ORIGINAL RESEARCH

The Association Between Household Financial Burden and Patient Mobility and Their Impact on Loss to Follow-Up Among Multidrug-Resistant Tuberculosis Patients in Guizhou, China

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Purpose: We aimed to assess the household financial burden due to multidrug-resistant tuberculosis (MDR-TB) treatment and its predictors, examine its association with patient mobility, and test their impact on patient loss to follow-up (LTFU).

Methods: A cross-sectional study combining follow-up data collection was conducted at the largest designated MDR-TB hospital in Guizhou. Data were collected from medical records and questionnaires. Household financial burden was measured by the incidence of 2 indicators: catastrophic total costs (CTC) and catastrophic health expenditure (CHE). Mobility was classified as mover or non-mover after the patient's address was verified twice. A multivariate logistic regression model was used to identify associations between variables. Model I and Model II were separated by CHE and CTC.

Results: Out of 180 households, the incidence of CHE and CTC was 51.7% and 80.6%, respectively. Families with low income and patients who were primary income earners were significantly associated with catastrophic costs. 42.8% of patients were movers. Patients from households with CHE ($OR_{adj}=2.2, 95\%$ CI: 1.1–4.1) or with CTC ($OR_{adj}=2.6, 95\%$ CI: 1.1–6.3) were more likely to move. Finding a job against financial difficulty (58.4%) was the top reason for movers. 20.0% of patients experienced LTFU. Patients from households with catastrophic payments (CHE: $OR_{adj}=4.1, 95\%$ CI 1.6–10.5 in Model I; CTC: $OR_{adj}=4.8, 95\%$ CI 1.0–22.9 in Model II), patients who were movers ($OR_{adj}=6.1, 95\%$ CI 2.5–14.8 in Model I; $OR_{adj}=7.4, 95\%$ CI 3.0–18.7 in Model II) and primary income earners ($OR_{adj}=2.5, 95\%$ CI: 1.0–5.9 in Model I; $OR_{adj}=2.7, 95\%$ CI 1.1–6.6 in Model II) had an increased risk of LTFU.

Conclusion: There is a significant association between household financial burden due to MDR-TB treatment and patient mobility in Guizhou. They impact patients' treatment adherence and cause LTFU. Being a primary breadwinner increases the risk for catastrophic household payments and LTFU.

Keywords: household catastrophic costs, migration, loss to follow-up, Guizhou, MDR-TB

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is an infectious disease that is defined as resistance to at least isoniazid and rifampin.¹ Treating MDR-TB requires long-term, costly and multidrug regimens.² It has been estimated that the latest treatment success rate is only 60% among MDR-TB and RR-TB (rifampicin-resistant TB) patients worldwide,¹ and the rate of loss to follow-up (LTFU) is 16%.³ The Philippines and China have the highest LTFU rates of 33% and 29%, respectively.³ LTFU impedes the successful treatment and control of MDR-TB globally. Various factors are correlated

with LTFU, including adverse drug events,⁴ limitations of economic status⁵ and social health insurance.⁶ MDR-TB disproportionately affects poor people.⁷ Treatment due to MDR-TB imposes a financial burden on patients and their families.⁷

The magnitude of the financial burden is documented by the total cost and distribution of cost components.⁷ The total costs of treatment include 3 parts: direct medical costs (such as drug costs), direct non-medical costs (such as transportation expenses), and indirect costs (such as income loss). These three types of costs are used to calculate the incidence of two indicators: catastrophic health expenditure (CHE) and catastrophic total costs (CTC).⁷ Both are used to measure patients' household financial burden under the financial and social protection of local health policies. CHE is incurred mainly by direct medical costs after reimbursement. CTC is caused by the total costs of treatment. Families with MDR-TB patients suffering catastrophic payments are often unable to support their completion of the full course of treatment.⁷ Thus, patients of working age may interrupt their treatment and move out of the home to work.

The mobility of MDR-TB patients contributes to the spread of this disease and treatment failure. Previous studies have reported that infection acquired before migration contributes to higher TB morbidity in migrant and host countries.^{8–10} The cross-border travel of MDR-TB patients challenges disease control in border countries.^{11,12} Migrants infected with TB may have a high risk of LTFU and disease progression.^{10,13–15} However, few studies have examined the association between household financial burden due to MDR-TB treatment and patients' mobility status and their relationship with patients' LTFU.

