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The extent and determinants of catastrophic health expenditure for tuberculosis care in southwest of China: a cross-sectional study

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Title page

The extent and determinants of catastrophic health expenditure for tuberculosis care in southwest of China: a cross-sectional study

Running title: The extent and determinants of CHE for TB care

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ABSTRACT

Objective: To investigate the extent and determinants of catastrophic health expenditure (CHE) for tuberculosis(TB) care in representative southwest region of China.

Design: A cross-sectional study

Setting: Four counties of Chongqing municipality, China

Participants: 1199 active pulmonary TB patients beyond 16 years and without mental disorders were consecutively recruited in the four counties' designated TB medical institutions.

Outcome measures Socio-demographic and clinical characteristics of the study participants, direct medical costs, incidence and intensity of CHE for TB care were described. Univariable and multivariable logistic regression analyses were performed to assess the determinants of CHE.

Results The incidence of CHE was 52.8%. Out-of-pocket payments were 93% of the total costs for TB care. Compared with patients without delay, the incidence and intensity of CHE were greater in patients who had patient delay or diagnostic delay. Incurring CHE was independently associated with patient delay (adjusted odds ratio [aOR], 1.359; 95% confidence interval (CI), 1.062–1.740), diagnostic delay (aOR, 1.449; 95% CI, 1.131–1.857), being male (aOR, 1.511; 95% CI, 1.149–1.987), inhabitant (aOR, 1.477; 95% CI, 1.107–1.971) and high educational level (aOR, 0.611; 95% CI, 0.505–0.739).

Conclusion The findings might be considered as baseline data about the extent of

catastrophic costs that TB-related households faced in southwest of China. Our findings will provide valuable information for policymakers to take fine-tuned interventions to decrease catastrophic costs for TB-affected households.

Keywords: Tuberculosis, Catastrophic health expenditure, Patient delay, Diagnostic delay

Strengths and limitations of this study

1. The study first provides the baseline data about TB-related households facing catastrophic costs and the determinants of CHE for TB care in southwest of China.

2. The study highlights the importance of early care seeking and diagnosis of TB.

3. Our findings will provide valuable information for policymakers to take fine-tuned interventions to decrease catastrophic costs for TB-affected households.

4. Due to some data were collected based on self-reporting, which may be subjected to a recall bias.

5. The non-medical costs and indirect costs were not taken into account, which may underestimate the extent of CHE for TB care and should be considered in the future study.

INTRODUCTION

Tuberculosis (TB) is the first leading cause of death among communicable diseases worldwide. China ranks third among the countries in the world with the heaviest TB burden.[1] Poverty is not only strongly associated with TB incidence, but also a cause and a devastating outcome of TB in China.[2] Therefore, TB is not only a serious infectious disease but also a major public health problem worldwide. "End TB strategy," a plan announced by the World Health Organization (WHO) to end the global TB epidemic, aims to reduce TB death rate by 95% and cut new cases by 90% between 2015 and 2035, and to ensure that no affected families will face catastrophic costs due to TB by 2020.[3] The last target is so urgent and important to ascertain the progress of universal health coverage and social protection. However, the projected 2015 baseline is not yet available.[3]

To reduce the economic burden on TB patients, a "free TB service policy" was implemented in many continents.[5-7] In China, the "free TB service policy" includes free X-ray examination and free sputum smear test for patients once with suspected TB at first visit, free anti-TB drugs (6 months for new patients and 8 months if previously treated), three free sputum smear tests, and one free X-ray test during anti-TB treatment. Although the policy has been implemented for 25 years in China, TB patients still suffer from the high costs of TB treatment, which often forces their families into catastrophe and poverty. [8-12]

Catastrophic health expenditure (CHE) is a measure of financial risk protection and is often incurred by households who have to pay out of pocket (OOP) for health services. Thus, the household may have to sacrifice the consumption of other goods and services necessary for their well-being.[4] A series of studies reported that the incidence of CHE for TB care in China ranges between 46.7% and 66.8%, which is higher than the incidence of other illnesses despite the patients' access to free TB treatment.[10-12] Additionally, households with members having TB are approximately 1.8 times more likely to experience CHE than those without. [13] Therefore, it is essential to reduce the economic burden of TB patients and save their families from CHE.

According to a few studies conducted in China, Nigeria, and Benin, the factors determining CHE for TB care include age, sex, number of family members, urban residence, educational level, being a breadwinner, job loss, health insurance status, poor households, adverse pre-diagnosis stage (i.e., patient delay over 1 month and seeking of informal care), treatment at a private facility, ratio of patient income to total household income, hospitalization, and previous of TB treatment.[11 14-16]. However, the factors associated with CHE among TB patients remain not well elucidated.

As an economic and industrial hub of southwest region of China, Chongqing municipality has experienced rapid economic development. The TB epidemic is high in southwest China and Chongqing ranks in the top 10 among the highest TB burden provinces in China. The TB notification rate of Chongqing in 2015 has declined to 70.8 cases per 100,000 population from the peak of 106 cases per 100,000 in 2005. Recent five years, approximately 20,000 patients were reported with TB in Chongqing, making up 2.5% of all notified TB cases in China.[17] Consideration the high TB burden and great challenges in controlling TB, as well as no baseline data about the TB-related families facing catastrophic costs in southwest of China, we conducted a cross-sectional study to investigate the extent and determinants of CHE for TB care, taking Chongqing as an example.

METHODS

Study sites and participants

There are 39 counties in Chongqing. This cross-sectional study was conducted in four counties of Chongqing from March 2013 to August 2014. According to the Chongqing Statistical Yearbook 2015, the real GDP per capita was 47850 RMB. Urban population accounts for 59.6% of the total population in 2014. The four counties with similar levels of economic development and similar human geographical environment as the study sites. These four counties are among the middle-income counties in southwest region of China, have both villages and cities, and are in the process of urbanization.

From March to December in 2013, all the registered active pulmonary TB (PTB) patients excluding those aged below 16 years or with mental disorders were recruited consecutively in the designated TB medical institutes of the four counties. Totally, 1290 PTB patients were qualified, of whom 61 refused to participate due to poor clinical conditions and 30 questionnaires were not completed. Thus, a total of 1199 patients were included in the study. All participants had access to free TB treatment and were prospectively followed throughout the treatment period.

Data collection

All data were collected in these four counties' designated TB medical institutes. The study was based on a well-structured questionnaire and patients' medical records. All participants at the local TB-designated medical institutes were interviewed face to face by a trained TB staff using the questionnaire. The following data were obtained:

covered personal information, socioeconomic information (age, sex, residence, occupation, education, marital status, number of family members, medical insurance status, household income, etc.), and history of disease (forms of TB, date of first onset of suspected TB symptoms, date of first visit to any health provider, date of PTB diagnosis, and direct medical costs for TB care). Clinic information and exact date of TB diagnosis were checked against the patients' medical records. A 6-month or 8-month treatment regimen was recommended by the WHO. The treatment costs were collected every month. Out-of-pocket (OOP) payments and reimbursements of the direct medical costs for TB care in different periods of services (pre-diagnosis, diagnosis, and treatment) were collected per individual and checked according to the invoices. All costs were indicated in Ren Min Bi (RMB).

Definitions

Pulmonary TB was diagnosed based on the pathological, clinical, and radiological findings, and confirmed through bacteriological and histological examinations, which were strictly performed according to the Chinese Diagnostic criteria for PTB (WS-288-2008) .[18]

Patient delay is determined as a time interval from the first onset of TB symptoms to the first visit to any health provider; if the time interval lasts for more than 14 days, it is considered as a "delay" .[19]

Diagnostic delay is defined as a time interval between a patient's first visit to any health provider and the final diagnosis as TB; if the time interval lasts for more than 14 days, it is considered as a "delay".[19]

Pre-diagnosis is the period from the onset of TB symptoms to first visit to a local designated TB medical institutions. **The period of diagnosis** is from the first visit to a local designated TB medical institution to the diagnosis of TB. **The period of treatment** is the full course of TB treatment.

Direct medical costs are composed of consultation fees, laboratory tests, X-rays, medical tests, and drugs during the period of pre-diagnosis, diagnosis, and treatment.

OOP payments are regarded as the direct medical costs paid by patients themselves.

Catastrophic health expenditure is defined as OOP expenditure for healthcare that exceeds a specified proportion of household income, often set at a threshold of 10% or 40% for the proportion of OOP in total household income or household capacity to pay, respectively. [14] The 40% for the proportion of OOP in household capacity to pay is recommended by the WHO and is widely used. The 10% for the proportion of OOP in total household income is also used in many studies. In this study, the OOP payments of direct medical costs for TB care exceeding the 10% of household annual income are defined as catastrophic.

