider) constraints; ii) individuals who sought care at providers without TB diagnosis and care provision or at private clinics (both with and without TB diagnosis and care provision), who may not receive a TB diagnosis or notification to NTPs; and iii) individuals who sought care at providers with TB diagnosis and care provision who were not reported to NTPs, even after receiving a diagnosis and treatment [2].

Globally, people with TB often make multiple visits to different types of healthcare providers before being tested for and diagnosed with TB [1, 2, 5, 13]. This is because the majority of people with TB make their initial visit to healthcare providers that do not offer point-of-care TB diagnostics and treatment. This scenario demonstrates the misalignment between people with TB's care-seeking preferences and the availability of TB services [6, 14–17].

The World Health Organization's (WHO) End TB Strategy advocates for a person-centred approach that delivers services which respect and respond to people's preferences, needs, and values, with a focus on ensuring that people access services that are convenient to them, ideally at the lowest cost possible [18–21]. Cumbersome diagnostic pathways with utilization of many healthcare providers along the way can lead to high out-of-pocket expenditures and lost income [5]. A systematic review estimated that the average total cost related to TB illness, care seeking, diagnosis, and treatment was 58% of the annual income of affected individual in low- and middle-income countries, with approximately half of these costs being incurred before TB treatment initiation [22]. This can impose socioeconomic hardship and compound poverty amongst TB-affected individuals and households from which it can be difficult to recover [3].

To the best of our knowledge, only one study from Mozambique, conducted in a region of Mozambique with lower TB case notification rates and fewer health facilities than our study setting, described factors associated with diagnostic delays [23]. In addition, two recently published studies investigated the health system costs associated with treatment of people with multi-drug resistant or rifampicin-resistant TB (MDR/RR-TB) [24] and indirect costs incurred by people with MDR/RR-TB [25]. Neither study aimed to determine TB diagnostic and treatment pathways and their associated direct and indirect costs to people with TB. We aimed to fill this critical knowledge gap in an often-neglected aspect of TB care in Mozambique.

Methods

Study design

This cross-sectional study was conducted between 11 December 2017 and 31 January 2020 in Maputo City and Maputo Province, Mozambique. We enrolled adults with TB at the time of their TB treatment initiation, within the TB Sequel framework [26]. TB Sequel, which is ongoing at the time of writing, is a longitudinal prospective cohort study recruiting people with TB in four countries: Mozambique, South Africa, The Gambia, and Tanzania. TB Sequel aims to: i) understand the clinical, microbiological, immunological, and socioeconomic risk factors affecting or predicting long-term pulmonary function outcome among people with pulmonary TB; and ii) determine costs to the individual and health system of

TB illness, care-seeking, treatment and post-TB sequelae. Clinical and pulmonary assessments, biological sample collection and socio-economic questionnaires were performed according to TB Sequel schedule of events, which is reported in more detail elsewhere [26].

Study setting and population

This study was conducted in Maputo City and Maputo Province, Mozambique. Mozambique is a Sub-Saharan African country with an estimated population of 31 million inhabitants [27], an illiteracy rate of 39%, and 62.8% of people living below the national poverty line [28]. The TB incidence in 2023 was 361 (95% CI: 220–537) per 100,000 population, and the country is listed by WHO as one of the high-burden countries for TB, HIV-associated TB and MDR/RR-TB [29]. TB diagnosis and treatment, including microbiological testing of sputum, chest X-ray and anti-TB treatment, is provided free of charge by the NTP at designated public health facilities [9]. In 2022, 110,674 people with TB were notified to the Mozambican NTP and 25% of those had HIV co-infection [30].

The Mozambican public healthcare system encompasses four levels of care: Primary (health facilities); secondary (rural, district and general hospitals); tertiary (provincial hospitals); and quaternary (central and specialised hospitals) [31]. Maputo City, the capital city of Mozambique, is densely populated, comprising 1,127,565 inhabitants (3,768 inhabitant/km^2) [32]. It has a healthcare network of 38 public healthcare providers including 33 health facilities, 4 general hospitals and one central hospital [33]. Sputum-smear microscopy, GeneXpert MTB/RIF and culture testing capacity is available in 35 (92.1%), 28 (73.7%) and 1 (2.6%) public laboratories, respectively [34]. In 2022, Maputo City notified 6,574 cases of which 152 (2.3%) were MDR/RR-TB (see Supplementary File 1) [30]. Maputo Province, within which Maputo City lies, has a population of 2,302,891 inhabitants (92 inhabitants/km^2) [35]. It has a healthcare network of 124 public healthcare providers including 117 health facilities, 3 general hospitals, and one provincial hospital [36]. Sputum smear microscopy and GeneXpert MTB/RIF are available in 40 (32.2%) and 17 (13.7%) public laboratories, respectively [34]. There is no mycobacterial culture testing capacity established in Maputo Province. In 2022, Maputo Province reported 7,799 cases of TB, of which 117 (1.5%) were MDR/RR-TB [30]. Anecdotally private clinics, pharmacies, traditional healers and practitioners are commonly consulted throughout Mozambique, including in Maputo City and Province, but there is limited empirical data on their use, onward referral mechanisms, and their networks.

Participants were pre-recruited by trained NTP nurses at 12 health facilities with TB services (nine in Maputo City and three in Maputo Province) where treatment was provided, which had been selected through convenience sampling. Participants were then referred to TB Sequel health facilities for further data collection, with a referral form detailing the TB diagnostic tests already done (see Supplementary File 1). Recruitment, screening and eligibility criteria were conducted by study team members at TB Sequel health facilities following the TB Sequel study protocol as described elsewhere [26]. In brief, adults 18 years or older with microbiologically confirmed pulmonary drug-sensitive TB (DS-TB) or MDR/RR-TB were recruited within 7 days of TB treatment initiation (see Supplementary File 2).

Definition of variables

Operational definitions of the key study variables (TB disease, healthcare seeking behaviour, healthcare providers and costs) are summarised in Table 1. 'Pathways' was defined as the route people with TB take from symptom onset to TB treatment initiation. 'Healthcare seeking' was defined as the action taken by individuals with symptoms compatible with TB to seek relief, diagnosis, and care for their symptoms. A 'healthcare provider with TB service' was defined as a location where anti-TB treatment is available and GeneXpert MTB/RIF or smear microscopy is either available or sample referral mechanisms are in place.

