DISPARITIES IN "CATASTROPHIC" OUT-OF-POCKET COST INCURRED FROM MULTI-DRUG RESISTANT TUBERCULOSIS TREATMENT AMONG MIGRANT AND RESIDENT PATIENTS IN GUANGZHOU, GUANGDONG PROVINCE, PR CHINA

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Abstract. Out-of-pocket (OOP) costs of multidrug-resistant tuberculosis (MDR-TB) treatment before and after reimbursement of resident and migrant patients (n = 162) were estimated using hierarchical multiple logistic regression models. Total OOP cost of migrant and resident patients was USD 15,138 (interquartile range (IQR) = USD 9,646-20,199) and USD 3,871 (IQR = 2,584-7,637) respectively, with 46 and 90% suffering from ruinous cost respectively (p-value<0.01). Low annual household income (adjusted odds ratio (adjusted OR) = 17.30, 95% confidence interval (CI): 4.93-60.78) and loss of employment (adjusted OR = 4.14, 95% CI: 1.46-11.76) increased risk of incurring "catastrophic" MDR-TB treatment cost. As expected reimbursement program contributed to reduction in OOP cost of a larger proportion of resident compared to migrant patients. These findings indicate increasing reimbursement of MDR-TB treatment to both low-income migrant and resident patients will mitigate "catastrophic cost", and more reimbursement should be given to migrant patients.

Keywords: China, migrant, multidrug-resistant tuberculosis, out-of-pocket cost, resident, "catastrophic" cost

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INTRODUCTION

Multi-drug resistant tuberculosis (MDR-TB) is a global crisis, with an estimated 7.0 million accounting for 97% of notified new cases in low- and middle-income countries in 2018 (WHO, 2019a). China is one of the three countries with the highest MDR-TB burden: in 2018, there were an estimated 66,000 new MDR-TB or rifampicin-resistant TB (MDR/RR-TB) cases in China (WHO, 2019a), but only 14,636 (22%) cases were notified, among which 8,965 (61%) were enrolled in a treatment program (WHO, 2019a).

Financial burden creates a significant barrier to adherence and treatment success (Tanimura *et al*, 2014). In developing countries MDR-TB treatment cost ranges USD 1,838-6,680, with 54~85% of households suffering from what the World Health Organization (WHO) calls "catastrophic" cost (explained below) (Laokri *et al*, 2014; Wingfield *et al*, 2014; Ruan *et al*, 2016; Fuady *et al*, 2018). Financial limitation prevents 3-45% of MDR-TB patients from receiving a complete course of TB treatment (Long *et al*, 2011; Xu *et al*, 2017). Thus, reducing the financial burden of MDR-TB patients is not only a conducive way to improve the treatment compliance, but also an effective tool to promote disease control (Suarez *et al*, 2002).

Migrants are the most vulnerable population for risk of MDR-TB infection and transmission (Liu *et al*, 2012). In addition, infected migrant patients are less likely to be covered by social health protection scheme and face higher economic barriers in accessing health-care services than resident patients (WHO WPRO, 2016; Thetkathuek *et al*, 2017; Shete *et al*, 2018). At a TB-designated hospital in Beijing, PR China, 67.2% of MDR-TB were migrants from other cities (An *et al*, 2016). More adverse events, complications and additional non-medical costs stemming from transport, accommodation, food and lower reimbursement rate from a basic health insurance (BHI) can result in higher expenses for migrant MDR-TB patients (An *et al*, 2016). In order to safeguard health of MDR-TB patients and equity of access to health care services, there is urgent need to understand factors impacting financial burden and "catastrophic cost" of migrant patients. However, only a few studies have been able to shed light on the financial burden of MDR-TB patients and no study focused on migrant patients (Suarez *et al*, 2002; Ruan *et al*, 2016; Hutchison *et al*, 2017; Fuady *et al*, 2018; Nam *et al*, 2018). Additionally, there is a dearth of research on disparities in out-of-pocket (OOP) and "catastrophic" costs from MDR-TB treatment between migrant and resident patients. Whether BHI and other reimbursement measures can reduce financial burden and "catastrophic cost" of migrant and resident MDR-TB patients are unknown.