Measuring the incidence and intensity of catastrophic health expenditure

CHE is usually assessed by incidence and intensity. Head count (HC) is used to measure the incidence of CHE, while mean gap (MG) and mean positive gap (MPG) are used to reflect the intensity of CHE. HC means the percentage of households whose OOP payments equal or exceed 10% of their annual income to the total number of households. MG is the average amount by which OOP payments, as a proportion of household annual income, exceeds the threshold. MPG is equal to MG/HC, the excess expenditure per household experiencing CHE. The methods used in measuring HC, MG, and MPG are based on the previous study. [20]

Statistical analysis

Data were double entered and checked using EPI Data Version 3. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 18.0 (SPSS Inc. Chicago, IL, USA). Continuous variables were presented as means, or medians and interquartile (IQR) ranges, while categorical variables were presented as numbers and percentages (%). Comparisons among groups were analyzed using the Pearson's chi-square test. Odds ratios (ORs) and their 95% confidence intervals (CIs) were estimated. All variables that showed association with outcome variable ($p<0.05$) in the univariable analysis were included in the multivariable model. A multivariate logistic regression analysis, using a backward elimination method, was performed to assess the determinants of CHE in a multivariate model. A two sided p-value of <0.05 was considered statistically significant.

Ethics approval

The study was approved by the Ethical Committee of the Chongqing Institute of Tuberculosis Prevention and Treatment, Chongqing, China. A written informed consent was obtained from each participant prior to inclusion in the survey.

Patient and public involvement

No applicable for this study.

RESULTS

Patient characteristics

The characteristics of these pulmonary TB patients are summarized in Table 1. A total of 1199 PTB patients were enrolled in the study. The proportion of men to women involved in this study is 2.3:1. More than three-quarters of patients were in their labor age (16–59 years), and the average age of the patients were 43.9 years, with a median age of 44 years. Approximately 30% of patients were migrants. Two-thirds of patients were married and received at least junior high school education. The patients included in this study were either unemployed, employed, or peasant. Approximately three-quarters of the households had one to three family members. In majority, 89.2% of the patients had medical insurance. Only 15.9% of patients had been hospitalized in the intensive period. Approximately three-quarters of patients were smear negative. Of the total participants, 53.0% (635/1199) and 43.0% (516/1199) experienced patient and diagnostic delay, respectively. Patients' average annual household income was 42,200 RMB, with a median (IQR) of 35,000 RMB (20,000–56,000 RMB).

Direct medical costs for TB in different periods of medical treatment

The OOP costs and medical insurance reimbursement in the pre-diagnosis, diagnosis, and treatment period are presented in Table 2. Costs in the pre-diagnosis period were all paid by OOP, accounting for nearly half of the total cost. Excluding the fees covered by free TB treatment, the average diagnosis cost was 528 RMB, which could not be reimbursed by medical insurance, while the average treatment cost was 3107 RMB, of which approximately 85% was paid by OOP. Overall, the average medical cost of a TB patient was 7,000 RMB, with a median of 4,085 RMB and 93% of which were paid by OOP. Average annual household OOP payment was 6,518 RMB (a median of 3,789 RMB), which accounts for 15.4% of the mean household annual income.

Incidence and intensity of CHE

Table 3 shows that 52.8% (633/1199) of all TB-related households experienced CHE. On average, healthcare payments for TB were 18.1% higher than the threshold value (10%). For households experiencing CHE, the mean positive gap was 34.2% higher than the threshold. The incidence of CHE in patients experiencing patient delay or diagnostic delay was 11% or 9.7% more than those not experiencing patient delay or diagnostic delay, respectively. The intensity measure was also greater for the group of experiencing patient delay or diagnostic delay than the group without delay.

Determinants of CHE

In Table 4, the impacts of different variables on the incidence of CHE are compared among various patients or households using a Pearson's chi-square test. There are many factors associated with CHE, including patient delay, diagnostic delay, sex, age, resident status, marital status, educational level, occupation, medical insurance status, and hospitalization.

Logistic regression analysis showed that the independent determinants of CHE include patient delay (adjusted odds ratio [aOR], 1.359; 95% CI, 1.062–1.740), diagnostic delay (aOR, 1.449; 95% CI, 1.131–1.857), sex (aOR, 1.511; 95% CI, 1.149–1.987), resident status (aOR, 1.477; 95% CI, 1.107–1.971), and educational level (aOR, 0.611; 95% CI, 0.505–0.739). That is to say, patients who have experienced patient delay or diagnostic delay have greater risks of CHE. The probability of incurring CHE increases if the patient is male, a permanent resident, or has a low educational background (Table 5).

DISCUSSION

This study revealed that the incidence of CHE for TB care is 52.8% after reimbursement. It is lower than the reported rates of 66.8%, 66% and 78.1% using the same CHE measurement methods in other cities of China, Nigeria, and Benin, respectively. [10 14 15] However, compared with the incidence of CHE incurred by common disease or non-communicable chronic disease in China and other countries, CHE incidence is still higher in TB-related households.[4 21 22] Recently, WHO changes the definition of "catastrophic costs due to TB", which is the total [direct and indirect] costs exceeding 20% of annual household income.[23] Although the threshold (10%) we set is lower than the recent definition, it may also be valuable to present the proportion of TB-affected patients (and their households) facing catastrophic costs if direct costs alone are counted.[23] A previous study in China demonstrated that non-medical costs relating to TB treatment are a serious financial burden for many TB patients.[24] Since the non-medical costs and indirect costs were not taken into account in the current study, the incidence of patients incurring catastrophic costs in this study population may be underestimated. Further studies are needed to evaluate the catastrophic costs accurately.

Although all patients in this study have access to free TB treatment and the majority of them have medical insurance, there was still a considerable amount of money spent before diagnosis and during treatment and a low ratio of reimbursement result in very high OOP payment. There may be three reasons to explain the phenomena: (i) many associated health-care costs are not covered in the free TB policy, for example, payment for drugs of ancillary and liver protection, and extra diagnostic tests.[2 6 12] (ii) Driven by profits, doctors may prescribe additional drugs and tests.[25] (iii) The costs before diagnosis are usually not reimbursed and the reimbursement level for outpatient TB treatment after diagnosis is very low due to a limited outpatient quota in China.[9] Furthermore, the patients' average annual household income is lower than the the real GDP per capita in 2014 in Chongqing, which reconfirmed that TB inequitably affects poor people.[26] This is another reason why the incidence of CHE is so high in the study.

In contrast with the previous study conducted in China, [11] the present study found that age, number of family members, health insurance status, and hospitalization are not the major determinants of CHE. It may be due to the different study settings and different participants in the two studies. Being male and having low educational level are independent determinants of CHE, which is consistent with a study carried out in Nigeria. [14] Men are the breadwinner of a family and patients with low education may have low income. Surprisingly, the migrant population is less likely to experience CHE. The reason need to be further investigated.

In this study, we found that patient delay and diagnostic delay are very important determinants of CHE. Therefore, patients who encountered patient or diagnostic delay are more likely to incur CHE than those without delay. Prolonged delays in TB diagnosis are still prevailing problems in many countries in many low- and middle-income countries, such as Southern, Ethiopia， Zambia， Tanzania， Mozambique，Indonesia and so on. [27-33] Delay in diagnosis have a huge impact on TB transmission in the community, aggravating the severity and mortality and resulting in an unfavorable treatment outcome, as well as increasing patient's expenses. [17 34-38] Therefore, it is vital to take measures to shorten the delay in diagnosis.

Patient delay may be related to the fact that patients do not take minor symptoms seriously in its early stage and will pay greater attention to it until symptoms become more severe. [9 39] In addition, many sociodemographic and economic factors contribute to patient delay. [18 40] Therefore, we should adopt comprehensive measures to facilitate patients to seek care early, such as strengthening TB health education to the public and adopting a precise poverty alleviation to increase the income of poverty-stricken patients. Early diagnosis is difficult due to the great percentage of asymptomatic PTB patients and non-availability of rapid, accurate, and cost-effective tests in many settings. [2 41] In this study, only one-quarter of patients has been confirmed bacteriological and mainly based on traditional methods. In fact, rapid molecular methods were not frequently used in Chongqing in 2013. Smear microscopy is rapid and cheap but with low sensitivity, whereas sputum culture is gold standard but labor intensive and time consuming. Various molecular TB diagnosis methods such as GeneXpert, line probe assay, and loop-mediated isothermal amplification are rapid and accurate but expensive and not covered by public medical insurance in China. [42-44] Methods based on immunology and protein biomarkers are rapid but limited due to their low accuracy. [45 46] Considering the limitations of diagnostic methods, more rapid, accurate, and affordable methods are urgently needed to shorten the time of diagnosis.