Direct out-of-pocket (OOP) medical costs included costs of diagnosis (laboratory tests, chest X-ray), consultations fees, drugs other than TB drugs, and hospitalization costs. Direct OOP non-medical costs included food, transportation and other costs incurred while seeking care and waiting at the health facility. Indirect costs, collected using both output approach (estimation of the participants' loss of income by calculating the money they would have earned if they were not ill or seeking care) and human capital approaches (estimation of the participants' productivity reduction by calculating the reduction in work output, absenteeism hours lost due to TB illness and care-seeking) [37]. For individual and household income, we asked participants to recall what their income was "before" the TB illness (onset of symptoms) and at the time of the interview (e.g., at TB treatment initiation or enrolment into the TB Sequel study).

Wealth quintiles were generated following a principal component analysis of standard household assets measured in the Mozambican Health Demographic Survey [38–40]. Time to TB treatment initiation was calculated from what participants reported as the onset of their TB symptoms until the date of TB treatment initiation (as

Table 1 Glossary of operational definitions of providers and costs

TB Disease related definitions
TB Illness: the period of time from the onset of TB-related symptoms to the end of the continuation treatment phase
Pre-treatment: the period of time from self-reported onset of TB-related symptoms until treatment initiation
TB treatment initiation: start of anti-tuberculosis medicines intake after the diagnosis of TB (i.e. the day on which they first took TB medications)
Health seeking behaviour
Delay of the person with TB (patient delay): time interval between onset of symptoms and first contact with the health care system;
Health system delay: time interval between the first visit to the healthcare provider and TB treatment initiation
Total delay: the sum delay of the person with TB and the health system delay
Providers
Healthcare providers: formal medical professionals, informal traditional healers or alternative practitioners, private clinics, health facilities, pharmacies, and hospitals
Primary care health facility (health facility): Primary level of care in the Mozambican healthcare system with TB service provision
Public hospital: any public healthcare provider in the Mozambican healthcare system at the secondary, tertiary, or quaternary level of care
Private clinics[a]: private and formal healthcare providers
Pharmacy: private healthcare provider that dispenses medication as well as various other products
TB costs
Direct ("out of pocket") costs: the sum of the direct out-of-pocket medical and direct out-of-pocket non-medical costs
Direct out of pocket medical costs: out of pocket payments made directly by the person with TB or their households member for assessing TB treatment (ex. consultation fee, medicines, diagnostics, lab tests and procedures), net of any reimbursement
Direct out of pocket non-medical costs: out-of-pocket payment made by TB affected people and /or their guardian related to transportation, accommodation, food, day charges for time in hospital etc., net of any reimbursements
Indirect costs (Income/productivity loss): self-reported household income loss net of welfare or social assistance payments or time spent away from the daily productive routine
Total costs: The sum of direct "out of pocket" costs and indirect costs
Earnings: the monthly money actually received by the household
Income before: estimates of the monthly money that was received by the individual or household before the TB illness
Income now: estimates of the monthly money that was received by the individual or household during the TB illness

[a] Private clinic network is not clearly described in the existing Mozambican levels of care

reported in medical records or in the TB Sequel source documents). Mean Monthly Household Income (MMHI) was estimated using monthly household income before TB. Total TB treatment initiation delay was categorised into shorter delay or longer delay based on a median delay of 4 weeks calculated for the whole sample size. The TB treatment initiation delay was calculated based on the duration of the oldest and longest symptom, as the data on time to TB treatment initiation was not directly collected.

Data collection

Study procedures, including data collection, only commenced after obtaining the informed consent and checking the eligibility criteria at TB Sequel health facilities. All study participants were given a participant Identification number (Participant ID) for data anonymisation. Following informed consent, we used a version of the WHO's TB Patient Cost Survey tools, adapted for the TB sequel study to collect socioeconomic and clinical data including presence and duration of TB symptoms, the type and number of healthcare providers visited since symptom onset, employment status and individual and household income [41]. Due to the eligibility check that included GeneXpert testing, the questionnaire was conducted on the second study day (baseline/D0) or later, as appropriate. Data were collected by the first author with support from hired research assistants with backgrounds in sociology. They were trained on study protocol, study procedures and socioeconomic questionnaires. The questionnaires were conducted on paper-based case report form (CRF), in Portuguese or another language most appropriate to the participants and then entered into OpenClinica (OpenClinica LLC, an open-source password-protected clinical trial management system). Socio-demographic data were collected in a separate CRF. Participants were also asked to estimate the direct OOP costs they incurred during visits to healthcare providers from the time which they perceived to be the onset of their TB symptoms until diagnosis of TB. Cost data was collected using local currency units (Mozambican New Metical, MZN) directly reported from participants. All local currency amounts were converted into United States Dollars ($) using the mean rate exchange provided by the Bank of Mozambique during the data collection period (between December 2017 and January 2020 [$1.00 = 62.21 MZN]). As per the TB Sequel protocol, participants who were diagnosed and initiated on TB treatment at first visit to a health facility were assumed to have incurred no healthcare seeking costs and had no costs data collected. Thus, only participants who had more than one visits to providers before diagnosis and TB treatment initiation had costs data collected. Socioeconomic and socio-demographic data were merged using the participant identification (Participant ID). A dedicated team of study monitors regularly checked the data for completeness, inconsistencies, and discrepancies.

Statistical analysis

We performed descriptive analysis to summarise the data and used Mann–Whitney U or Kruskal Wallis tests where appropriate to assess differences between groups (i.e., no pre-treatment visits versus pre-treatment visits to healthcare providers). The healthcare seeking costs, stratified by the order or number of providers, were mostly described by their arithmetic means and standard deviation (SD) whether the data was Gaussian or non-Gaussian because this approach is considered robust for health economic data analysis [3, 42–44]. All significance tests were two-sided with a confidence level of 95%.