Here, medical records of MDR-TB patients together with a cross-sectional survey were employed to estimate

OOP costs in treatment of migrant and resident MDR-TB patients and to understand the extent to which reimbursement measures including BHI contributed to reducing OOP and "catastrophic" costs of MDR-TB patients.

MATERIALS AND METHODS

Study site

A cross-sectional survey was conducted in Guangzhou, capital city of Guangdong Province, South China, from 15 January to 10 May 2018. The per capita GDP of Guangdong Province is USD 12,225 in 2017 (Guangdong Province, 2017). Guangzhou Chest Hospital is the only designated hospital for MDR-TB treatment in the city, and the MDR-TB care of Guangdong Province is centralized in this hospital.

Participants enrollment

Inclusion criteria of participants were (i) diagnosed with MDR-TB (resistant to at least rifampicin and isoniazid) and (ii) treated in outpatient department ≥1 month. Exclusion criteria were (i) diagnosed with extra-pulmonary TB, (ii) >1 MDR-TB patient in the family, (iii) unavailable medical record, and (iv) unable to provide annual household income. Migrant participant is defined one who does not have a permanent household registration (known as "Hukou" in mainland China) in Guangzhou; otherwise participant is defined as resident.

According to previous research (Ruan *et al*, 2016), estimated prevalence of MDR-TB patients incurring "catastrophic cost" is 85.5%. Sample size at 95% confidence interval with tolerance error (δ) of 0.1, and taking into account 5% of non-response among MDR-TB patients, a minimum sample size of 59 resident and migrant patients respectively was calculated using a Power Analysis and Sample Size (PASS) software version 11.0 (NCSS, LLC, Kaysville, UT).

The research protocol was approved by the School of Public Health Institutional Review Board, Sun Yat-Sen University (approval no. 2018-004). Prior written informed consent was obtained from all participants.

Data collection

Data were obtained from the hospital information system and a questionnaire.

Hospital information system

Medical records obtained from Guangzhou Chest Hospital information database were date of MDR-TB diagnosis, list of all prescribed services and drugs related to MDR-TB diagnosis and treatment, prescription dates, costs of services and drugs, reimbursement from BHI and Local Subsidy Program, and OOP medical payments. Medical records prior to MDR-TB diagnosis date were excluded.

Questionnaire content

Participants were interviewed face-to-face in a private room by trained investigators. The questionnaire, designed according to WHO (2017) guidelines, is to obtain (i) demographic characteristics of the participants

(age, gender, marital status, education level, occupation, household registration category (resident or migrant), household income for the previous year, and type of BHI), (ii) OOP payments paid by both patients and caregivers, and (iii) average time spent on each visit.

OOP costs include direct medical costs (minus reimbursement), direct non-medical costs and indirect costs. Direct non-medical costs are payments related to the use of health services, such as payment for transportation, accommodation, food, and nutritional supplements. The former three items are calculated by multiplying typical cost of these items by the number of visits to health care facilities. Costs for nutritional supplements include total payments covering the complete treatment period and average monthly costs. Indirect costs are income loss of patients and their caregivers due to time for travel and medical service, calculated based on number of working hours lost and average hourly wage in Guangdong Province for 2018. OOP costs for the complete treatment phase and direct and indirect costs incurred during outpatient treatment were extrapolated over a period of 24 months (WHO, 2014; WHO, 2019b). If the patient has been treated >24 months, the patient is assumed to be in the last month of treatment and extrapolation is not applied.

"Catastrophic" total cost calculation

WHO defines "catastrophic" total cost as total cost (sum of direct medical, direct non-medical and indirect costs) that exceeds a given threshold (*eg* 20%) of a household annual income (WHO 2015; WHO, 2017). As indicated above, the period of expenditure is 24 months and thus double of household annual income is used as the denominator (Ruan *et al*, 2016). Headcount (H) is defined as percent households suffering from catastrophic total cost and reflects the frequency of catastrophic cost. Mean gap (G) is defined as the average amount by which total cost, as a proportion of the annual household income, exceeds the threshold and reflects intensity of catastrophic cost. Mean positive gap (MPG) is defined as G/H and reflects specific intensity of catastrophic total cost for an affected household (O'Donnell *et al*, 2008).

Statistical analysis

Socio-demographic information is reported as frequency and percentage for categorical variables, and median plus interquartile range (IQR, Q1-Q3) for quantitative variables. A currency exchange rate of Chinese RMB 662 to USD 100 is used (Li, 2019).