This study has some other limitations. Firstly, due to some data were collected based on self-reporting, which may be subjected to a recall bias. Secondly, the data in this study were collected four years ago and the per capita income has increased from 2014 to 2017. However, China's free TB service policy has not changed in recent years and TB inequitably affects poor people. Therefore, the CHE remains a problem for TB now in China. The results of this study still have a guiding significance in future practice. Furthermore, based on the results of this study we have taken some effective measures to shorten the delay in diagnosis, including strengthen TB health education to the public, adopt a precise poverty alleviation policy and promote rapid diagnostic tests for detection of TB.

CONCLUSION

The results indicate that the incidence and intensity of CHE for TB care are high, which provide baseline data of TB-related households facing CHE in southwest of China. Male patients, inhabitants, those with low educational level, and those who experience patient delay and diagnostic delay are more likely to incur CHE. Although the study was completed at four counties and results cannot be generalized to all TB patients in China, it still provides valuable information for policymakers to take fine-tuned interventions to decrease catastrophic costs for TB-affected households. Multi-center studies should be implemented in the future study.

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Competing interests None

Patient consent Obtained

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Table 1 Socio-demographic and clinical characteristics of the study participants (n=1199).

Variables	Patients No.	Percent (%)
Sex		
Male	839	70.0
Female	360	30.0
Age		
≤40	532	44.4
41-59	402	33.5
≥60	265	22.1
Residential status		
Inhabitant	848	70.7
Migrant	351	29.3
Marital status		
Single	340	28.4
Married	795	66.3
Divorced/widow	64	5.3
Educational level		
Primary or below	382	31.9
Junior high	356	29.7
High school and above	461	38.4
Occupation		
Unemployed	302	25.2
Employed	327	27.3
Peasant	353	29.4
Student	96	8.0
Retiree	121	10.1
Family size		
1~3	887	74.0
4~8	312	26.0
Medical insurance		
Yes	1069	89.2

No	130	10.8
Hospitalization		
Yes	191	15.9
No	1008	84.1
Forms of TB		
Smear-negative PTB	892	74.4
Smear-positive PTB	307	25.6
Patient delay		
Yes	635	53.0
No	564	47.0
Diagnostic delay		
Yes	516	43.0
No	683	57.0
Household annual income(RMB)		
Mean	42,200	
Median (IQR)	35,000(20,000-56,000)	

Note: IQR represents interquartile range. TB represents tuberculosis.

Table 2 Direct medical costs for TB care in different periods of services (n=1199). RMB

Costs in different periods (services)	Out of pockets		Medical insurance reimbursement		Total	
	Mean	Median(IQR)	Mean	Median(IQR)	Mean	Median(IQR)
Pre-diagnosis	3282	750(250-3000)	0	0	3282	750(250-3000)
Diagnosis*	528	157(121-250)	0	0	528	157(121-250)
Treatment #	2638	1792(834-3050)	482	0(0-501)	3107	1966(1000-3723)
Total	6518	3789(2106-6645)	482	0(0-501)	7000	4085(2222-7371)

Note:The expenses excludes the costs of the free-TB policy reduction and exemption. *The expenses excluded the cost of one time free chest X-ray and sputum smear examination. #The expenses excluded anti-TB drugs (6 months for new patients, 8 months if previously treated), three times sputum smear tests and one time X-ray test during anti-TB treatment.

Table 3 Incidence and intensity of CHE for TB care stratified by patient and diagnostic delay.

Catastrophic health expenditure	Patient delay		Diagnostic delay		All (n=1199)
	Yes	No	Yes	No	
Head count (%)	58.0	47.0	58.3	48.6	52.8
Mean gap (%)	21.1	14.6	19.3	17.2	18.1
Mean positive gap (%)	36.5	31.1	33.0	35.3	34.2

Table 4 Single factor analysis of catastrophic health expenditure in patients.

Variables		Experiencing CHE (n,%)	Not experiencing CHE (n,%)	OR (95% CI)	Chi-square	*P-value*
Patient delay	No	265 (47.0)	299(53.0)	1.0		
	Yes	368(58.0)	267(42.0)	1.555(1.238-1.954)	14.415	0.000
Diagnostic delay	No	332(48.6)	351(51.4)	1.0		
	Yes	301(58.3)	215(41.7)	1.480(1.175-1.864)	11.153	0.001
Sex	Female	151(41.9)	209(58.1)	1.0		
	Male	482(57.4)	357(42.6)	1.869(1.455-2.400)	24.300	0.000
Age	≤40	200(37.6)	332(62.4)	1.0		
	41-59	242(60.2)	160(39.8)	2.511(1.925-3.275)	46.936	0.000
	≥60	191(72.1)	74(27.9)	4.285(3.109-5.904)	84.156	0.000
Resident status	Migrant	129(36.8)	222(63.2)	1.0		
	Inhabitant	504(59.4)	344(40.6)	2.521(1.951-3.259)	51.246	0.000
Marital status	Single	133(39.1)	207(60.9)	1.0		
	Married	450(56.7)	344(43.3)	2.036(1.571-2.638)	29.377	0.000

	Divorced/widow	50(76.9)	15(23.1)	5.188(2.800-9.613)	31.488	0.000
Educational level	Primary or below	277(72.5)	105(27.5)	1.0		
	Junior high	190(53.4)	166(46.6)	0.434(0.319-0.589)	29.058	0.000
	High school and above	166(36.0)	295(64.0)	0.213(0.159-0.286)	111.600	0.000
Occupation	Unemployed	139(46.0)	163(54.0)	1.0		
	Employed	128(39.1)	199(60.9)	0.754(0.549-1.036)	3.044	0.081
	Peasant	261(73.9)	92(26.1)	3.327(2.396-4.519)	53.331	0.000
	Student	37(38.5)	59(61.5)	0.735(0.460-1.176)	1.654	0.198
	Retiree	68(56.2)	53(43.8)	1.505(0.984-2.300)	3.577	0.059
Family size	1~3	479(54.0)	408(46.0)	1.0		
	4~8	154(49.4)	158(50.6)	0.830(0.641-1.075)	1.997	0.158
Medical insurance status	No	47(36.2)	83(63.8)	1.0		
	Yes	586(54.8)	483(45.2)	2.143(1.469-3.125)	16.200	0.000
Hospitalization	No	517(51.3)	491(48.7)	1.0		
	Yes	116(60.7)	75(39.3)	1.469(1.071-2.014)	5.746	0.017

Forms of TB	Smear-negative PTB	480(53.8)	412(46.2)	1.0		
	Smear-positive PTB	153(49.8)	154(50.2)	0.853(0.658-1.105)	1.448	0.229

Note: PTB, pulmonary tuberculosis. OR, odds ratio. 95% CI,95% confidence interval for the odds ratio.

Table 5 Independent determinants of CHE for TB care using logistic regression model.

Variables	B	Standard error	Wald	*P-value*	Odds ratio(95% CI)
Patient delay	0.307	0.126	5.943	0.015	1.359(1.062-1.740)
Diagnostic delay	0.371	0.127	8.585	0.003	1.449(1.131-1.857)
Sex	0.413	0.14	8.703	0.003	1.511(1.149-1.987)
Residential status	0.39	0.147	7.033	0.008	1.477(1.107-1.971)
Educational level	-0.493	0.097	25.779	*P*<0.001	0.611(0.505-0.739)
Constant	-0.905	0.306	8.753	0.003	

Note: The variables that showed association with patient delay (p<0.05) in the univariable analysis were included in the multivariable model. The results showed association with CHE (p<0.05) were presented here. OR, odds ratio. 95% CI,95% confidence interval for the odds ratio.

1

The extent and determinants of catastrophic health expenditure for tuberculosis care in southwest of China: a cross-sectional study

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Title page

The extent and determinants of catastrophic health expenditure in tuberculosis care in Chongqing Municipality, China: cross-sectional study

Running title: The extent and determinants of CHE for TB care

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ABSTRACT

Objective: To investigate the extent and associations of patient /diagnostic delay and other potential factors with catastrophic health expenditure (CHE) for tuberculosis (TB) care in Chongqing Municipality, China.

Design: A cross-sectional study

Setting: Four counties of Chongqing municipality, China

Participants: A total of 1199 active pulmonary TB patients beyond 16 years and without mental disorders were consecutively recruited in the four counties' designated TB medical institutions.

Outcome measures The incidence and intensity of CHE for TB care were described. The association between patients' "social-demographic and clinical characteristics such as patient delay, diagnostic delay, forms of TB, health insurance status and hospitalization" and CHE were analyzed using univariate and multivariate logistic regression.