We used logistic regression to identify socioeconomic and clinical factors associated with visiting multiple providers (no pre-treatment visits *versus* pre-treatment visits to healthcare providers) prior to TB treatment initiation. We used a multiple logistic regression model to estimate the odds ratio and corresponding 95% confidence interval for variables independently associated with the primary outcome of having no pre-treatment visits versus having pre-treatment visits to healthcare providers prior to TB treatment initiation. From the univariate logistic regression, variables with a p-value less than 0.2 entered the multivariable analysis [45]. Multicollinearity was assessed in the final multivariable regression model using the evaluation of the variance inflation factor (VIF). Variables with VIF > 10 were considered to contribute to multicollinearity [46, 47]. In case of multicollinearity, continuous variables were considered for centering (by subtracting their mean from each observation), while categorical variables were considered for exclusion from the model [48]. Then, a stepwise backward elimination process was used to further build the model whereby the variables with the weakest association were eliminated sequentially from the model and a likelihood ratio test was used to compare nested models. This process was continued until no further variables could be excluded from the model without a statistically significant loss of fit. All analyses were performed in STATA version 16 and data visualization was performed in R version 4.3.1.

Participants' involvement

Participants were not involved in the development, design, and analysis of this study. Ethical approval was received from the National Bioethics Committee (CNBS—IRB0002657) in Maputo, Mozambique (Reference number 291/CNBS/2017) and all participants gave written, informed consent to participate. The reporting of the study findings adheres to the STROBE guidelines [49].

Results

Participant characteristics

Of 498 people screened for study participation, 82 (16.5%) were not eligible mainly due to the absence of microbiological confirmation of TB diagnosis (Fig. 1). Of the 416 eligible participants enrolled in the study: 268 (64.4%) were male; median age was 34 years (IQR: 27–42); 221 (53.1%) completed a secondary school education; 320 (76.9%) were unemployed and 172 (41.4%) were primary income earners of their households. The median monthly individual income before TB was $56.3 (IQR: 0–96.4). Nearly half, 190 (45.7%), of the participants were HIV positive; 51 (12.3%) had a previous episode of TB disease; 68 (16.4%) had other comorbidities; 285 (68.5%) were alcohol consumers; and 32 (7.7%) and 47 (11.3%) were current smokers and illicit drug users respectively. At TB treatment initiation, 261 (62.7%) participants had three or more symptoms consistent with TB. Just over one third, 160 (38.5%), of participants were diagnosed and initiated on TB treatment at their first and only healthcare provider (Table 2).

Pathways and delays to TB treatment initiation

Participants sought initial care from both private and public healthcare providers. The longest pathway involved up to five different healthcare providers before TB treatment initiation (see pathways to care as Supplementary File 3). The 416 participants' pathways to different providers, were divided into 25 pathways. The mean time between symptom onset and visit to the first healthcare provider was 1.5 weeks (SD = 4.9) and to TB treatment initiation was 7.7 weeks (SD = 5.5) (Table 3). Health facilities were the most visited provider during the healthcare seeking process (n = 160; 38%). Specifically, 322/416 (77.4%) sought initial care at a health facility of whom 162/322 (50%) did not have TB treatment initiated. A similar trend was observed among those who visited a second pre-treatment healthcare provider, with 223/256 (87%) going to a health facility of whom the majority (191/223, 86%) initiated TB treatment. Among those whose pathway involved a third pre-treatment healthcare provider, 62/65 (95.4%) went to a health facility of whom the majority (56/62, 90.3%) initiated TB treatment

(Fig. 2). Overall, 48% of people presented to a healthcare provider with TB services available at least once during the healthcare seeking pathways, but they were not diagnosed and consequently, not initiated on treatment. Public hospitals (40/256, 15.6%) and pharmacies (38/256, 14.8%) were, respectively, the second and the third most commonly visited initial healthcare provider.

Cost associated with care-seeking prior to TB treatment initiation

Of the 256 participants who had visits to providers before diagnosis and TB treatment initiation and, contributed data to the costs analysis as per the TB Sequel protocol, 249 (97.3%) incurred any type of pre-treatment direct OOP costs. The mean total cost was equivalent to 53.7% (95% CI = 38.8–68.5) of the MMHI and increased significantly with each additional visit to healthcare providers, ranging from 34.3% (95% CI = 21.2–74.9%) for those who had two visits to 98.8% (95% CI = 45.4–152.2%) for those who had four or more visits to healthcare providers ($p = 0.0002$, Table 3). Indirect costs were consistently higher than the direct OOP costs regardless of the number of visits to healthcare providers. Those who had four or more visits to healthcare providers incurred significantly higher total direct OOP costs ($27.5, SD = 51) compared to those with two or three visits ($17.6, SD = 51.7, and $4.7, SD = 16.1, respectively, $p < 0.001$). Among direct OOP medical costs, medicine costs were the major contributor (Mean = $11.0, SD = 34.7), followed by consultation fees (Mean = $1.2, SD = 5.5). Income loss was the major contributor to the total costs and mean cost ranged from $25.6 (SD = 58.3) among those who had two visits to healthcare providers to $53.6 (SD = 145.0) for those who had four or more visits. People attending private providers (pharmacies and private clinics) had disproportionally higher costs compared to those attending any public services with the mean OOP costs of first healthcare seeking visit at a private clinic being $64.0 (SD = 16.0) (Table 4). The cost associated with care seeking was also summarised as median and IQR (see Supplementary File 4) and disaggregated according to delay to treatment initiated (see Supplementary File 5).