Relationship between household registration status and catastrophic total cost is determined using a four-step hierarchical multiple logistic regression as follows: in step 1, household registration status is included in the model to evaluate its independent effect on catastrophic total cost; in step 2, demographic variables are included considering the difference of demographic characteristics between migrant and resident patients; in step 3,

social-economic variables are included as previous studies (Fuady *et al*, 2018) reported household income level and income-earning jobs contribute significantly to catastrophic total cost; and in step 4, BHI is included to evaluate disparity in reimbursement for tuberculosis care among different health insurance schemes. In addition, in order to understand the contribution of reimbursement in reducing OOP and catastrophic total costs in MDR-TB treatment, OOP cost, frequency and intensity of catastrophic total costs (including H, G and MPG) before and after reimbursement are calculated according to the definitions. A *p*-value <0.05 is considered statistically significant. Statistical analyses were performed using Statistical Analysis System (SAS) version 9.4 (SAS Institute, Cary, NC).

RESULTS

Socio-demographic characteristics

Participating patients (*n* =162; consisting of 103 migrants and 59 residents) were (mean ± SD) 39 ± 16 years of age, 62% males, 57% married, and 49% with junior or lower school level of education (Table 1). Most (83%) resident patients in our research were from urban areas, while most (76%) of the migrant patients were from rural areas (*p*-value <0.001). Twenty-four (40.7%) resident patients had no income-earning jobs, compared to 61 (59.2%) migrant patients (*p* = 0.023). Median annual income is significantly higher among resident compared to migrant patients (*p* = 0.026). Nearly three quarters of migrant patients had urban and rural resident basic medical insurance coverage, while resident patients are covered by either urban and rural resident basic medical insurance, urban employee-based basic medical insurance or other types of medical insurances (Table 1).

OOP expenses and catastrophic total costs of MDR-TB treatment

OOP expenses for MDR-TB treatment of migrant patients were 2.5 folds higher than those of resident patients (Table 2). Direct medical expenses constituted the major portion of OOP expenditure, with those (74%) of migrant patients significantly higher compared to those (65%) of resident patients (*p*-value <0.001), with anti-TB drugs costs accounting for some 30% of the expenses. In addition, migrant patients incurred significantly more non-medical costs than resident patients (*p*-value <0.001), but indirect costs were similar for both groups.

Using the definition of "catastrophic" cost as that constituting >20% of a household annual income, total medical cost for MDR-TB treatment of patients taken as a whole were categorized as catastrophic, but not when adjusted for demographics (model 2) or for demographics, social-economic variables (model 3) and health insurance (model 4) (Table 3). On closer inspection, migrant MDR-TB patients were at greater risk for incurring catastrophic total treatment,

Table 1

Demographic and socio-economic characteristics of participating patients attending an out-patient department for treatment of multi-drug resistant tuberculosis at Guangzhou Chest Hospital, Guangdong Province, PR China (15 January - 10 May 2018)

Characteristic	Resident patient Number (%) (n = 59)	Migrant patient Number (%) (n = 103)	All patient Number (%) (n = 162)	χ^2	p-value*
Age, years, mean ± SD	42 ± 18	38 ± 14	39 ± 16	1.64	0.201
Gender					
Male	38 (64)	62 (60)	100 (62)	0.28	0.596
Female	21 (36)	41 (40)	62 (38)		
Marital status					
Single/divorced/widowed	25 (42)	44 (43)	69 (43)	0.002	0.966
Married	34 (58)	59 (57)	93 (57)		
Education					
Junior school or lower	24 (41)	55 (53)	79 (49)	6.52	0.038
High school	19 (32)	36 (35)	55 (34)		
College or higher	16 (27)	12 (12)	28 (17)		
Household registration					
Urban	49 (83)	25 (24)	74 (46)	52.23	<0.001
Rural	10 (17)	78 (76)	88 (54)		

Table 1 (cont)