China is one of the countries with a high burden of MDR-TB.¹ The median direct medical cost per person treated for MDR-TB in 2019 globally was US\$ 5659, and the cost is positively correlated with GDP per capita.³ In China, the estimated drug cost per MDR-TB patient ranges from \$2648 to \$6090 in the first year of treatment based on different regimens stated in the national guidelines.^{16,17} Costs for MDR-TB treatment are co-paid by medical insurance and out-of-pocket (OOP) expenses. Patients from poor families can receive additional financial support from the targeted poverty alleviation program (TPAP),¹⁸ which increases the co-payment ratio of insurance and provides conditional cash compensation. However, the beneficial level of insurance and TPAP coverage depends on the local economic status.

Guizhou is a low-income province in China with the second largest rural population and high MDR-TB epidemic.^{19,20} The average per capita annual income was only US \$5263 for urban residents and US \$1636 for rural residents during the last 5 years (2014–2020) in this province.²⁰ Limited by the low economic level in Guizhou, the maximum liability of reimbursement from insurance is insufficient, and TPAP cannot cover all families affected by MDR-TB.²¹ Thus, we hypothesized that household financial burden due to MDR-TB treatment would be common in Guizhou patients, and this may lead some patients who were still under treatment to migrate for work; consequently, they may drop out of treatment. To address this issue, we conducted this study to evaluate the level of household financial burden due to MDR-TB treatment in Guizhou, explore its predictors, examine its association with patient mobility status, and test their impact on LTFU.

Methods

Study Design, Setting and Participants

A cross-sectional study combining methods of follow-up data collection was conducted from January 2018 to December 2019. Participants were recruited from Guiyang Public Health Clinical Center (GPHCC), the largest hospital designated for MDR-TB diagnosis and treatment in Guizhou. Each year, three-quarters of MDR-TB patients in the whole province are diagnosed and treated at GPHCC. MDR-TB treatment is implemented in accordance with the chemotherapy regimen recommended by the national guidelines.¹⁷ Patients are required to visit the outpatient department every month for physical examinations and to receive their drugs. In this study, the eligible participants were patients who were diagnosed with MDR-TB from 2016 to 2017 at GPHCC, received treatment, were reachable and had treatment outcomes during the study period. The excluded patients were those who refused to participate in the study and could not be traced during the study. A total of 180 eligible patients who agreed to participate in the study were included. The study sample met the sample size estimation, which was calculated as 187 based on a pooled proportion of LTFU (14.2%)²² with 95% confidence limits. After providing written informed consent, the patients were interviewed face-to-face either in the

hospital or at their home by a trained research team under the supervision of the principal investigator. Follow-up data of treatment outcomes were obtained from the medical records.

Variable Definitions and Measurements

Household Annual Financial Status

Household annual financial status was measured by household annual income and capacity to pay.

Household annual income refers to any kind of income earned by all members of a household, such as the sale of goods or property, fixed salary, or a profit from investments.⁷ Pre-disease annual income means the household annual income before diagnosis with MDR-TB.

Household capacity to pay is defined as a household's nonfood expenditure, which is equal to total household expenditure minus food expenditure.²³ Total household expenditure includes daily necessities, food, accommodation, transportation and communication, OOP health expenditure, education and other spending.

Household Catastrophic Costs

Household catastrophic costs were measured by two indicators: catastrophic total costs (CTC) and catastrophic health expenditure (CHE). CTC is defined as total costs for MDR-TB treatment reaching or exceeding 20% of the household's annual pre-disease income.⁷ CHE is defined as a household's direct medical OOP expenses reaching or exceeding 40% of its capacity to pay.²³ The variable of catastrophic costs was constructed as a dummy variable with yes indicating a household with CTC or CHE and no indicating a household without CTC or CHE. The incidence of catastrophic costs is defined as the total number of households with CTC or CHE divided by the total number of households in the study.²³

Mobility Status

Participants were classified as movers if they had ever left the address registered at the time of MDR-TB diagnosis in GPHCC and non-movers if they were still living at the same address.