Socioeconomic and clinical factors associated with TB treatment initiation pathways

Several socioeconomic and clinical variables were associated with having pre-treatment visits to healthcare provider before TB treatment initiation. In the univariable logistic regression model, it was observed that people with three or more symptoms (cOR 0.6 [95% CI = 0.4–0.9], $p = 0.016$), who used illicit drugs (cOR 0.42 [95% CI = 0.2-0.08], $p = 0.005$), or who were HIV-positive (cOR 0.6 [95% CI = 0.4–0.8], $p = 0.005$) were less likely to have

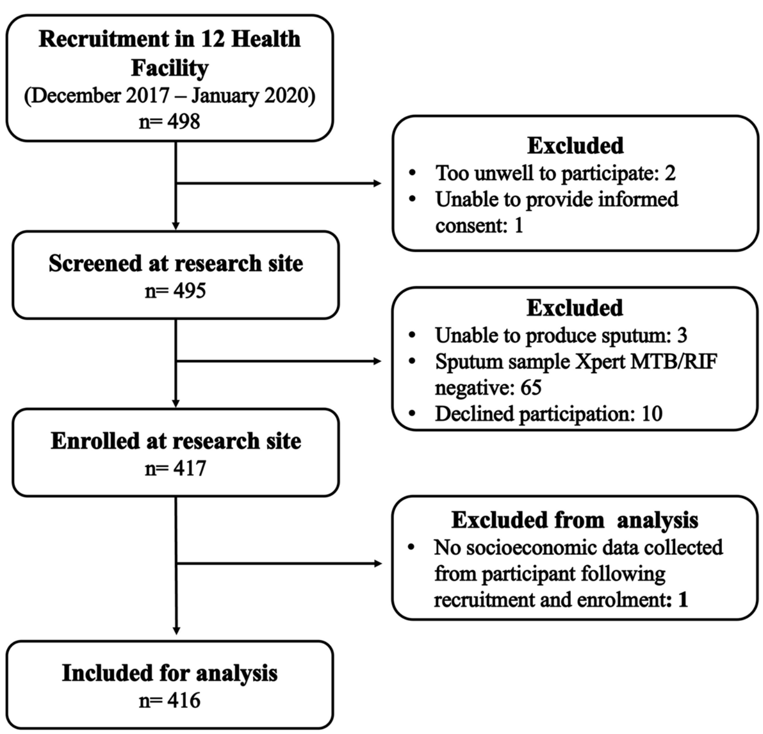

Fig. 1 Study participants flow chart

Table 2 Study population sociodemographic and health characteristics and comparison of participants based on the pre-treatment pathways to diagnosis and treatment

	All participants	**Pathways to TB treatment initiation**	
	***n* = 416**	**Diagnosed and initiated on treatment at first healthcare provider (no pre-treatment visit) (*n* = 160)**	**Visits to healthcare providers before diagnosis and treatment initiation (pre-treatment visits) (*n* = 256)**
Sociodemographic variables	**n (%)**	**n (%)**	**n (%)**
Median age in years (IQR)	34 (27–42)	34 (28–43)	34 (26–42)
Age groups in years			
18–29	147 (35.5)	49 (30.8)	98 (38.4)
30–39	135 (32.6)	58 (36.5)	77 (30.3)
40–49	72 (17.4)	26 (16.4)	46 (18.0)
> 50	60 (14.5)	26 (16.4)	34 (13.3)
Sex			
Female	148 (35.6)	57 (35.6)	91 (35.6)
Male	268 (64.4)	103 (64.4)	165 (64.5)
Education level			
No education	34 (8.2)	20 (12.5)	14 (5.5)
Primary	141 (33.9)	57 (35.6)	84 (32.8)
Secondary	221 (53.1)	76 (47.5)	145 (56.6)
University	20 (4.8)	7 (4.4)	13 (5.1)
Occupation			
Unemployed	320 (76.9)	125 (78.1)	195 (76.2)
Employed	96 (23.1)	35 (21.9)	61 (23.8)
Primary income earner			
Patient	172 (41.4)	67 (41.9)	105 (41)
Other household member	244 (58.6)	93 (58.1)	151 (59)
Monthly income in USD			
Mean individual monthly income before TB, (SD) n = 380	77.3 (115.4)	69.9 (83)	81.6 (130.7)
Median individual monthly income before TB, (IQR) n = 380	56.3 (0–96.4)	56.3 (0–96.4)	56.3 (0–104.5)
Mean current individual monthly income, (SD) n = 378	39.4 (105)	28.1 (88.7)	46.6 (113.8)
Median current individual monthly income, (IQR) n = 378	0 (0–48.2)	0 (0)	0 (0–56.3)
Mean monthly household income before TB, (SD) n = 292	127.5 (146.3)	114.1 (132.7)	135.3 (153.5)
Median monthly household income before TB, (IQR) n = 292	96.4 (61.9–160.7)	80.4 (56.3–152.7)	96.4 (64.3–160.7)
Mean current monthly household income, n = 251	124.6 (151.8)	112.1 (143.4)	130.9 (155.9)
Median current monthly household income, (IQR) n = 251	96.4 (56.3–96.4)	80.4 (48.2–144.7)	96.4 (48.2–144.7)
Wealth quintile			
First (Poorest)	84 (20.2)	44 (27.5)	40 (15.6)
Second	85 (20.4)	33 (20.6)	52 (20.3)
Third	81 (19.5)	32 (20.0)	49 (19.1)
Fourth	83 (20.0)	28 (17.5)	55 (21.5)
Fifth (Least poor)	83 (20.0)	23 (14.4)	60 (23.4)
Food insecurity			
Yes	209 (50.2)	85 (53.1)	124 (48.4)

Table 2 (continued)

	All participants	Pathways to TB treatment initiation	
	n **= 416**	**Diagnosed and initiated on treatment at first healthcare provider (no pre-treatment visit) (*n* = 160)**	**Visits to healthcare providers before diagnosis and treatment initiation (pre-treatment visits) (*n* = 256)**
No	207 (49.8)	75 (46.9)	132 (51.6)
Health variables at TB treatment initiation (enrolment into TB Sequel study)			
TB Symptoms			
Fewer symptoms (1 or 2)	155 (37.3)	48 (30.0)	107 (41.8)
More symptoms (3 or more)	261 (62.7)	112 (70.0)	149 (58.2)
Treatment initiation delay			
Shorter delay	242 (58.2)	128 (80.0)	114 (44.5)
Longer delay	174 (41.8)	32 (20.0)	142 (55.5)
BMI (kg/m2)			
< = 18	142 (34.1)	54 (33.6)	88 (34.4)
18–25	250 (60.1)	100 (62.5)	150 (58.6)
25–30	20 (4.8)	5 (3.1)	15 (5.9)
> 30	4 (1.0)	1 (0.6)	3 (1.2)
Previous TB episode			
No	365 (87.7)	141 (88.1)	224 (87.5)
Yes	51 (12.3)	19 (11.9)	32 (12.5)
1 episode	49 (96.1)	19 (100)	30 (93.8)
2 episodes	2 (3.92)	0 (0)	2 (6.3)
HIV status			
Positive	190 (45.67)	87 (54.4)	103 (40.2)
Negative	226 (54.33)	73 (45.6)	153 (59.8)
Comorbidities			
No	348 (83.7)	134 (83.8)	214 (83.6)
Yes	68 (16.4)	26 (16.3)	42 (16.4)
1 Comorbidity	63 (92.6)	25 (95.2)	38 (90.5)
2 + Comorbidities	5 (7.4)	1 (3.8)	4 (9.5)
Alcohol consumption			
Yes	285 (68.5)	118 (73.8)	167 (65.2)
No	131 (31.5)	42 (26.3)	89 (34.8)
Smoking			
Yes	32 (7.7)	17 (10.6)	15 (5.9)
No	384 (92.3)	143 (89.4)	241 (94.1)
Previous smoker	98 (23.6)	46 (28.8)	52 (20.3)
Never smoked	286 (68.8)	97 (60.6)	189 (73.8)
Illicit drug use			
Yes	47 (11.3)	27 (16.9)	20 (7.8)
No	369 (88.7)	133 (83.1)	236 (92.2)
Formerly incarcerated			
Yes	30 (7.2)	16 (10.0)	14 (5.5)
No	386 (92.8)	144 (90.0)	242 (94.5)