Characteristic	Resident patient Number (%) (n = 59)	Migrant patient Number (%) (n = 103)	All patient Number (%) (n = 162)	χ^2	p-value*
Income-earning job					
Yes	35 (59)	42 (40)	77 (47)	5.17	0.023
No	24 (41)	61 (59)	85 (53)		
Monthly household income (USD), median (IQR)	14,073 (7,553-27,190)	10,574 (5,740-15,589)	11,782 (7,251-19,637)	4.95	0.026
High income level†	44 (75)	87 (85)	131 (81)	2.37	0.124
Low income level†	15 (25)	16 (15)	31 (19)		
Health insurance					
URRBMI	25 (43)	75 (73)	100 (62)	16.42	<0.001
UEBMI	19 (32)	20 (19)	39 (24)		
Other types of insurance	15 (25)	8 (8)	23 (14)		

*Significant at p<0.05

†Low- and high-income level based on annual median household income of working class in China (RMB 150,000 or USD 22,658)
IQR: interquartile range; UEBMI: urban employee-based basic medical insurance; URRBMI: urban and rural resident basic medical insurance

Table 2

Out-of-pocket costs of participating patients attending an out-patient department for treatment of multi-drug resistant tuberculosis (TB) at Guangzhou Chest Hospital, Guangdong Province, PR China (15 January - 10 May 2018)

Cost (USD)[a]	Resident patient (n = 59)			Migrant patient (n = 103)			p-value*
	Mean ± SD	Median (IQR)	Percent[b]	Mean ± SD	Median (IQR)	Percent[b]	
Total cost	6,387 ± 6,535	3,727 (2,638-7,541)	100	15,783 ± 7,770	15,138 (9,646-20,199)	100	<0.001
Direct medical cost	4,124 ± 5,956	2,182 (1,381-3,790)	64.8	11,766 ± 5,909	11,502 (6,902-15,374)	74.5	<0.001
Hospitalization	635 ± 946	0 (0-1,012)	8.6	2,883 ±,2,747	2,181 (1,303-3,448)	13.8	<0.001
Outpatient	3,575 ± 5,554	1,820 (1,075-3,010)	56.2	9,583 ± 5,239	8,991 (5,125-13,555)	60.7	<0.001
Anti-TB drugs	1,940 ± 5,420	24 (5-629)	30.4	6,184 ± 4,502	5,866 (1,990-9,466)	39.2	<0.001
Adjuvant drugs	1,047 ± 563	1,010 (618-1,403)	16.4	1,281 ± 845	1,139 (649-1,733)	8.1	0.171
Laboratory tests	261 ± 417	85(0, 373)	4.1	1,429 ± 790	1,271 (919-1,702)	9.1	<0.001
Others	341 ± 306	323 (92-464)	5.3	685 ± 717	488 (332-734)	4.3	<0.001
Direct non-medical cost	1,081 ± 1,619	362 (136-1,590)	17.0	2,681 ± 2,901	1,953 (491-3,601)	17.0	<0.001
Transport	222 ± 355	98 (25-246)	3.5	977 ± 1,346	620 (130-1,239)	6.2	<0.001
Food	248 ± 298	154 (54-289)	3.9	420 ± 552	255 (69-529)	2.7	0.057
Hotel	24 ± 181	0 (0-0)	0.4	272 ± 466	6 (0-453)	1.7	<0.001
Nutrition supplements	587 ± 1,449	0 (0-159)	9.2	1,013 ± 2,134	0 (0-997)	6.4	0.282
Indirect cost	1,182 ± 750	1,134 (715-1,565)	18.2	1,335 ± 1,155	1,042 (553-1,803)	8.5	0.798

*Significant at p <0.05

[a]USD 100 = Chinese RMB 662 (second quarter of 2018); [b]Proportion of expenses relative to total cost

RMB: Renminbi (Chinese Yuan); USD: US dollar

Table 3

Hierarchical multiple logistic regression analysis of factors associated with catastrophic total cost (after reimbursement) of multi-drug resistant tuberculosis treatment of participating patients attending an out-patient department at Guangzhou Chest Hospital, Guangdong Province, PR China (15 January - 10 May 2018)