Lost to Follow-Up (LTFU)

A patient was considered lost to follow-up if their treatment was interrupted for 2 or more consecutive months.²⁴

Data Collection

Variables obtained from the structured questionnaire and medical records included 1) demographic and socioeconomic status (gender, age, marital status, education level, home address, household composition, household income and expenditure, insurance scheme and TPAP situation); 2) treatment outcome; and 3) total costs for the entire MDR-TB episode, which included 3 parts: direct medical costs, direct non-medical costs, and indirect costs.

The collection of direct medical costs came from two sources: 1) medical records reflecting inpatient costs and outpatient costs. These costs are co-paid by partial OOP expenses and reimbursement from insurance. Inpatient costs include costs for medicines, examinations, materials, laboratory tests, bed fees, and nursing fees. The outpatient costs cover registration, medicines and examination. 2) Self-reported costs for injections and liver-protecting drugs bought from drug stores. These costs are OOP payments, net of any reimbursements.

Direct non-medical costs and indirect costs were collected from self-reports. Direct non-medical costs are OOP expenses related to accommodation and transportation costs during hospital visits by the patients and/or their caregivers. Indirect costs refer to income lost by the patients and/or their caregivers due to being absent from work because of MDR-TB treatment. The amount of income lost was calculated by multiplying the number of workdays lost by the total daily wages of the patients and/or their caregivers. The costs were ascertained from the diagnosis of MDR-TB to the end of treatment or investigation.

Patients' treatment outcomes were collected from the medical records. Data on demographic and socioeconomic status were obtained from self-reports. The patient's home address was verified twice, once at the diagnosis of MDR-TB from the medical records and again during the home visit, by telephone, or face-to-face interview when patients visited the hospital again. Movers were also asked their reasons for moving.

Statistical Analysis

Data were entered into EpiData (version: 3.1, Odense, Denmark) and analyzed using R (version 3.4.2, Vienna, Austria). Descriptive analysis was presented to understand the distribution of total costs and household financial status. Means, medians and interquartile ranges (IQR) were used for continuous variables; otherwise, frequencies and percentages were used. Variables associated with CTC, CHE, mobility or LTFU were explored initially by univariate analysis, and variables with a p value < 0.2 were included in the separate multivariate logistic regression modeling process. The likelihood ratio test was assessed at each step and used to determine the final model where only variables with a p value < 0.05 remained. Model I and Model II were separated by CHE and CTC; Model I presents the association of CHE, mobility and LTFU, while Model II shows the association of CTC, mobility and LTFU.

Results

Distribution of Total Costs Due to MDR-TB Treatment and Household Financial Status

Figure 1 shows the distribution of total costs due to MDR-TB treatment among 180 households. The mean and median (IQR) of total cost are 70,636 and 60,629 yuan (44,528–83,784), respectively, which consist of 75.6% direct medical costs, 7.0% direct non-medical costs and 17.4% indirect costs. Direct medical costs are co-paid by OOP expenses (42.6%) and reimbursement (33.0%). A total of 63.4% of the pre-disease annual income (74,728 yuan) and 57.8% of the capacity to pay (52,047 yuan) was reportedly spent when the participants fell ill. Figure 2 shows that the incidence of CTC and CHE among 180 households is 80.6% and 51.7%, respectively. Both incidences decline as income increases. Respondents in the lowest tertile (poorest) experience more catastrophic costs than others.

Characteristics of Households and Their Association with Catastrophic Costs

Table 1 shows the characteristics of households and their association with two measures of catastrophic costs by univariate and multivariate analysis. Of the 180 households, 80.0% are from rural areas, and 66.1% have at least 2 members earning income. For 51.1% of families, the patients themselves were the primary income earners before being diagnosed with MDR-TB. A total of 32.2% of families have at least 2 students and 19.4% are covered by the TPAP. For patients living in these households, the majority are young to middle-aged, married males with a low educational level.



Figure 1 Distribution of total costs due to MDR-TB treatment among 180 households. Abbreviations: MDR-TB, Multidrug-resistant tuberculosis; IQR, interquartile range; OOP, out-of-pocket.