Results The incidence of CHE was 52.8% and out-of-pocket payments were 93% of the total costs for TB care. Compared with patients without delay, the incidence and intensity of CHE were higher in patients who had patient delay or diagnostic delay. Patients who experienced patient delay or diagnostic delay, who was a male, elderly (≥60 years), an inhabitant, a peasant, divorced/widow, NCMS membership had greater risks of incurring CHE for TB care. Having a higher educational level appeared to be a protective factor. However, hospitalization was not associated with CHE after controlling for other variables.

Conclusion The incidence and intensity of CHE for TB care are high, which provides baseline data about catastrophic costs that TB-related households faced in Chongqing of China. Variety of determinants of CHE implicate that it is essential to take effective measures to promote early seeking care and early diagnosis, improve

the actual reimbursement rates of health insurance, especially for outpatients, and need more fine-tuned interventions such as precise poverty alleviation to reduce catastrophic costs of the vulnerable population.

Keywords: Tuberculosis, Catastrophic health expenditure, Patient delay, Diagnostic delay, Health insurance

Strengths and limitations of this study

1. The study provides new data about TB-related households facing catastrophic costs and the determinants of CHE for TB care in China.

2. The study highlights the importance of early care seeking and diagnosis of TB.

3. Our findings will provide valuable information for policymakers to take fine-tuned interventions to decrease catastrophic costs for vulnerable TB-affected households.

4. Due to some data were collected based on self-reporting, which may be subjected to recall bias.

5. The non-medical costs and indirect costs were not taken into account, which may underestimate the extent of CHE for TB care and should be considered in the future study.

INTRODUCTION

Tuberculosis (TB) is one of the top 10 causes of death and the leading cause of a single infectious disease (above HIV/AIDS) worldwide. In 2017, about 10.0 million people developed TB disease and 1.6 million deaths caused by TB globally. China has the second largest burden of TB in the world, accounting for 9% of all cases.[1] Poverty is not only strongly associated with TB incidence, but also a cause and a devastating outcome of TB.[2] Therefore, TB is not only a serious infectious disease but also a severe public health problem worldwide. "End TB strategy," a plan announced by the World Health Organization (WHO) to end the global TB epidemic, aims to reduce TB death rate by 95% and cut new cases by 90% between 2015 and 2035, and no affected families face catastrophic costs due to TB by 2020.[3] However, the projected 2015 baseline is not yet available.[3] Achieving zero TB-induced catastrophic costs for households is too great to realize because the financial burden for TB patients is extremely high in low-income, middle-income and high-income countries. [4-7] For instance, the mean treatment costs per drug-sensitive (DS-TB) TB patient are $39 to $858 in Africa, $149 to $724 in China and €3,427 to €10,282 in the EU. [4 6 8]

Catastrophic health expenditure (CHE) is a widely used index to calculate the burden of medical costs upon households at a national level and is often incurred by households who have to pay out-of-pocket (OOP) for health services.[9 10] Thus, the family may have to sacrifice the consumption of other goods and services necessary for their well-being.[10] There are various definitions of CHE and no one gold standard for measuring it. [11 12] WHO has defined CHE as OOP payment for direct health care spending exceeds 40% of a household's capacity, [10] while many studies defined CHE as OOP payment for health-care that exceeds a specified proportion of annual household income which often set the threshold at 10%-25%. [11 13 14] According to the End TB Strategy, it is now recommended to measure catastrophic costs incurred when the total costs exceed 20% of the annual household income.[15] Eradicating catastrophic costs for TB-affected families is essential to ascertain the progress of universal health coverage and social protection. However, the data about CHE for TB care are limited.

A recent systematic review indicated that approximately a third of households with a TB patient experienced TB-associated catastrophic costs.[5] For instance, the incidence of CHE for TB was 32.4% in Puducherry of India, 78.1% in Benin, and 44% in Nigeria. [11 16] In China, more than two-thirds of TB-related households experienced CHE overall, and 46.7 % of the households still experienced CHE after reimbursement by NCMS in rural areas.[17 18] Additionally, households with members having TB are approximately 1.8 times more likely to suffer CHE than those without.[19] Therefore, it is essential to reduce the economic burden of TB patients and save their families from CHE.

To reduce the economic burden on TB patients, a "free TB service policy" has been implemented in many countries.[8 20 21] Although the policy has been conducted for many years, TB patients still suffer from the high costs of TB treatment, which often forces their families into catastrophe and poverty in low- and middle-income countries, such as in China, India, Peru, Ethiopia, and Tajikistan. [16-18 22 23] In China, the "free TB service policy" includes free X-ray examination and free sputum smear test for patients once with suspected TB at first visit, free first-line anti-TB drugs (6 months for new patients and 8 months if previously treated), three free sputum smear tests, and one free X-ray test during anti-TB treatment.[18] Also, there are three essential government-led complementary health insurances to cover some extra expenditures beyond the "free-TB service policy" in China, including the New Cooperative Medical Scheme (NCMS) for rural farmers, the Medical Insurance for Urban Residents scheme (MIUR) and the Medical Insurance for Urban Employees (MIUE). [18] Health insurance is the least for rural farmers followed by that for local urban residents, while it for urban employees is the most. However, the financial protection remains insufficient though China has dramatically expanded health insurance coverage. [19]

According to a few studies conducted in China, Nigeria, Indonesia and Benin, the factors determining CHE for TB care include age, sex, number of family members, urban residence, educational level, being a breadwinner, job loss, health insurance status, poor households, adverse pre-diagnosis stage, treatment at a private facility, ratio of patient income to total household income, hospitalization, and previous of TB treatment.[11 13 17 24] However, the factors associated with CHE among TB patients remain not well elucidated. Considering fact that delay in TB diagnosis was not only a significant challenge of TB control and prevention programs in low- and middle-income settings but also was an vital risk factor increases the risk of transmission and economic costs to patients and communities at large, [25 26] we planned to explore the associations between the patient and diagnostic delay and CHE for TB care. Also, the extent of CHE and other risk factors related to CHE are investigated as well. Consequently, a cross-sectional study was performed in Chongqing municipality, which was an economic and industrial hub of the southwest region of China with a heavy burden of TB.

METHODS

Study sites and participants

This cross-sectional study was conducted in four counties of Chongqing from March 2013 to August 2014. The TB epidemic was high in Chongqing, which ranked in the top 10 among the most upper TB burden provinces in China. The TB notification rate of Chongqing in 2015 had declined to 70.8 cases per 100,000 populations from the peak of 106 cases per 100,000 in 2005, but still above the average TB incidence of China. Recent years, approximately 20,000 patients were reported with TB in Chongqing, making up 2.5% of all notified TB cases in China.[27] There are 39 districts/counties in Chongqing. According to the Chongqing Statistical Yearbook 2015, the real GDP per capita was 47850 RMB. Urban population accounts for 59.6% of the total population. The four counties with similar levels of economic development and similar human geographical environment were selected as the study sites. These four counties are among the middle-income counties in Chongqing, have both villages and cities, and are in the process of urbanization. In Chongqing, the reimbursement ratio in different counties was different. The reimbursement ratio of medical expenses was 0-60% by MIUE, 0-50% by MIUR and 0-45% by NCMS for outpatients and 65% by MIUE, 35% by MIUR and 35% by NCMS for inpatients in Chongqing.

From March to December in 2013, all registered active pulmonary TB (PTB) patients excluding those aged below 16 years or with mental disorders were recruited consecutively in the designated TB medical institutes of the four counties. Because extrapulmonary TB, tuberculous pleuritis, drug-resistant pulmonary TB and PTB patients not registered in counties' designated TB medical institutes were not covered by the free TB service policy during the period of research, only registered active pulmonary TB were included. Totally, 1290 PTB patients were qualified, of who 61 refused to participate due to poor clinical conditions and 30 questionnaires were not completed. Thus, a total of 1199 patients were included in the study. All participants had access to free TB treatment and were prospectively followed throughout the treatment period.

Data collection

All data were collected in these four counties' designated TB medical institutes. The study was based on a well-structured questionnaire and patients' medical records. All participants at the local TB-designated medical institutes were interviewed face to face by a trained TB staff using the questionnaire. The following data were obtained: covered personal information, socioeconomic information (age, sex, residence, occupation, education, marital status, number of family members, household income, etc.), and history of disease (forms of TB, date of first onset of suspected TB symptoms, date of first visit to any health provider, date of PTB diagnosis, and direct medical costs for TB care). Clinic information (patient delay, diagnostic delay, forms of TB, health insurance status and hospitalization) and exact date of TB diagnosis were checked against the patients' medical records. A 6-month or 8-month treatment regimen was recommended by the WHO. The follow-up survey was conducted with TB patients till completion of the treatment. The treatment costs were collected every month by the trained TB staff. The staff interviewed each participant and then checked invoices or financial accounting systems to ensure accuracy. OOP payments and reimbursements of the direct medical costs in different periods of services (pre-diagnosis, diagnosis, and treatment) were collected per individual and checked invoices or financial accounting systems as well. All costs were indicated in Ren Min Bi (RMB).