The cost was estimated in Meticais and converted to US dollars using a mean conversion rate of $1.00 = 62.21 MZN (mean conversion rate during the data collection period)

Table 3 Direct out-of-pocket and indirect costs associated with health care seeking

Pre-treatment cost	All Participants	Total number of pre-treatment visits to healthcare providers			*p*-value*
	n = 256	2 (*n* = 122)	3 (*n* = 79)	4 + (*n* = 55)	
Time to first health facility visit (weeks)	1.5 (4.9)	1.7 (4.6)	0.9 (4.8)	1.9 (5.6)	0.64
Time to Treatment initiation (weeks)	7.7 (5.5)	6.8 (5.2)	7.4 (4.2)	9.9 (7.2)	0.016
Direct Medical costs in USD, mean (SD)	**12.9 (39.7)**	**4.4 (16.1)**	**16.9 (51.8)**	**25.5 (51.2)**	**0.0001**
Consultation fee	1.2 (5.5)	0.3 (1.3)	2.2 (8.8)	1.7 (4.6)	
Radiography or other imaging (e.g., X-ray)	0	0	0	0	
Other procedures	0.1 (1)	0.01 (0.1)	0.2 (1.8)	0.04 (0.3)	
Lab tests	0.5 (3.6)	0.1 (1.1)	1 (5.6)	0.6 (3.3)	
Medication	11.0 (34.7)	3.9 (15)	13.5 (41.6)	22.9 (49.1)	
Other (e.g., supplements)	0.1 (1.1)	0.05 (0.5)	0.03 (0.3)	0.3 (2.2)	
Hospitalisation (day charges for time in hospital)	0	0	0	0	
Direct non-medical costs in USD, mean (SD)	**0.8 (2.2)**	**0.3 (0.5)**	**0.7 (1.36)**	**2.0 (4.2)**	**0.0001**
Transportation	0.6 (1.6)	0.2 (0.3)	0.6 (1.3)	1.4 (3)	
Food	0.2 (1)	0.1 (0.4)	0.1 (0.3)	0.6 (1.9)	
Accommodation	0.01 (0.2)	0	0.04 (0.4)	0	
Other non-medical payments	0.01 (0.1)	0	0	0.03 (0.2)	
TOTAL medical and non-medical Costs in USD, mean (SD)	**13.7 (39.7)**	**4.7 (16.1)**	**17.6 (51.7)**	**27.5 (51)**	**0.0001**
Income loss, mean (SD)	**34.6 (87.9)**	**25.6 (58.3)**	**27.5 (75)**	**53.6 (145)**	**0.26**
TOTAL COSTS in USD, mean (SD)	**48.3 (93.3)**	**30.6 (56.5)**	**45.1 (78.7)**	**81.1 (152.6)**	**0.0001**
Cost of care seeking as % of MMHI (95% CI)	**53.7 (38.8 – 68.5)**	**34.3 (21.2 – 47.4)**	**52.1 (29.3 – 74.9)**	**98.8 (45.4 – 152.2)**	**0.0002**

MMHI Mean Monthly Household Income

* *p*-value provided by Kruskal–Wallis test

visits to healthcare provider before diagnosis and TB treatment initiation. Conversely, people who were in the least poor quintile (cOR 2.9 [95% CI = 1.5–5.5], p = 0.001) or had longer time from TB symptom onset to TB treatment initiation (cOR 4.0 [95% CI = 3.1–7.9], *p* = *0.001*) were more likely to have visits to healthcare provider before diagnosis and TB treatment initiation.

In the multivariable logistic regression model, adjusting for age, sex and occupation, the VIF was less that 10 for all variables included in the model. We found that belonging to the least poor quintile of households (aOR 2.6 [95% CI = 1.5–5.5], *p* = *0.011*) and having longer time from TB symptom onset to TB treatment initiation (aOR 6.0 [95% CI = 3.6–9.9], *p* < *0.001*) was independently associated with having visits to healthcare provider before diagnosis and TB treatment initiation. Having more symptoms at the time of TB treatment initiation (aOR 0.4 [95%CI = 0.3–0.7], *p* = *0.011*) or reporting illicit drug use was associated with lower likelihood of having visits to healthcare provider before diagnosis and TB treatment initiation (Table 5).