Figure 2 Incidence of catastrophic costs based on income tertiles among 180 households affected by MDR-TB. Abbreviations: MDR-TB, Multidrug-resistant tuberculosis; CTC, catastrophic total cost; CHE, catastrophic health expenditure; T, tertile.

After multivariate analysis, both indicators are found to increase the OR if the patient is from the poorest family (CTC: $OR_{adj}=34.0, 95\%$ CI 3.8–307.5, CHE: $OR_{adj}=9.7, 95\%$ CI 3.6–26.3) and if the patient is the primary income earner (CTC: $OR_{adj}=2.4, 95\%$ CI 1.1–5.5; CHE: $OR_{adj}=2.0, 95\%$ CI 1.1–3.7). In addition, families with young to middle-aged TB patients are more likely to experience CTC ($OR_{adj}=9.9, 95\%$ CI 2.6–38.0).

Characteristics	Total	стс				CHE			
	n (%) ^a	Rate n (%) ^b	p-value ^c	OR _{adj} (95% CI) ^d	p-value (LR Test)	Rate n (%) ^b	p-value ^c	OR _{adj} (95% CI) ^d	p-value (LR Test)
Overall	180 (100)	145 (80.6)				93 (51.7)			
Household information									
Area of residence									
Urban	36 (20.0)	27 (75.0)	0.480	-	-	20 (55.6)	0.737	-	-
Rural	144 (80.0)	118 (81.9)				73 (50.7)			
Household annual income after MDR-TB									
(RMB yuan)									
T3 (richest)	60 (33.3)	34 (56.7)	0.001	Ref	0.001	15 (25.0)	0.001	Ref	0.001
T2	60 (33.3)	52 (86.7)		4.3 (1.6, 11.8)		33 (55.0)		3.7 (1.6, 8.2)	
TI (poorest)	60 (33.3)	59 (98.3)		34.0 (3.8,		45 (75.0)		9.7 (3.6, 26.3)	
				307.5)					
Number of employed household members									
2 or more	119 (66.1)	91 (76.5)	0.083	Ref	0.101	56 (47.1)	0.116	Ref	0.302
1	61 (33.9)	54 (88.5)		2.4 (0.8, 7.1)		37 (60.7)		1.5 (0.7, 3.0)	
Primary income earner									
Others	88 (48.9)	64 (72.7)	0.016	Ref	0.027	37 (42.0)	0.017	Ref	0.030
Patient	92 (51.1)	81 (88.0)		2.4 (1.1, 5.5)		56 (60.9)		2.0 (1.1, 3.7)	
Number of students									
0 or I	122 (67.8)	100 (82.0)	0.622	-	-	66 (54.1)	0.431		
2 or more	58 (32.2)	45 (77.6)				27 (46.6)			

Table I Characteristics of Households and Their Association with Catastrophic Costs by Univariate and Multivariate Analysis

(Continued)

Table I (Continued).

Characteristics	Total	стс				СНЕ			
	n (%)*	Rate n (%) ^b	p-value ^c	OR _{adj} (95% CI) ^d	p-value (LR Test)	Rate n (%) ^b	p-value ^c	OR _{adj} (95% CI) ^d	p-value (LR Test)
Family with TPAP									
Yes	35 (19.4)	32 (91.4)	0.116	Ref	0.938	22 (62.9)	0.198	Ref	0.457
No	145 (80.6)	113 (77.9)		1.1 (0.2, 5.4)		71 (49.0)		1.5 (0.5, 3.9)	
MDR-TB patient in household									
Gender									
Female	65 (36.I)	53 (81.5)	0.957	-	-	30 (46.2)	0.338	-	-
Male	115 (63.9)	92 (80.0)				63 (54.8)			
Age (years)									
≥ 60	17 (9.4)	6 (35.3)	0.001	Ref	0.002	8 (47.1)	0.637	-	-
≤ 25	43 (23.9)	33 (76.7)		7.2 (1.6, 32.2)		20 (46.5)			
25–59	120 (66.7)	106 (88.3)		9.9 (2.6, 38.0)		65 (54.2)			
Marital status									
Single	70 (38.9)	56 (80.0)	1.000	-	-	37 (52.9)	0.919	-	-
Married	110 (61.1)	89 (80.9)				56 (50.9)			
Education level									
Primary school or less	55 (30.6)	44 (80.0)	0.647	-	-	27 (49.1)	0.971	-	-
Middle school	56 (31.1)	48 (85.7)				30 (53.6)			
High school	50 (27.8)	38 (76.0)				26 (52.0)			
University	19 (10.6)	15 (78.9)				10 (52.6)			

Notes: ^aColumn percent; ^bPercent of total subjects in each group; ^cUnivariate analysis; ^dMultivariate logistic regression analysis.