Indicator	Model[a]			
	1	2	3	4
R^2 ($\triangle R^2$)	0.211	0.225 (0.014)	0.370 (0.145)	0.376 (0.006)
Chi-square[b]	38.412	2.807	33.594	1.67
p-value[c]	<0.001	0.121	<0.001	0.224
Step 1: Migration status, odds ratio (interquartile range)				
Resident patient	Reference	Reference	Reference	Reference
Migrant patient	11.02 (4.81-25.26)	14.2 (4.76-42.38)	17.26 (4.7-63.47)	15.55 (4.18-57.81)
Step 2: Demographics, adjusted odds ratio (interquartile range)				
Age	-	1.12 (0.44-2.81)	1.28 (0.44-3.71)	1.39 (0.46-4.18)
Gender				
Male	-	Reference	Reference	Reference
Female	-	0.98 (0.95-1.02)	0.98 (0.94-1.03)	0.98 (0.94-1.03)
Marital status				
Single/divorced/widowed	-	Reference	Reference	Reference
Married	-	1.56 (0.46 5.34)	1.49 (0.36-6.17)	1.45 (0.34-6.25)

Table 3 (cont)

Indicator	Model[a]			
	1	2	3	4
Step 2 (cont)				
Education				
Junior school or lower	-	Reference	Reference	Reference
High school	-	0.48 (0.17-1.33)	0.49 (0.15-1.63)	0.49 (0.15-1.63)
College or higher	-	0.65 (0.16-2.66)	0.87 (0.16-4.79)	0.88 (0.16-4.97)
Household registration				
Urban	-	Reference	Reference	Reference
Rural	-	0.6 (0.19-1.85)	1.04 (0.27-3.96)	1.04 (0.27-3.97)
Step 3: Social-economic variable, adjusted odds ratio (interquartile range)				
Household income level[d]				
Higher	-	-	Reference	Reference
Lower	-	-	17.26 (4.95-60.1)	17.30 (4.93-60.78)
Income-earning job				
No	-	-	Reference	Reference
Yes	-	-	3.67 (1.33-10.09)	4.14 (1.46-11.76)

Table 3 (cont)

Indicator	Model[a]			
	1	2	3	4
Step 4: Health insurance, adjusted odds ratio (interquartile range)				
Health insurance				
No insurance	-	-	-	Reference
URRBMI	-	-	-	1.25 (0.27-5.68)
UEBMI	-	-	-	2.35 (0.43-12.8)
Other types of insurances	-	-	-	0.92 (0.09-9.47)

[a]Model 1: unadjusted; Model 2: adjusted for demographics; Model 3: adjusted for demographics and social-economic variables; Model 4: adjusted for demographics, social-economic variables and health insurance

[b]The chi-square corresponding to the changes of -2lnL between two adjacent models

[c]Significant at p <0.05

[d]Median household income of working class = RMB 150,000 or USD 22,658

RMB: Renminbi (Chinese Yuan); URRBMI: urban and rural resident basic medical insurance; UEBMI: urban employee-based basic medical insurance; USD: US dollar

even if demographics, social-economic variables and health insurance were taken into account (model 4). In both groups, not having a job and coming from a household with lower than median annual income were risk factors, even using adjustments according to model 4, but having a medical insurance coverage was a mitigating factor (Table 3). Migrant status was a strong factor related to catastrophic total costs of MDR-TB patients, which explained 21.1% of the variance of catastrophic total costs.

Causes of disparities in OOP expenses and incidence of catastrophic total medical cost between migrant and resident patients

For resident patients, reimbursement from Local Subsidy Program accounted for 60.8% of the total medical costs, and with assistance from BHI, payment of OOP expenses accounted for 23.2% (Fig 1). On the other hand, for migrant patients, reimbursement from Local Subsidy Program and BHI accounted for 1.6 and 10.4% of the total medical costs respectively. As a result, OOP payments for migrant patients remained at a relatively high level (88.0% of the total medical costs) (Table 4).

At 20% threshold, frequency of catastrophic total cost after reimbursement was 45.8 and 90.3% for resident and migrant patients respectively (Table 5). For resident patients, reimbursement from BHI and Local Subsidy Program were substantial contributions towards reducing frequency of catastrophic total costs (from 88.1 to 45.8%). Similarly, intensity of catastrophic total costs was also alleviated in this group, MG and MPG reduced by 60.2 and 57.2% respectively. For migrant patients, due to the low level of reimbursements, both BHI and the Local Subsidy Program did not to assist in lowering the incidence of catastrophic total medical cost (Table 5).