Definitions

Pulmonary TB was diagnosed based on the pathological, clinical, and radiological findings, and confirmed through bacteriological and histological examinations, which were strictly performed according to the Chinese Diagnostic criteria for PTB (WS-288-2008) .[28]

Patient delay is determined as a time interval from the first onset of TB symptoms to the first visit to any health provider; if the time interval lasts for more than 14 days, it is considered as a "delay".[29]

Diagnostic delay is defined as a time interval between a patient's first visit to any health provider and the final diagnosis as TB; if the time interval lasts for more than 14 days, it is considered as a "delay".[29]

Pre-diagnosis is the period from the onset of TB symptoms to the first visit to a local designated TB medical institution. **The period of diagnosis** is from the first visit to a local designated TB medical institution to the diagnosis of TB. **The period of treatment** is the full course of TB treatment.

Direct medical costs are composed of consultation fees, laboratory tests, X-rays, medical tests, and drugs during the period of pre-diagnosis, diagnosis, and treatment.

OOP payments are regarded as the direct medical costs paid by patients themselves.

Measuring the incidence and intensity of catastrophic health expenditure

CHE is usually assessed by incidence and intensity. According to the definition of CHE in several previous studies[11 13 14], we defined 'catastrophic' as the OOP payments of total medical costs for TB care exceeding 10% of the annual household income in this study. Head count (HC) is used to measure the incidence of CHE, while the mean gap (MG) and mean positive gap (MPG) are used to reflect the intensity of CHE. HC means the percentage of households whose OOP payments equal or exceed 10% of their annual income to the total number of households. MG is the average amount by which OOP payments, as a proportion of annual household income, exceeds the threshold. MPG is equal to MG/HC, the excess expenditure per household experiencing CHE. The methods used in measuring HC, MG, and MPG are based on the previous study.[14]

Statistical analysis

Data were double entered and checked using EPI Data Version 3. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 18.0 (SPSS Inc. Chicago, IL, USA). Continuous variables were presented as medians and interquartile (IQR) ranges, while categorical variables were presented as numbers and percentages (%). Pearson's chi-square test was used in univariate analyses to identify factors associated with the CHE and odds ratios with 95% confidence intervals (95% CIs) were computed. All variables with a *P*-value <0.05 in the univariate analysis were included in the multivariate model. A multivariate logistic regression model using a backward elimination method was used to assess the determinants of CHE and to calculate adjusted odds ratios (aOR) and 95% CIs. A two-sided *P*-value of <0.05 was considered statistically significant.

Ethics approval

The study was approved by the Ethical Committee of the Chongqing Institute of Tuberculosis Prevention and Treatment, Chongqing, China. Written informed consent was obtained from each participant prior to inclusion in the survey.

Patient and public involvement

Not applicable to this study.

RESULTS

Patient characteristics

The characteristics of these pulmonary TB patients are summarized in Table 1. A total of 1199 PTB patients were enrolled in the study. The proportion of men to women involved in this study is 2.3:1. More than three-quarters of patients were in their labor age (16–59 years), and the average age of the patients was 43.9 years, with a median age of 44 years. Approximately 30% of patients were migrants. Two-thirds of patients were married and received at least junior high school education. About one-quarter of patients were unemployed, about 30% patients were peasants and 8.0% patients were students. Approximately three-quarters of the households had one to three family members. In the majority, 89.2% of the patients had health insurance and about half of the patients had NCMS. Only 15.9% of patients had been hospitalized in the intensive period. Approximately three-quarters of patients were smearing negative. Of the total participants, 53.0% and 43.0% patients experienced patient and diagnostic delay, with a median (IQR) of 16(3-52) and 9 (3-33) days measured in days, respectively. Patients' average annual household income was 42,200 RMB, with a median (IQR) of 35,000 RMB (20,000–56,000 RMB).

Direct medical costs for TB in different periods of medical treatment

The OOP costs and health insurance reimbursement during the pre-diagnosis, diagnosis, and treatment period are presented in Table 2. Expenses in the pre-diagnosis period were all paid by OOP, accounting for nearly half of the total cost. Excluding the fees covered by free TB service policy, around 7% of costs were reimbursed by health insurance during the treatment period, but no costs were reimbursed during the period of pre-diagnosis and diagnosis. The median total direct medical costs paid by a TB patient were 4085 RMB, about 93% of which was paid by patients themselves.

Incidence and intensity of CHE

Table 3 shows that 52.8% (633/1199) of all TB-related households experienced CHE. On average, healthcare payments for TB were 18.1% higher than the threshold value (10%). For households experiencing CHE, the mean positive gap was 34.2% higher than the threshold. The incidence of CHE in patients experiencing patient delay or diagnostic delay was 11% or 9.7% more than those not sufferring patient delay or diagnostic delay, respectively. The intensity measure was also higher for the group of experiencing patient delay or diagnostic delay than the group without delay.

Determinants of CHE

Table 4 shows the influence of different variables on CHE for TB care using a Pearson's chi-square test. There are many factors associated with CHE, including patient delay, diagnostic delay, sex, age, resident status, marital status, educational level, occupation, health insurance status, and hospitalization. Those factors were included in the multivariate logistic regression.

Logistic regression produced a wide range of determinants related to catastrophic health expenditure (Table 5). Independent determinants of CHE were: patient delay (aOR, 1.342; 95% confidence interval (CI), 1.043–1.726), diagnostic delay (aOR, 1.540; 95% CI, 1.195–1.983), male (aOR, 1.141; 95% CI, 1.066–1.877), age≥60 years (aOR, 2.117; 95% CI, 1.281–3.498), inhabitant (aOR, 1.455; 95% CI, 1.084–1.951), divorced or a widow (aOR, 2.211; 95% CI, 1.093–4.475), peasant (aOR, 2.205; 95% CI, 1.522–3.194), high school and above (aOR, 0.542; 95% CI, 0.356–0.826) and as NCMS membership (aOR, 1.688; 95% CI, 1.071-2.661). However, hospitalization was not related to CHE after controlling for other variables (aOR, 1.342; 95% CI, 0.950-1.897).

DISCUSSION

For the first time, global TB targets aimed to decrease catastrophic costs associated with TB. Evaluating the incidence and intensity of TB-related CHE not only provided insight into the universal health coverage (UHC) but also reflected the economic burden of TB patients and their families. In this study, the incidence of CHE for TB care was 52.8% after reimbursement, which was lower than the reported rates of 66.8%, 65% and 78.1% in other cities of China, Nigeria, and Benin, respectively, using the same CHE measurement methods. [11 13 17] However, the figure was a little higher than that in Indonesia (50%) when they involved in MDR-TB patients, [24] and much higher than the rate of CHE incurred by general population or patients with non-communicable chronic disease in China. [19] In that TB inequitably affects poor people and households in poorer economic quintiles are more at risk of suffering CHE and impoverishment.[19 30] The mean gap was 18.1% and the mean positive gap was 34.2% for TB in our study, both were higher than that in Nigeria (6.0%, 9.3%) [11 13] and in Benin (7.8%,14.8%) [13] but lower than that in other cities of China (40.8%, 62.2%) [17] because we did not take non-medical costs into account while other studies did. Although many studies claimed that non-medical costs and indirect costs related to TB care were a severe financial burden for TB patients and their households, [5 31 32] some studies found that these costs were not high compared with direct medical costs.[18 33 34] Thus, the extent of patients incurring catastrophic costs in this study population may be underestimated but remain reliable.

Although all patients in this study have access to free TB treatment and the majority of them have health insurance, they had a heavy financial burden of out-of-pocket payments and more than half of them incurred catastrophic costs. The phenomena is common in China, [8 18 35] there may be three reasons to explain it: (i) Many associated health-care costs are not covered in the free TB policy, for example, payment for drugs of ancillary and liver protection, and extra diagnostic tests.[2 8 36] (ii) Driven by profits, doctors may prescribe additional medicines and tests.[37] (iii) The reimbursement ratio for outpatient services is low and often ignored, as well as the actual implementation strength of inpatients reimbursement was weak. [38-40] Besides, we also found nearly half of all OOP payments were paid before diagnosis, which was similar to many previous studies. [6 23 41] This cost had aroused particular concern in that it not only reflected the economic burden on families for obtaining a diagnosis, but also may act as an obstacle for poor patients to access timely TB care.