Abbreviations: CTC, catastrophic total cost; CHE, catastrophic health expenditure; OR_{adj.} adjusted odds ratio; CI, confidence interval; LR test, likelihood ratio test; ref, reference group; T, tertile; TPAP, targeted poverty alleviation program; MDR-TB, Multidrug-resistant tuberculosis.

Reasons for Patient Mobility and Its Association with Household Catastrophic Costs

Among 180 participants, 77 patients (42.8%) had changed their address after being diagnosed with MDR-TB. The four main reasons answered by movers are shown in Figure 3. Finding a job against financial difficulty (58.4%) was the top reason. Figure 4 summarizes the separate estimates for the association between two measures of catastrophic costs and mobility status from univariate analysis and multivariate logistic regression models, adjusting for covariates. In Model I,



Figure 3 Ranking of main reasons for mobility among 77 MDR-TB patients. Abbreviation: MDR-TB, Multidrug-resistant tuberculosis.

Characteristics	Total N (%)	Mobility	Mobility status		OR _{adj}		P value
Characteristics		Non-mover	Mover	P value	(95%CI)°		(LR-test)
Overall	180 (100%)	103 (57.2)	77 (42.8)				
Model I							
Household with CHE							
No	87 (48.3)	57 (55.3)	30 (39.0)	0.043	ref		0.017
Yes	93 (51.7)	46 (44.7)	47 (61.0)		2.2 (1.1, 4.1)		
Covariates							
Number of students in							
household							
0 or 1	122 (67.8)	76 (73.8)	46 (59.7)	0.046	ref		0.029
2 or more	58 (32.2)	27 (26.2)	31 (40.3)		2.1 (1.1, 3.9)		
Model II							
Household with CTC							
No	35 (19.4)	26 (25.2)	9 (11.7)	0.037	ref		0.024
Yes	145 (80.6)	77 (74.8)	68 (88.3)		2.6 (1.1, 6.3)		
						0 1 2 3 4 5 6 7 ORe (95% Cle)	

Figure 4 Association between household with catastrophic costs and mobility status adjusting for covariates^a.

Notes: ^aAdjusted for area of residence, number of students in household, number of employed household members, primary income earner in household, family with TPAP, gender, age, marital status, education level; ^bUnivariate analysis; ^cMultivariate logistic regression analysis.

Abbreviations: CTC, catastrophic total cost; CHE, catastrophic health expenditure; OR_{adj}, adjusted odds ratio; CI, confidence interval; LR test likelihood ratio test; ref, reference group.

patients from families who experience CHE ($OR_{adj}=2.2, 95\%$ CI: 1.1–4.1) or families containing two or more students ($OR_{adj}=2.1, 95\%$ CI: 1.1–3.9) are more likely to move. In Model II, only one factor, namely, patients from families with CTC ($OR_{adj}=2.6, 95\%$ CI: 1.1–6.3), has statistical significance for moving. (full results for association between all relevant variables and mobility status are shown in Supplementary Table 1).

The Impact of Households with Catastrophic Costs and Patient Mobility on LTFU

Table 2 provides the incidence of LTFU and shows the association between households with two measures of catastrophic costs, patient mobility and LTFU from univariate analysis and separate multivariate logistic regression models after adjusting for other covariates. Twenty percent of patients experience LTFU. Patients from households with