DISCUSSION

In a designated hospital, the national "free TB treatment service policy" of the country provided free diagnosis and first-line anti-TB drugs according to the national treatment protocol to reduce costs to tuberculosis patient (Chen *et al*, 2015). However, this policy does not include any second-line anti-TB drugs, which are becoming crucial for successful treatment of MDR-TB (Chen *et al*, 2015). In 2014, the Guangzhou government introduced a reduction and exemption policy (Local Subsidy Program) for examination and treatment costs of resident MDR-TB patients as a successor to the Global Fund (Wang *et al*, 2017). This Program provides free diagnosis and payment for a 24-month treatment service up to a maximum of USD 14,857 per patient.

To the best of our knowledge, this is the first study comparing financial burden of treatment of both resident and migrant MDR-TB patients. Over 90% of migrant patients suffered from catastrophic total cost, even with reimbursement from BHI, and were

ten times more likely to experience catastrophic total cost compared to resident patients. However, in both groups, unemployment and a household with lower annual income were risks for incurring catastrophic total medical costs.

A previous study by Xu *et al* (2003) identified health services requiring payment, low capability to pay and lack of prepayment or health insurance as key conditions for acquiring a catastrophic total cost, findings that applied to migrant patients participating in our

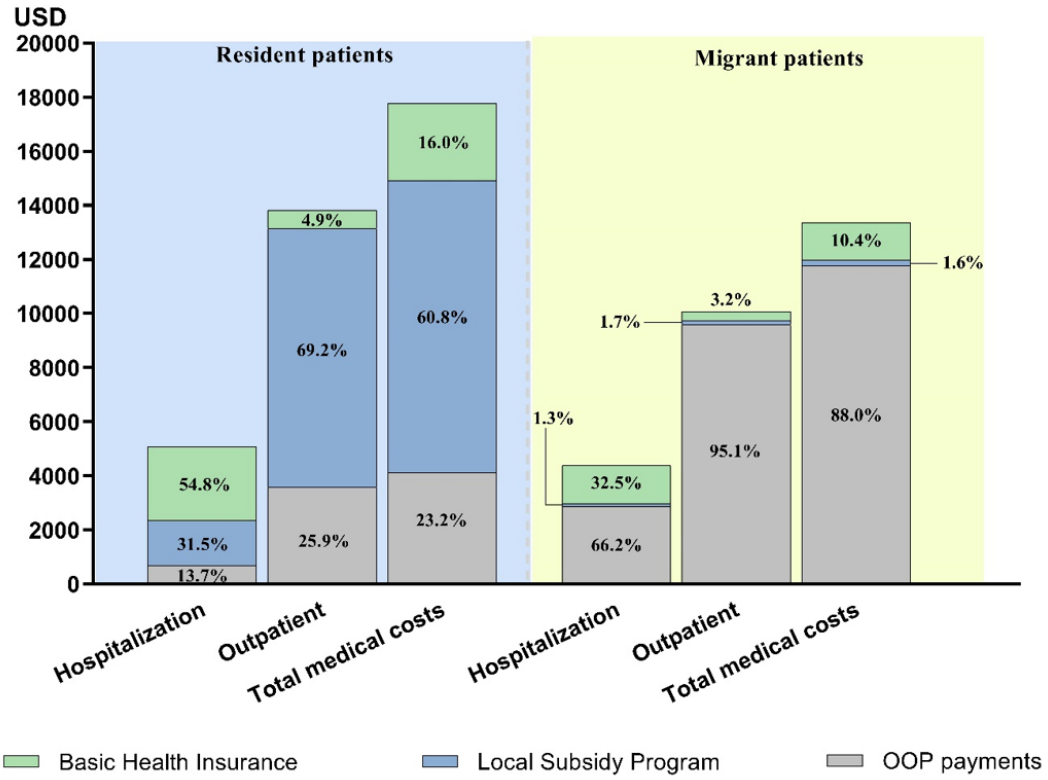

Fig 1 - Proportion of multi-drug resistant tuberculosis treatment cost reduced by reimbursement programs (Basic Health Insurance and Local Subsidy Program) among participating migrant and resident patients attending an out-patient department at Guangzhou Chest Hospital, Guangdong Province, PR China (15 January - 10 May 2018)

OOP: out-of-pocket
Chinese RMB 662 = USD 100 (second quarter of 2018)
RMB: Renminbi (Chinese Yuan); USD: US dollar