Delay in diagnosis had a massive impact on TB transmission in the community, aggravating the severity and mortality, resulting in an unfavorable treatment outcome and significantly increasing total patient costs.[42-45] This study, we further investigated the relationship between patient/diagnostic delay and CHE for TB care among TB patients. We found about half patients encountered patient delay or diagnostic delay, who incurred more serious CHE than those without delay. Also, we demonstrated that patient delay and diagnostic delay were crucial determinants of CHE. Consistently, Laokri et al found that patient delay over 1 month was an independent determinant of incurring catastrophic expenditure. [11] In addition, a large number of studies had revealed that patient delay and diagnostic delay were independent factors associated with total out-of-pocket costs. [23 25 34 35 46] Actually, prolonged delays in TB diagnosis are still prevailing problems in many countries in many low- and middle-income countries, such as in Ethiopia，Zambia，Tanzania，Mozambique，Indonesia and so on. [43 47-50] Therefore, it is vital to take measures to shorten the delay in diagnosis.

Patient delay may be related to the fact that patients do not take minor symptoms seriously in its early stage and will pay greater attention to it until symptoms become more severe. [38] In addition, many sociodemographic and economic factors contribute to patient delay. [29] Therefore, we should adopt comprehensive measures to facilitate patients to seek care early, such as strengthening TB health education to the public and adopting a precise poverty alleviation to increase the income of poverty-stricken patients. Early diagnosis is difficult due to the vast percentage of asymptomatic PTB patients and non-availability of rapid, accurate, and cost-effective tests in many settings.[51] In this study, only one-quarter of patients has been confirmed bacteriological and mainly based on traditional methods. Rapid molecular methods were not frequently used in Chongqing in 2013. Hence, more rapid, accurate, and affordable methods are urgently needed to shorten the time of diagnosis.

Multivariate regression analysis indicated that demographic factors such as age, sex, marital status, occupation, resident status, and education level independently affected the risk of catastrophic costs for TB care. Consistent with previous studies in Nigeria and other cities of China, age was an essential determinant of CHE, [11 17] but only patients who were ≥60 years significantly affect CHE after removing the confounding factors in our study. Usually, men were the breadwinner of a family, thus we and Ukwaja et al found male patients were more easily to experience CHE, [11] but Zhou et al showed that gender had no significant associations with CHE.[17] In contrast with a previous study in China, [17] we found marital status was an independent factor related with CHE, but the family size and hospitalization were not determinants of CHE because we grouped different segments of the household population. Besides, only 15.9% of patients had been hospitalized during the treatment, much lower than the figure in a previous study of 55%.[17] Generally, people with low educational level also have less economic income, and thus we all demonstrated patients with less education were more likely to incur CHE.[11 13] Compared with inhabitants, migrants had a smaller proportion of patients being male, elderly, or peasant and a higher proportion of patients with high educational level, thus migrant patients were less likely to experience CHE compared with inhabitant patients.

We found that patients covered by NCMS, compared with those without any type of health insurance, were more likely to experience CHE. A series of studies conducted in China have demonstrated that NCMS could not relieve the financial burden of TB-related medical costs and had a partial effect on protecting TB-related households from CHE. [17 39 52] Compared with patients not covered by NCMS, patients with TB covered by the NCMS only had a 5% higher reimbursement rate regarding outpatient and total medical costs in Zhejiang and Sichuan provinces of

China. [39] NCMS is designed exclusively for rural residents particular for peasants, who are usually in low-income status. Also, the majority of patients without health insurance were migrants. In contrast with the previous study in China, we did not find MIUR or MIUE has any positive effect on reducing CHE. [17] It may be due to in-effective reimbursement rates of health insurance in China. Although health insurance had reimbursement to both outpatient and inpatient services at a certain proportion, a lot of areas existed to ignore reimbursement to varying degrees, especially for outpatient services.[40] In research, there was no reimbursement for medical costs during pre-diagnosis and diagnosis, which indicated that the implementation effect of reimbursement rates was weak. Thus, so far health insurance plan did not actually help to relieve the financial burden for patients with PTB in China. Consequently, the health insurance policy should be implemented effectively.

This study has some limitations. Firstly, some data collected based on self-reporting could not be checked, which may be subjected to recall bias. Secondly, the data in this study were collected four years ago, and the per capita income has increased from 2014 to 2017. However, China's free TB service policy has not changed in recent years, and TB inequitably affects poor people. Therefore, the CHE remains a problem for TB now in China. Thirdly, we did not use the new definition of "catastrophic costs due to TB" recommended by WHO, which is the total [direct and indirect] costs exceeding 20% of annual household income recently.[15] Although the threshold (10%) we set was lower than the new definition and we did not take indirect costs into account, it may also be valuable to present the proportion of TB-affected patients (and their households) facing catastrophic costs if direct costs alone are counted.[15] Furthermore, the data about the CHE associated with TB were limited worldwide and correlational research has been conducted only in three cities in China. Consequently, our study may add some new data of CHE for TB care in China.

CONCLUSION

Although all patients have access to free TB service policy and the majority of them have health insurance, TB patients still shoulder a high burden of OOP payments and experience high incidence and intensity of CHE for TB care in Chongqing, China. Except for social-demographic factors, patient delay and diagnostic delay are essential determinants of CHE for TB care, which highlights the significance of early care seeking and early diagnosis. In addition, NCMS aggravates the catastrophic costs, which implicates that it is essential to improve the actual reimbursement rates of health insurance, especially for outpatients. Furthermore, more fine-tuned interventions such as precise poverty alleviation are essential to taken for vulnerable TB patients to reduce their catastrophic costs. Overall, our results have provided some baseline data about CHE for TB, which may give some clues for a further prospective study.

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Contributors DH: designed the study and drafted the manuscript; YL: designed the study, implemented the survey and analyzed the data; WD: designed the study, analyzed the data and drafted the manuscript; WZ, CW, QW, and YY: implemented the survey and collected data; HL: analyzed the data and drafted the manuscript. All authors read and approved the final version of the manuscript.

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Competing interests None

Patient consent Obtained

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Data sharing statement No additional data are available

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Table 1 Social-demographic and clinical characteristics of the study participants (n=1199).

Variables	Patients No.	Percent (%)
Sex		
Male	839	70.0
Female	360	30.0
Age		
≤40	532	44.4
41-59	402	33.5
≥60	265	22.1
Residential status		
Inhabitant	848	70.7
Migrant	351	29.3
Marital status		
Single	340	28.4
Married	795	66.3
Divorced/widow	64	5.3
Educational level		
Primary or below	382	31.9
Junior high	356	29.7

High school and above	461	38.4
Occupation		
Unemployed	302	25.2
Employed	327	27.3
Peasant	353	29.4
Student	96	8.0
Retiree	121	10.1
Family size		
1~3	887	74.0
4~8	312	26.0
Health insurance status		
None	130	10.8
NCMS	548	45.7
MIUR	230	19.2
MIUE	249	20.8
Other insurance plan	42	3.5
Hospitalization		
Yes	191	15.9
No	1008	84.1

Forms of TB		
Smear-negative PTB	892	74.4
Smear-positive PTB	307	25.6
Patient delay		
Yes	635	53.0
No	564	47.0
Median (IQR) (days)	16 (3-52)	
Diagnostic delay		
Yes	516	43.0
No	683	57.0
Median (IQR) (days)	9 (3-33)	
Household annual income(RMB)		
Mean	42,200	
Median (IQR) (days)	35,000(20,000-56,000)	

Note: IQR represents interquartile range. TB represents tuberculosis.

NCMS, New Cooperative Medical Scheme; MIUR, Medical Insurance for Urban Residents; MIUE, Medical Insurance for Urban Employees.

Table 2 Direct medical costs for TB care in different periods of services (n=1199). RMB

Costs in different periods (services)	Out-of-pockets		Health insurance reimbursement		Total	
	Median	IQR	Median	IQR	Median	IQR
Pre-diagnosis	750	250-3000	0	0	750	250-3000
Diagnosis*	157	121-250	0	0	157	121-250
Treatment #	1792	834-3050	0	0-501	1966	1000-3723
Total	3789	2106-6645	0	0-501	4085	2222-7371

Note: Expenses excludes the costs of the free-TB policy reduction and exemption. *The expenses excluded the cost of one-time free chest X-ray and sputum smear examination. #The expenses excluded anti-TB drugs (6 months for new patients, 8 months if previously treated), three times sputum smear tests and one time X-ray test during anti-TB treatment. IQR: interquartile range.

Table 3 Incidence and intensity of CHE for TB care stratified by patient and diagnostic delay.

Catastrophic health expenditure	Patient delay		Diagnostic delay		All
	Yes	No	Yes	No	(n=1199)
Head count (%)	58.0	47.0	58.3	48.6	52.8
Mean gap (%)	21.1	14.6	19.3	17.2	18.1
Mean positive gap (%)	36.5	31.1	33.0	35.3	34.2

Table 4 Single factor analysis of catastrophic health expenditure in patients.