Characteristics	Total	LT	FU	p-value ^b	OR _{adj} (95% CI) ^c	p-value (LR Test)
	N (%)	Yes (n, %)	No (n, %)			
Overall	180 (100)	36 (20.0)	144 (80.0)			
Model I						
Household with CHE						
No	87 (48.3)	7 (19.4)	80 (55.6)	0.001	Ref	0.002
Yes	93 (51.7)	29 (80.6)	64 (44.4)		4.1 (1.6, 10.5)	
Mobility status						
Non-mover	103 (57.2)	8 (22.2)	95 (66.0)	0.001	Ref	0.001
Mover	77 (42.8)	28 (77.8)	49 (34.0)		6.1 (2.5, 14.8)	
Covariates						
Primary income earner						
Others	88 (48.9)	10 (27.8)	78 (54.2)	0.008	Ref	0.038
Patient	92 (51.1)	26 (72.2)	66 (45.8)		2.5 (1.0, 5.9)	

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Characteristics	Total	LTI	FU	p-value ^b		p-value
	N (%)	Yes (n, %) No (n, %)			(95% CI) ^c	(LR Test)
Model II						
Household with CTC						
No	35 (19.4)	2 (5.6)	33 (22.9)	0.034	Ref	0.022
Yes	145 (80.6)	34 (94.4)	111 (77.1)		4.8 (1.0, 22.9)	
Mobility status						
Non-mover	103 (57.2)	8 (22.2)	95 (66.0)	0.001	Ref	0.001
Mover	77 (42.8)	28 (77.8)	49 (34.0)		7.4 (3.0, 18.7)	
Covariates						
Primary income earner						
Others	88 (48.9)	10 (27.8)	78 (54.2)	0.008	Ref	0.032
Patient	92 (51.1)	26 (72.2)	66 (45.8)		2.7 (1.1, 6.6)	

Table 2 (Continued).

Notes: ^aAdjusted for area of residence, number of students in household, number of employed household members, primary income earner in household, family with TPAP, gender, age, marital status, education level; ^bUnivariate analysis; ^cMultivariate logistic regression analysis. **Abbreviations:** CTC, catastrophic total cost; CHE, catastrophic health expenditure; LTFU, loss to follow-up; OR_{adj,} adjusted odds ratio; CI, confidence interval; LR, test likelihood ratio test; ref, reference group; TPAP, targeted poverty alleviation program.

catastrophic costs are at increased risk for LTFU (CHE: $OR_{adj}=4.1$, 95% CI 1.6–10.5 in Model I; CTC: $OR_{adj}=4.8$, 95% CI 1.0–22.9 in Model II). In addition, being a mover ($OR_{adj}=6.1$, 95% CI 2.5–14.8 in Model I; $OR_{adj}=7.4$, 95% CI 3.0–18.7 in Model II) and being a primary income earner in the family ($OR_{adj}=2.5$, 95% CI: 1.0–5.9 in Model I; $OR_{adj}=2.7$, 95% CI 1.1–6.6 in Model II) are also significantly associated with LTFU (full results for association between all relevant variables and LTFU are shown in <u>Supplementary Table 2</u>).

Discussion

Our main findings are that households with MDR-TB patients in Guizhou bear a high financial burden mainly due to direct medical costs and income loss. Greater catastrophic payments occur in families with lower incomes. Nearly half of the patients move away from their original address after their diagnosis. Household financial burden is a significant predictor and main reason for patient mobility. A total of 20.0% of patients experience LTFU, which is associated with the household financial burden caused by MDR-TB treatment and patient mobility. The patient being the primary breadwinner must be considered as they increased risk for household catastrophic payments and LTFU.

This study demonstrates that more than half of the affected households with MDR-TB patients experience CHE and four-fifths face CTC in Guizhou. A high financial burden is borne mainly by direct medical OOP costs and income loss, which agrees with the findings of other studies.^{25,26} Lower annual income is a risk factor for households that faced catastrophic costs, regardless of the approach used. These results concur with previous studies.^{27–30} We also find that the risk of catastrophic costs is higher for families with TB patients as a primary income earner who were young to middle-aged, which is consistent with studies from other countries.^{30,31} A previous study conducted in four high-income provinces of China showed that 35% of the families with MDR-TB patients experienced CHE and 78% faced CTC.²⁷ In the previous study, the incidence of CHE was low because 90% of the direct medical fees for MDR-TB treatment were reimbursed from a piloted program. While the piloted program did not address direct non-medical costs and income loss, the incidence of CTC in the study was also high. These results indicate that for MDR-TB patients, both the financial and social protection of health policies seem particularly critical. Evidence has been shown from other studies that financial support covering direct medical costs,³² direct non-medical costs³³ and income loss^{34,35} can improve treatment adherence among TB patients. Thus, we suggest that financial and social protection in Guizhou should be expanded to improve the treatment adherence of MDR-TB patients.