Table 4

Medical cost and reimbursement of multi-drug resistant tuberculosis treatment of participating patients attending an out-patient department at Guangzhou Chest Hospital, Guangdong Province, PR China (15 January - 10 May 2018)

Treatment phase	Indicator	Medical cost (before reimbursement) (USD)	Reimbursement from BHI (USD)	Reimbursement from LSP (USD)	Out-of-pocket medical expenditure (USD)
Resident patient					
Hospitalization	Mean ± SD	4,965 ± 4,578	2,723 ± 2,989	1,670 ± 1,735	678 ± 972
	Median (IQR)	3,407 (1,984-6,112)	1,963 (927-2,963)	889 (676-2010)	0 (0-1,104)
	Proportion (%)*	100	54.8	31.5	13.7
Outpatient care	Mean ± SD	13,813 ± 7,369	672 ± 619	9,565 ± 5,370	3,575 ± 5,554
	Median (IQR)	13,002 (8,209-17,845)	691 (0-1047)	9,330 (5,519-13,041)	1,820 (1,075-3,010)
	Proportion (%)*	100	4.9	69.2	25.9
Total	Mean ± SD	17,768 ± 9,461	2,841 ± 3,028	10,811 ± 5,703	4,116 ± 5,956
	Median (IQR)	16,644 (10,806-22,236)	2,175 (788-3,398)	10,619 (6,731-14,647)	2,182 (1,381-3,700)
	Proportion (%)*	100	16.0	60.8	23.2

Table 4 (cont)

Treatment phase	Indicator	Medical cost (before reimbursement) (USD)	Reimbursement from BHI (USD)	Reimbursement from LSP (USD)	Out-of-pocket medical expenditure (USD)
Migrant patient					
Hospitalization	Mean ± SD	4,353 ± 3,495	1,415 ± 2,099	85 ± 316	2,883 ± 2,747
	Median (IQR)	2,915 (2,248-4,999)	828 (0-1,841)	0 (0-79)	2,181 (1,303-3,448)
	Proportion (%)*	100	32.5	1.3	66.2
Outpatient care	Mean ± SD	10,075 ± 5,847	321 ± 2,113	171 ± 1,233	9,583 ± 5,239
	Median (IQR)	9,407(5,361-13,715)	0 (0-0)	0 (0-0)	8,991 (5,125-13,555)
	Proportion (%)*	100	3.2	1.7	95.1
Total	Mean ± SD	13,371 ± 7,628	1,392 ± 3,369	213 ± 1,451	11,766 ± 5,909
	Median (IQR)	12,484 (7,651-16,688)	0 (0-1,560)	0 (0-0)	11,502 (6,902-15,374)
	Proportion (%)*	100	10.4	1.6	88.0

*Relative to the total medical cost

Chinese RMB 662 = USD 100 (second quarter of 2018)

BHI: basic health insurance; IQR: interquartile range; LSP: local subsidy program; RMB: Renminbi (Chinese Yuan); SD: standard deviation; USD: US dollar

Table 5

Reimbursement impact on frequency and intensity of catastrophic total cost of multi-drug resistant tuberculosis treatment of participating patients attending an out-patient department at Guangzhou Chest Hospital, Guangdong Province, PR China (15 January - 10 May 2018)

Indicator	Catastrophic total cost		
	Before reimbursement (%)	After reimbursement 1[a] (%)	After reimbursement 2[b] (%)
Resident			
Headcount	88.1	86.4	45.8
Mean gap	70.8	56.8	10.6
Mean positive gap	80.3	65.7	23.1
Migrant patient			
Headcount	91.3	91.3	90.3
Mean gap	113.6	103.9	103.6
Mean positive gap	124.5	113.8	114.7

[a]From basic health insurance; [b]From both basic health insurance and local subsidy program

study. Guangzhou Local Subsidy Program accounted for over half of the MDR-TB medical costs, reduced OOP payments of resident patients and prevented a substantial proportion of incurring a catastrophic total medical cost. In addition, loss of jobs was more frequent among migrant patients because of their trans-regional movement, thereby compromising their ability to pay for the long-term MDR-TB treatment. Furthermore, migrant patients were more likely to be excluded from receiving health insurance or lower reimbursement rate due to their status (Meng *et al*, 2018).