Discussion

This study investigated the healthcare-seeking pathways and associated costs of adults with microbiologically confirmed pulmonary TB in Maputo City and Province, Mozambique. The findings highlighted the complex pathways to TB treatment initiation, which often involved multiple visits to different healthcare providers and direct out-of-pocket costs. Notably, one quarter of participants had their first healthcare-seeking visit at healthcare providers that were not designated TB diagnosis and treatment facilities. Among those who had the first healthcare seeking visit at a healthcare provider

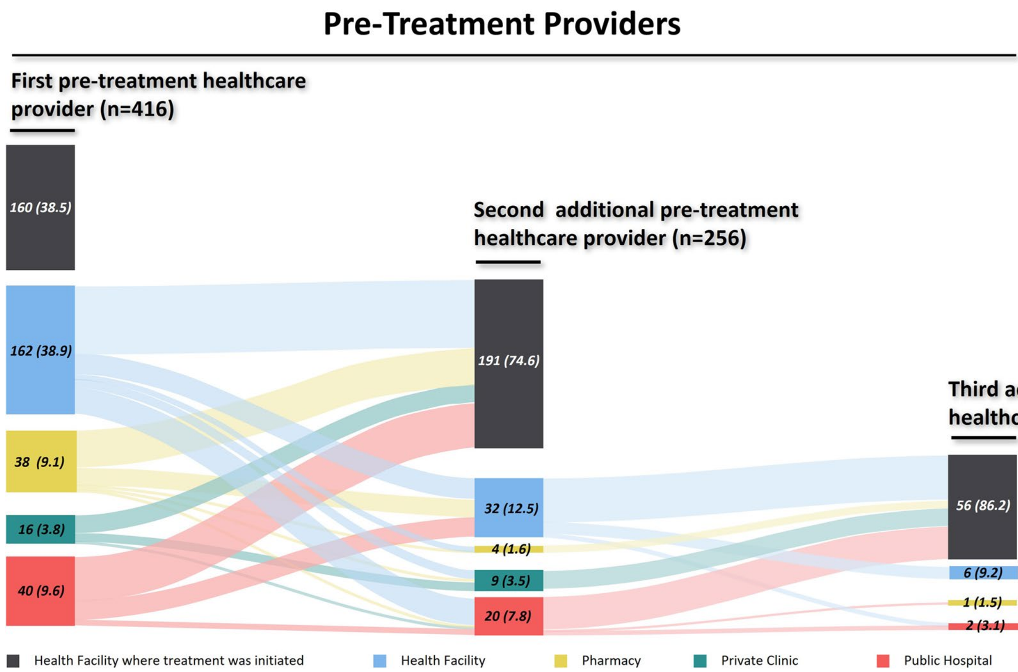

Fig. 2 Care-seeking pathways undertaken by people with TB from symptoms onset to treatment initiation. Nine participants were not diagnosed at a third healthcare provider and sought care at a fourth ($n = 8$) and fifth healthcare provider ($n = 1$). The numbers in the boxes represent the sample (n) and percentages (%) of people who sought care from a particular healthcare provider as a proportion of all participants seeking care at the respective provider

Table 4 Healthcare seeking and associated direct costs by order of healthcare providers visited. Presented costs are direct out-of-pocket during care-seeking in US dollars

Order of providers	Type of provider	n (%)	Number of times visited, mean (SD)	Total direct OOP costs, mean $ [SD]	Total direct OOP costs, median $ [IQR]
First healthcare provider (*n* = 256)	**Private providers**				
	Pharmacy	38 (14.8)	1.89 (1.20)	10.3 (24.1)	4.8 (1.3 – 8.0)
	Private clinic	16 (6.3)	1.93 (1.73)	64.0 (16.0)	22.4 (16.0 – 66.7)
	Public providers				
	Hospital	40 (15.6)	1.7 (1.26)	7.7 (2.8)	1.2 (0.4 – 5.2)
	Health Facility	162 (63.2)	1.89 (1.06)	4.2 (12.5)	0.5 (0.2 – 2.1)
Second healthcare provider (*n* = 65)	**Private providers**				
	Pharmacy	4 (6.2)	2 (0.8)	4.5 (4.6)	4.3 (0.6 – 8.4)
	Private clinic	9 (13.8)	2.4 (0.5)	45.6 (45.2)	24.1 (6.0 – 66.7)
	Public providers				
	Hospital	20 (30.8)	2.8 (1.4)	16.8 (46.2)	5.1 (0.1 – 8.8)
	Health Facility	32 (49.2)	2.9 (1.4)	9.5 (42.4)	0.5 (0.3 – 1.8)
Third healthcare provider (*n* = 9)	**Private providers**				
	Pharmacy	1 (11.1)	3 (0)	12.4 (0)	12.4 (0)
	Private clinic	0 (0)	–	–	–
	Public providers				
	Hospital	2 (22.2)	3.5 (0.7)	6.7 (5.4)	6.7 (2.9 – 10.4)
	Health Facility	6 (66.7)	5.2 (2.3)	1.2 (1.9)	0.1 (0.1 – 1.5)

Table 5 Univariable and multivariable logistic regression of health and social variables associated with visits to providers before diagnosis and start of treatment

Variables	Number of pre-treatment healthcare providers[a]			
	Univariable logistic Regression		Multivariable logistic regression	
	cOR (95%CI)	*p-value*	aOR (95%CI)	*p-value*
Age groups in years				
18 – 29	Ref	_	_	_
30 – 39	0.7 (0.4–1.1)	0.097	0.9 (0.5–1.6)	0.63
40 – 49	0.9 (0.5–1.6)	0.68	1.6 (0.8–3.3)	0.23
> 50	0.7 (0.4–1.2)	0.14	0.6 (0.3–1.2)	0.11
Sex				
Female	Ref	_	_	_
Male	1.0 (0.7–1.5)	0.99	1.4 (0.8–2.4)	0.38
Education level				
No education	Ref	_	_	_
Primary	2.1 (1.0–4.5)	0.055	1.4 (0.7–2.8)	0.33
Secondary	2.7 (1.3–5.6)	0.008	1.5 (0.8–6.2)	0.20
University	2.7 (0.8–8.3)	0.095	1.1 (0.3–3.9)	0.74
Occupation				
Unemployed	Ref	_	_	_
Employed	1.1 (0.7–1.7)	0.65	0.9 (0.5–1.6)	0.80
Primary income earner				
Patient	Ref	_	_	_
Other	1.0 (0.7–1.5)	0.86	_	_
Wealthy quintile				
First (Poorest)	Ref	_	_	_
Second	1.7 (0.9–3.2)	0.078	1.6 (0.8–3.2)	0.16
Third	1.7 (0.9–3.1)	0.098	1.4 (0.7–2.8)	0.95
Fourth	2.2 (1.2–4.0)	0.016	1.9 (0.9–3.9)	0.090
Fifth (Least poor)	2.9 (1.5–5.5)	0.001	2.6 (1.3–5.5)	0.011
Food insecurity				
No	Ref	_	_	_
Yes	0.8 (0.6–1.2)	0.35	_	_
TB symptoms				
Fewer symptoms (1 or 2)	Ref	_	_	_
More symptoms (3 or more)	0.6 (0.4–0.9)	0.016	0.4 (0.3–0.7)	0.001
Time from symptoms onset to treatment initiation				
< 4 weeks	Ref	_	_	_
> 4 weeks	4.0 (3.1–7.9)	< 0.001	6.0 (3.6–9.9)	< 0.001
BMI (kg/m2)				
< = 18	Ref	_	_	_
18 – 25	0.9 (0.6–1.4)	0.7	_	_
25 – 30	1.8 (0.6–5.4)	0.26	_	_
> 30	1.8 (0.2–18.2)	0.60	_	_
Previous TB episode				
No	Ref	_	_	_
Yes	1.1 (0.6–1.9)	0.85	1.7 (0.8–3.6)	0.17