Variables	Experiencing CHE (n,%)	Not experiencing CHE(n,%)	OR (95% CI)	Chi-square	*P-value*
Patient delay					
No	265 (47.0)	299(53.0)	1.0		
Yes	368(58.0)	267(42.0)	1.555(1.238-1.954)	14.415	0.000
Diagnostic delay					
No	332(48.6)	351(51.4)	1.0		
Yes	301(58.3)	215(41.7)	1.480(1.175-1.864)	11.153	0.001
Sex					
Female	151(41.9)	209(58.1)	1.0		
Male	482(57.4)	357(42.6)	1.869(1.455-2.400)	24.300	0.000

Age					
≤40	200(37.6)	332(62.4)	1.0		
41-59	242(60.2)	160(39.8)	2.511(1.925-3.275)	46.936	0.000
≥60	191(72.1)	74(27.9)	4.285(3.109-5.904)	84.156	0.000
Resident status					
Migrant	129(36.8)	222(63.2)	1.0		
Inhabitant	504(59.4)	344(40.6)	2.521(1.951-3.259)	51.246	0.000
Marital status					
Single	133(39.1)	207(60.9)	1.0		
Married	450(56.7)	344(43.3)	2.036(1.571-2.638)	29.377	0.000
Divorced/widow	50(76.9)	15(23.1)	5.188(2.800-9.613)	31.488	0.000

Educational level					
Primary or below	277(72.5)	105(27.5)	1.0		
Junior high	190(53.4)	166(46.6)	0.434(0.319-0.589)	29.058	0.000
High school and above	166(36.0)	295(64.0)	0.213(0.159-0.286)	111.600	0.000
Occupation					
Unemployed	139(46.0)	163(54.0)	1.0		
Employed	128(39.1)	199(60.9)	0.754(0.549-1.036)	3.044	0.081
Peasant	261(73.9)	92(26.1)	3.327(2.396-4.519)	53.331	0.000
Student	37(38.5)	59(61.5)	0.735(0.460-1.176)	1.654	0.198
Retiree	68(56.2)	53(43.8)	1.505(0.984-2.300)	3.577	0.059
Family size					

1~3	479(54.0)	408(46.0)	1.0		
4~8	154(49.4)	158(50.6)	0.830(0.641-1.075)	1.997	0.158
Health insurance status					
None	47(36.2)	83(63.8)	1.0		
NCMS	351(64.1)	197(35.9)	3.146(2.113-4.685)	31.853	0.000
MIUR	111(48.3)	119(51.7)	1.647(1.059-2.561)	4.910	0.027
MIUE	109(43.8)	140(56.2)	1.675(0.888-2.128)	2.042	0.153
Other insurance plan	15(35.7)	27(64.3)	0.981(0.475-2.027)	0.003	0.959
Hospitalization					
No	517(51.3)	491(48.7)	1.0		
Yes	116(60.7)	75(39.3)	1.469(1.071-2.014)	5.746	0.017

Forms of TB					
Smear-negative PTB	480(53.8)	412(46.2)	1.0		
Smear-positive PTB	153(49.8)	154(50.2)	0.853(0.658-1.105)	1.448	0.229

Note: PTB, pulmonary tuberculosis. OR, odds ratio. 95% CI, 95% confidence interval for the odds ratio.

NCMS, New Cooperative Medical Scheme; MIUR, Medical Insurance for Urban Residents; MIUE, Medical Insurance for Urban Employees.

Table 5 Independent determinants of CHE for TB care using a logistic regression model.

Variables	β	Standard error	Wald	*P-value*	OR(95% CI)
Patient delay (Ref: Without delay)	0.294	0.128	5.251	0.022	1.342(1.043-1.726)
Diagnostic delay (Ref: Without delay)	0.431	0.129	11.145	0.001	1.540(1.195-1.983)

Sex (Ref: Female)	0.347	0.144	5.764	0.016	1.141(1.066-1.877)
Age (Ref: ≤40)			8.557	0.014	
41-59	0.336	0.187	3.216	0.073	1.399(0.969-2.019)
≥60	0.75	0.256	8.554	0.003	2.117(1.281-3.498)
Resident status (Ref: Migrant)	0.375	0.15	6.247	0.012	1.455(1.084-1.951)
Marital status (Ref: Single)			6.239	0.044	
Married	-0.005	0.192	0.001	0.977	0.995(0.683-1.448)
Divorced/widow	0.794	0.36	4.87	0.027	2.211(1.093-4.475)
Educational level (Ref: Primary or below)			8.224	0.016	
Junior high	-0.294	0.187	2.485	0.115	0.745(0.517-1.074)
High school and above	-0.612	0.215	8.114	0.004	0.542(0.356-0.826)

Occupation (Ref: Unemployed)			28.975	0.000	
Employed	0.025	0.176	0.02	0.887	1.025(0.726-1.448)
Peasant	0.791	0.189	17.475	0.000	2.205(1.522-3.194)
Student	0.368	0.279	1.745	0.187	1.446(0.837-2.497)
Retiree	-0.318	0.257	1.53	0.216	0.727(0.439-1.204)
Health insurance (Ref: none)			6.355	0.174	
NCMS	0.524	0.232	5.087	0.024	1.688(1.071-2.661)
MIUR	0.358	0.248	2.085	0.149	1.431(0.880-2.327)
MIUE	0.158	0.266	0.353	0.553	1.171(0.695-1.974)
Other insurance plan	0.169	0.398	0.181	0.671	1.184(0.543-2.583)
Hospitalization (Ref: not hospitalization)	0.294	0.176	2.784	0.095	1.342(0.950-1.897)

Note: The variables that showed association with CHE ($p<0.05$) in the univariate analysis were included in the multivariate model. OR, odds ratio. 95% CI,95%

confidence interval for the odds ratio. Ref, reference group.

NCMS, New Cooperative Medical Scheme; MIUR, Medical Insurance for Urban Residents; MIUE, Medical Insurance for Urban Employees.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6 line 38-54
Methods			
Study design	4	Present key elements of study design early in the paper	Page 7 line 9-11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7 line 9-41
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 7 line 43-59
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 8 line 49-58 Page 9 line 3-58
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 8-9

Bias	9	Describe any efforts to address potential sources of bias	Page 8 line 11-46
Study size	10	Explain how the study size was arrived at	Page 7 line 43-59
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 10 line 6-26
		(*b*) Describe any methods used to examine subgroups and interactions	Page 10 line 6-26
		(*c*) Explain how missing data were addressed	No missing data
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	None
		(*e*) Describe any sensitivity analyses	None
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7 line 43-60
		(b) Give reasons for non-participation at each stage	Page 7 line 55-60
		(c) Consider use of a flow diagram	None
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 Page 11
		(b) Indicate number of participants with missing data for each variable of interest	No participant with missing data
Outcome data	15*	Report numbers of outcome events or summary measures	Table 2-5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Table 4 and 5

		interval). Make clear which confounders were adjusted for and why they were included	Page 12 line 18-47
		(*b*) Report category boundaries when continuous variables were categorized	Table 4 and 5
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	None
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17 line4-25
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 16 line 30-57
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 17 line 51-54

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The extent and determinants of catastrophic health expenditure for tuberculosis care in Chongqing Municipality, China: a cross-sectional study

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Title page

The extent and determinants of catastrophic health expenditure for tuberculosis care in Chongqing Municipality, China: a cross-sectional study

Running title: The extent and determinants of CHE for TB care

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ABSTRACT

Objective: To investigate the extent and associations of patient /diagnostic delay and other potential factors with catastrophic health expenditure (CHE) for tuberculosis (TB) care in Chongqing Municipality, China.

Design: A cross-sectional study

Setting: Four counties of Chongqing municipality, China

Participants: A total of 1199 patients with active pulmonary TB beyond 16 years and without mental disorders were consecutively recruited in the four counties' designated TB medical institutions.

Outcome measures The incidence and intensity of CHE for TB care were described. The association between patients' "social-demographic and clinical characteristics such as patient delay, diagnostic delay, forms of TB, health insurance status and hospitalization" and CHE were analyzed using univariate and multivariate logistic regression.

Results The incidence of CHE was 52.8% and out-of-pocket payments(OOP) were 93% of the total costs for TB care. Compared with patients without delay, the incidence and intensity of CHE were higher in patients who had patient delay or diagnostic delay. Patients who experienced patient delay or diagnostic delay, who was a male, elderly (≥60 years), an inhabitant, a peasant, divorced/widow, the New Cooperative Medical Scheme (NCMS) membership had greater risks of incurring CHE for TB care. Having a higher educational level appeared to be a protective factor. However, hospitalization was not associated with CHE after controlling for other variables.