As mentioned in previous studies, mobility is common among TB patients,^{36,37} which agrees with our results. Finding a job against financial difficulty was found to be the top reason for movers. Our study used two approaches of

catastrophic costs to confirm that household financial burden is a significant predictor of patient mobility. These results are supported by other studies.^{8,10,11} Another finding from our study is that patients living in families that have more dependent students are more likely to move. Patients from families without TPAP also tend to move more often compared to those with TPAP. These results may be attributed to the fact that financial pressure is a risk factor for moving, while financial support is a protective factor.¹²

The incidence of LTFU in our study is similar to that previously found in various countries: 21.1% in India³⁸ and 20.9% in South Africa.³⁹ In terms of determinants of LTFU, two separate multivariate logistic regression models involving CHE and CTC gave consistent results. First, our findings revealed that MDR-TB patients from households that experience catastrophic costs are significantly more likely to be LTFU. This finding is consistent with studies from China,⁴⁰ Pakistan⁴¹ and Argentina.⁴² Another significant factor for LTFU in our study is mobility status, where movers are more likely than non-movers to experience LTFU, which is in line with the findings of other studies.^{13,15,43} Additionally, having a patient as a family's primary income earner is also an associated factor with LTFU, which is supported by other studies.^{44,45} In those studies, men and those who are unemployed were found to be more likely to be LTFU, which can be explained by the fact that men are commonly the primary breadwinners in their families. When faced with economic pressure, they have to balance their own medical needs with their family obligations. A qualitative study from India revealed that one of the main reasons for MDR-TB patients not adhering to treatment is earning money to feed their family.⁴⁶ These results suggest that support for patients of working age should be enhanced to increase their retention.

Our study has some limitations. First, following the WHO protocol of cost surveys, the participants in our study registered for treatment under a national tuberculosis program network. Thus, they may have a better ability to cope with financial hardship. However, the study still demonstrates that households with MDR-TB patients face a high financial burden. Second, the cross-sectional study design may not provide a strong ability to indicate causation. However, it is clear that the time sequence from exposure to outcome in our study is based on a comprehensive literature review. Thus, we collected data combining cross-sectional and follow-up methods. We also learned the reasons for moving. Our study may enlighten further prospective studies. Third, recall bias is unavoidable for self-reported data. Fourth, we did not qualitatively address the reasons for LTFU due to the lack of information in this regard from the patients. We clarified the impact of household financial burden due to MDR-TB treatment and patient mobility on LTFU from a quantitative view, which is beneficial for the relevant departments to understand the magnitude of the problem and adopt targeted interventions. Finally, our study was conducted in a low-income province of China, which may limit the generalizability of the results to other parts of the country. However, our results could be useful for other countries or regions where the situation is similar to that of Guizhou.

Conclusion

This study quantified the level of financial burden, mobility and LTFU among MDR-TB patients in Guizhou. The household financial burden due to MDR-TB treatment is caused mainly by high direct medical costs, income loss and low household income. Poor financial status is a significant predictor and main reason for patient mobility. Patients are more likely to be LTFU if they experience financial hardship and are mobile. If the primary breadwinner in the family is diagnosed with MDR-TB, then either the family is at increased risk for catastrophic payments or the patient is more likely to drop out of treatment. Our study underscores the urgent need for the sufficient financial and social protection of policies in Guizhou to improve the adherence of these vulnerable groups and thus improve their treatment outcome.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article and its <u>Supplementary Information</u> <u>Files</u>.

Ethics Approval and Consent to Participate

This study complies with the Declaration of Helsinki. This study was approved by the Ethics Committee of Guizhou Medical University. The signed informed consent was obtained from all participants before investigation. The names and

identification numbers of all patients were encrypted before use to ensure anonymity. All methods were carried out in accordance with relevant guidelines and regulations.

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Disclosure

The authors report no conflicts of interest in this work.

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