Table 5 (continued)

Variables	Number of pre-treatment healthcare providers[a]			
	Univariable logistic Regression		Multivariable logistic regression	
	cOR (95%CI)	*p-value*	aOR (95%CI)	*p-value*
HIV status				
Negative	Ref	_	_	_
Positive	0.6 (0.4–0.8)	0.005	0.6 (0.4–1.0)	0.062
Comorbidities				
No	Ref	_	_	_
Yes	1.0 (0.6–1.7)	0.97	_	_
Alcohol consumption				
No	Ref	_	_	_
Yes	0.8 (0.4–1.0)	0.07	0.7 (0.4–1.2)	0.24
Smoking				
No	Ref	_	_	_
Yes	0.5 (0.3–1.1)	0.080	0.7 (0.3–1.9)	0.56
Illicit drug use				
No	Ref	_	_	_
Yes	2.4 (1.3–4.4)	0.005	0.4 (0.2–0.9)	0.20
Formerly incarcerated				
No	Ref	_	_	_
Yes	1.9 (0.9–4.1)	0.09	0.6 (0.3–1.4)	0.25

[a] Number of pre-treatment healthcare providers were categorised as no pre-treatment visits ($n = 160$) vs 1 or more pre-treatment visits ($n = 256$)

with such TB services, half still remained undiagnosed, requiring further visits to healthcare providers. Visiting more healthcare providers was associated with delays in TB treatment initiation and increased direct OOP expenditures and total costs for people with TB and their households.

Our results showed that the mean time from symptom onset to first healthcare provider visit was 1.5 weeks (SD = 4.9). This finding aligns with previous studies conducted in urban health catchment areas in China (10 days) and Iran (13 days) [50, 51]. In contrast, people with TB in Ethiopia (30 days) and Nepal (32 days) experienced significantly longer delays to first healthcare provider visit [52, 53]. The time from TB symptom onset to TB treatment initiation (total delay) was two months on average, which was consistent with that observed in Malawi (59 days) [54]. However, it differed from other settings, being substantially shorter than the 150 days of delay observed by Saifodine et al. in Beira, Mozambique [23] and longer than the delays observed in Ethiopia (24 days) [55] and Tanzania (3 weeks) [56]. The shorter time from symptom onset to first healthcare provider visit vs time to TB treatment initiation suggests that overall delays are more strongly related to health system rather than healthcare seeking issues. During the study recruitment phase, the study team maintained close contact with the health facilities, ensuring that people with microbiologically confirmed TB were promptly initiated on treatment and referred to TB Sequel health facility. Therefore, it is possible that the time between TB diagnosis and TB treatment initiation was artificially reduced and actually underestimates the treatment delay in people with TB receiving standard of care in Maputo City and Province [26].

Our study found that more than three-quarters (322/416, 77,4%) of people with TB had their first visits in a primary health facility which was slightly higher when compared to findings in Beira (65.7%) and Ethiopia (67%) [23, 52]. The finding that nearly one quarter of people with TB had their first visit at healthcare providers which did not provide TB diagnosis and care services differs from the evidence in Ethiopia (30%), Tanzania (42%) and Uganda (78%) [15, 57, 58]. Despite this, even amongst those whose first visit was to a healthcare provider with TB services, still approximately half were not initiated on treatment at that visit. This suggests there may be challenges in conducting the standard TB diagnostic procedures during the initial presentation of people with TB to healthcare providers. This could be the result of healthcare professionals not recognizing symptoms consistent with TB [56], insufficient resources available at the time for testing [59] and a tendency to consider alternative diagnosis such as bacterial lower respiratory tract infections and chronic lung disease rather than pulmonary TB [59, 60]. The presence of three or more symptoms was associated with seeking care from fewer providers. This association may be attributed to people experiencing multiple symptoms, in addition to cough, feeling consistently unwell, leading them to seek care promptly [15, 56, 61] and being more easily identified as appropriate for TB testing by the healthcare provider.

Nearly 98% of people visiting two or more providers incurred some form of direct OOP expenditures. Those who had their first healthcare seeking visit at private clinics incurred costs that were fifteen times higher ($64 versus $4.2) than at health facilities where TB services were available free of charge [9]. Nonetheless, seeking care at private providers did not necessarily lead to improved TB testing and faster TB treatment initiation. A significant proportion (13/38, 38%) of people who initiated their care-seeking journey at private clinics, and 6/16 (34%) of those who began at a pharmacy, visited at least three healthcare providers before TB treatment initiation. Our results are similar to those in settings where TB services are mostly provided by the public healthcare providers [5, 62]. Total OOP expenditures represented a significant proportion of monthly household income, varying from 34.3% to 98.8%, depending on the number of healthcare providers and repeated visits involved in the healthcare seeking pathways.