Our results show BHI, URRBMI or UEBMI did not substantially alleviate patients from catastrophic total costs. Previous studies in China reported reimbursements for TB treatment range 7.0-34.7% (Wei *et al*, 2015; Zhou *et al*, 2016; Duan *et al*, 2019). In comparison, other developing countries such as Vietnam and Indonesia, more than two thirds of the MDR-TB patients received reimbursement of >80% of the total medical cost (Fuady *et al*, 2018; Nam *et al*, 2018). One reason for the low reimbursement for MDR-TB treatment in China is the inadequate coverage (Pan *et al*, 2016), with BHI mainly reimbursing

medical cost for hospitalization, whereas, the major portion of medical costs is from outpatient treatment. Although specific outpatient reimbursement programs were established to improve reimbursement for diseases requiring long-term outpatient treatment, such as, coronary heart disease, diabetes, kidney disease, and TB, monthly ceiling rate is low and inadequate for MDR-TB patients' (Duan *et al*, 2019). The reimbursement rate was low could also be due to conditional or partial reimbursement of the second-line anti-TB drugs (Wang *et al*, 2019). For example, under BHI scheme, only 10% of cycloserine cost could be reimbursed, but not that of linezolid, recommended by WHO (2017).

This study suffers from several limitations. Firstly, all MDR-TB patient participants were treated at a designated hospital, but those who could not afford initial treatment were likely to have discontinued attendance, thereby leading to an underestimation of frequency and intensity of catastrophic total cost. Secondly, participants were recruited over a single short period with a possible high proportion of recall bias of non-medical costs and thus the findings could not be generalized for the whole population of Guangzhou. Thirdly, patients (especially migrant patients) might have received medical services at other hospitals or pharmacies, resulting in possible underestimation of the actual catastrophic total medical cost. Fourthly, impact of co-infection of such diseases as HIV and diabetes was not taken into consideration.

Nonetheless, the following important implications resulted from our study. Firstly, re-evaluation of subsidy policies for MDR-TB treatment, in particular of migrant patients, is urgently needed. With the financial support from the Global Fund, China was able to expand free MDR-TB diagnostic and treatment from two prefectures in 2006 to 92 prefectures, covering 921 of the country's 3,000 counties, by June 2014 (Wang *et al*, 2017). When the Global Fund revised its co-financing policies, as of 2014 China became ineligible to obtain further support (Global Fund, 2014). As a result, enrollment of MDR-TB patients for treatment declined by 70% nationwide (Wang *et al*, 2017). However, local governments of several metropolitans in the more developed areas of China, such as Guangzhou, Shanghai (Hu *et al*, 2017) and Chongqing (Chongqing Municipal Tuberculosis Control, 2018), introduced subsidy programs to continue provision free of charge of second-line anti-TB drugs for treatment MDR-TB patients, but these types of services were not able to be sustained in less developed prefectures or rural regions. Monthly OOP payment for MDR-TB patients in Yunnan rose from RMB 800-900 (USD 125-140) in 2013 to RMB 400-10,000 (US$D 63-1,571) in 2015 (Hutchison *et al*, 2017). Supply of second-line anti-TB drugs became less reliable in Shandong Province (Li, 2019). Not only TB patients in those areas are not able not receive free diagnosis and treatment, but they also have to travel to other regions to be

treated, leading to significant increase in non-medical costs. In order to enhance diagnosis and treatment of MDR-TB patients, it is necessary to provide adequate subsidies for all MDR-TB patients regardless of their migrant status. Secondly, social protection measures, such as conditional cash transfer programs and unemployment insurances, should be implemented to improve MDR-TB patients' ability to afford treatment without incurring catastrophic total medical costs (Andrade *et al*, 2018). Thirdly, policy makers are urged to improve the reimbursement rate and ceiling level for second-line anti-TB drugs in outpatient treatment, and to raise reimbursement for migrant TB patients.

In conclusion, our findings reveal disparity between migrant and resident patients in acquiring catastrophic total cost for MDR-TB treatment was mainly due to inadequate benefit from reimbursement programs for migrant patients, resulting in a disproportionally high out-of-pocket expense. In order to achieve the goal of eliminating catastrophic total costs from MDR-TB treatment, a universal medical coverage for MDR-TB patients (and those suffering from other chronic diseases) should be introduced.

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CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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