In our study, total direct OOP expenditures were influenced by both the number of healthcare providers visited and multiple visits to the same providers. In particular, the main driver of direct medical OOP expenditures was pre-treatment medication, which imposed a considerable financial burden [22]. Income loss related to healthcare seeking was identified as a significant contributor to the overall pre-treatment costs [58]. To put this into perspective, a $35 income loss equated to 52% ($35/67) of the monthly earnings for an individual earning minimum wage. In many contexts, similar income loss has been demonstrated to increase the burden of pre-treatment costs and negatively affect the economic capacity of households [22]. Lastly, multiple variables were associated with visits to healthcare providers before diagnosis and TB treatment initiation and, consequently, longer pathways to care. Particularly, the least poor individuals were more likely to visit multiple providers, potentially due to their initial choice of private services, which were perceived to have a reputation for better quality care and shorter waiting times. Additionally, people with more symptoms, those living with HIV and using illicit drugs were less likely to visits to healthcare provider before diagnosis and TB treatment initiation. The reason behind this is unclear, however, we can speculate that previous and regular contact with health facilities due to these comorbidities contribute to this healthcare seeking behaviour.

Strengths and limitations

Our study is the first to look at pathways to care and assess the costs of care before the start of treatment in people with TB in the semi-urban sub-Saharan African setting of Mozambique City and Province. However, the study has several limitations. Recall bias is a concern when inquiring about healthcare seeking costs, potentially affecting the accuracy of the reported costs and pathways. To mitigate this, we linked cost-related questions with memorable events such as the onset of symptoms or visit to a healthcare provider. Additionally, there was a lack of pre-treatment data in a subset of study participants who had no pre-treatment visits to healthcare provider and, as per the wider TB Sequel protocol, they were assumed to have incurred no healthcare seeking costs. This approach may have resulted in an under-representation of certain cost profiles and pathways to care. Furthermore, we were only able to collect data to estimate the delay of people with TB and total delay. We did not collect data to estimate delays in diagnosis because we assumed that time to obtain the diagnosis was similar to time to TB treatment initiation as people diagnosed with TB were enrolled in the study and were immediately initiated on treatment. This is likely to be different to standard of care in which there may be delays between diagnosis and TB treatment initiation. Third, our cohort was restricted to adults with microbiologically confirmed pulmonary TB and excluded children and people with non-bacteriologically confirmed TB, people with extrapulmonary TB or tuberculous meningitis (TBM). This limits the generalizability of our results to the wider spectrum of TB seen routinely in TB services in Mozambique. In addition, the presence of comorbidities such as HIV, diabetes and hypertension among participants may have contributed to individual and family financial burdens, potentially affecting overall cost estimates. Lastly, the use of the stepwise method for variable selection is often associated with bias and overfitting, potentially affecting the stability and generalizability of the model. We detailed the process of building and adjusting the models so that the limitations of the methods can be assessed. Future studies should consider alternative approaches, such as Bayesian model averaging or least absolute shrinkage and selection operator (LASSO), to enhance the robustness of the analysis.

Conclusions

In conclusion, our study highlights the complex healthcare-seeking pathways and associated financial burdens faced by individuals with pulmonary TB in Maputo City Region, Mozambique. It reveals a concerning scenario where a substantial proportion of people with TB initially sought care from providers lacking designated TB services, leading to delayed diagnoses and increased costs. Although the time from symptom onset to TB treatment initiation was shorter compared to some low- and middle-income countries, a significant two-month average delay persisted, primarily attributed to health system-related delays. Indirect costs, such as income loss, were substantial and contributed significantly to the total costs. Enhancing the availability of TB services in health facilities is crucial to ensure that individuals have access to accurate diagnosis and timely TB treatment initiation through implementation of standard diagnostic procedures, particularly during initial presentations, to minimise delays in TB treatment initiation. Frontline healthcare professionals should receive adequate training to recognise TB symptoms early when individuals are present at health facilities, enabling timely testing, diagnosis, and treatment initiation. Policymakers should explore options to reduce the financial burden on people with TB, including support for those facing income loss, to achieve the WHO End TB Strategy of zero TB-affected families experiencing catastrophic costs. Public health campaigns and healthcare worker training are essential to raise awareness about TB symptoms and encourage prompt healthcare-seeking behaviour and diagnostic suspicion, especially at healthcare providers with TB services.

Developing streamlined referral systems is crucial to ensure that people with symptoms compatible with TB are promptly referred to facilities with diagnostic capabilities without unnecessary delays. Additional awareness training for healthcare providers, including pharmacists and private providers, should be considered to ensure prompt referral to appropriate public TB services. Awareness campaigns should also cover community education about TB symptoms, transmission, and the importance of early diagnosis and treatment initiation to enhance early detection and improve treatment outcomes.

Abbreviations

aOR	Adjusted Odds Ratio
CI	Confidence Interval
cOR	Crude Odds Ratio
CRF	Case Report Form
MDR-TB	Multi-Drug Resistant TB
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
M	Mean
MMHI	Mean Monthly Household Income
NTP	National Tuberculosis Programme
MZN	Mozambican New Metical
OOP	Out-of-Pocket
TB	Tuberculosis
RR-TB	Rifampicin Resistant TB
SD	Standard Deviation
VIF	Variance Inflation Factor
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-22333-y.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

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Authors' contributions

PN, OI, DE, CK and KL applied for the fund and designed the study. PN, CN, CM, and DB were responsible for the data collection and resolution of data discrepancies. PN, CN, CK, TW conceived the plan of analysis and MU and PN analysed the data. PN, SA, CN, MU, CM, CK and TW wrote the first draft of the manuscript and all authors reviewed, edited, and approved the final version of the manuscript.

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Data availability
The datasets generated and analysed in the present study are currently not available to the public due to ongoing further analyses. However, they are anticipated to be released in the near future once the primary analysis has been concluded and might be obtained from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was carried out following the TB Sequel study protocol,(26) the Declaration of Helsinki (last updated in October 2013), and the WHO Handbook for Good Clinical Research Practice (July 2002). The TB Sequel protocol received approval from the Mozambican National Bioethics Committee (IRB00002656—Comité Nacional de Bioética para a Saúde/CNBS, Reference number: 291/CNBS/2017) and in all other countries implementing the study (South Africa, Tanzania, and The Gambia). Before participating in the study, all participants were provided with clear and comprehensive information about the procedures and gave their written informed consent. A unique participant identification number (Participant ID) was assigned to each participant to identify their data as study documents did not contain any identifying information to ensure participant confidentiality.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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