Conclusion The incidence and intensity of CHE for TB care are high, which provides baseline data about catastrophic costs that TB-related households faced in Chongqing of China. Variety of determinants of CHE implicate that it is essential to

take effective measures to promote early seeking care and early diagnosis, improve the actual reimbursement rates of health insurance, especially for outpatients, and need more fine-tuned interventions such as precise poverty alleviation to reduce catastrophic costs of the vulnerable population.

Keywords: Tuberculosis, Catastrophic health expenditure, Patient delay, Diagnostic delay, Health insurance

Strengths and limitations of this study

1. The study provides new data about TB-related households facing catastrophic costs and the determinants of CHE for TB care in China.

2. The study highlights the importance of early care seeking and diagnosis of TB.

3. Our findings will provide valuable information for policymakers to take fine-tuned interventions to decrease catastrophic costs for vulnerable TB-affected households.

4. Some self-reported data such as dates for onset of symptoms and healthcare seeking may have been affected by recall bias.

5. The non-medical costs and indirect costs were not taken into account, which may underestimate the extent of CHE for TB care and should be considered in the future study.

INTRODUCTION

Tuberculosis (TB) is one of the top 10 causes of death and the leading cause of a single infectious disease (above HIV/AIDS) worldwide. In 2017, about 10.0 million people developed TB disease and 1.6 million deaths caused by TB globally. China has the second largest burden of TB in the world, accounting for 9% of all cases.[1] Poverty is not only strongly associated with TB incidence, but also a cause and a devastating outcome of TB.[2] Therefore, TB is not only a serious infectious disease but also a severe public health problem worldwide. "End TB strategy," a plan announced by the World Health Organization (WHO) to end the global TB epidemic, aims to reduce TB death rate by 95% and cut new cases by 90% between 2015 and 2035, and no affected families face catastrophic costs due to TB by 2020.[3] However, the projected 2015 baseline is not yet available.[3] Achieving zero TB-induced catastrophic costs for households is too great to realize because the financial burden for patients with TB is extremely high in low-income, middle-income and high-income countries. [4-7] For instance, the mean treatment costs per drug-sensitive (DS-TB) TB patient are $39 to $858 in Africa, $149 to $724 in China and €3,427 to €10,282 in the EU. [4 6 8]

Catastrophic health expenditure (CHE) is a widely used index to calculate the burden of medical costs upon households at a national level and is often incurred by households who have to pay out-of-pockets for health services.[9 10] Thus, the family may have to sacrifice the consumption of other goods and services necessary for their well-being.[10] There are various definitions of CHE and no one gold standard for measuring it. [11 12] WHO has defined CHE as OOP payment for direct health care spending exceeds 40% of a household's capacity, [10] while many studies defined CHE as OOP payment for health-care that exceeds a specified proportion of annual household income which often set the threshold at 10%-25%. [11 13 14] According to the End TB Strategy, it is now recommended to measure catastrophic costs incurred when the total costs exceed 20% of the annual household income.[15] Eradicating catastrophic costs for TB-affected families is essential to ascertain the progress of universal health coverage and social protection. However, the data about CHE for TB care are limited.

A recent systematic review indicated that approximately a third of households with a TB patient experienced TB-associated catastrophic costs.[5] For instance, the incidence of CHE for TB was 32.4% in Puducherry of India, 78.1% in Benin, and 44% in Nigeria. [11 16] In China, more than two-thirds of TB-related households experienced CHE overall, and 46.7 % of the households still experienced CHE after reimbursement by the New Cooperative Medical Scheme (NCMS) in rural areas.[17 18] Additionally, households with members having TB are approximately 1.8 times more likely to suffer CHE than those without.[19] Therefore, it is essential to reduce the economic burden of patients with TB and save their families from CHE.

To reduce the economic burden on patients with TB, a "free TB service policy" has been implemented in many countries.[8 20 21] Although the policy has been conducted for many years, patients with TB still suffer from the high costs of TB treatment, which often forces their families into catastrophe and poverty in low- and middle-income countries, such as in China, India, Peru, Ethiopia, and Tajikistan. [16-18 22 23] In China, the "free TB service policy" includes free X-ray examination and free sputum smear test for patients once with suspected TB at first visit, free first-line anti-TB drugs (6 months for new patients and 8 months if previously treated), three free sputum smear tests, and one free X-ray test during anti-TB treatment.[18] Also, there are three essential government-led complementary health insurances to cover some extra expenditures beyond the "free-TB service policy" in China, including the NCMS for rural farmers, the Medical Insurance for Urban Residents scheme (MIUR) and the Medical Insurance for Urban Employees (MIUE). [18] Health insurance is the least for rural farmers followed by that for local urban residents, while it for urban employees is the most. However, the financial protection remains insufficient though China has dramatically expanded health insurance coverage. [19]

According to a few studies conducted in China, Nigeria, Indonesia and Benin, the factors determining CHE for TB care include age, sex, number of family members, urban residence, educational level, being a breadwinner, job loss, health insurance status, poor households, adverse pre-diagnosis stage, treatment at a private facility, ratio of patient income to total household income, hospitalization, and previous of TB treatment.[11 13 17 24] However, the factors associated with CHE among patients with TB remain not well elucidated. Considering fact that delay in TB diagnosis was not only a significant challenge of TB control and prevention programs in low- and middle-income settings but also was an vital risk factor increases the risk of transmission and economic costs to patients and communities at large, [25 26] we planned to explore the associations between the patient and diagnostic delay and CHE for TB care. Also, the extent of CHE and other risk factors related to CHE are investigated as well. Consequently, a cross-sectional study was performed in Chongqing municipality, which was an economic and industrial hub of the southwest region of China with a heavy burden of TB.

METHODS

Study sites and participants

This cross-sectional study was conducted in four counties of Chongqing from March 2013 to August 2014. The TB epidemic was high in Chongqing, which ranked in the top 10 among the most upper TB burden provinces in China. The TB notification rate of Chongqing in 2015 had declined to 70.8 cases per 100,000 populations from the peak of 106 cases per 100,000 in 2005, but still above the average TB incidence of China. Recent years, approximately 20,000 patients were reported with TB in Chongqing, making up 2.5% of all notified TB cases in China.[27] There are 39 districts/counties in Chongqing. According to the Chongqing Statistical Yearbook 2015, the real GDP per capita was 47850 RMB. Urban population accounts for 59.6% of the total population. The four counties with similar levels of economic development and similar human geographical environment were selected as the study sites. These four counties are among the middle-income counties in Chongqing, have both villages and cities, and are in the process of urbanization. In Chongqing, the reimbursement ratio in different counties was different. The reimbursement ratio of medical expenses was 0-60% by MIUE, 0-50% by MIUR and 0-45% by NCMS for outpatients and 65% by MIUE, 35% by MIUR and 35% by NCMS for inpatients in Chongqing.

From March to December in 2013, all registered active pulmonary TB (PTB) patients excluding those aged below 16 years or with mental disorders were recruited consecutively in the designated TB medical institutes of the four counties. Because extrapulmonary TB, tuberculous pleuritis, drug-resistant pulmonary TB and patients with PTB not registered in counties' designated TB medical institutes were not covered by the free TB service policy during the period of research, only registered active pulmonary TB were included. Totally, 1290 patients with PTB were qualified, of who 61 refused to participate due to poor clinical conditions and 30 questionnaires were not completed. Thus, a total of 1199 patients were included in the study. All participants had access to free TB treatment and were prospectively followed throughout the treatment period.

Data collection

All data were collected in these four counties' designated TB medical institutes. The study was based on a well-structured questionnaire and patients' medical records. All participants at the local TB-designated medical institutes were interviewed face to face by a trained TB staff using the questionnaire. The following data were obtained: covered personal information, socioeconomic information (age, sex, residence, occupation, education, marital status, number of family members, household income, etc.), and history of disease (forms of TB, date of first onset of suspected TB symptoms, date of first visit to any health provider, date of PTB diagnosis, and direct medical costs for TB care). Clinic information (patient delay, diagnostic delay, forms of TB, health insurance status and hospitalization) and exact date of TB diagnosis were checked against the patients' medical records. A 6-month or 8-month treatment regimen was recommended by the WHO. The follow-up survey was conducted with patients with TB till completion of the treatment. The treatment costs were collected every month by the trained TB staff. The staff interviewed each participant and then checked invoices or financial accounting systems to ensure accuracy. OOP payments and reimbursements of the direct medical costs in different periods of services (pre-diagnosis, diagnosis, and treatment) were collected per individual and checked invoices or financial accounting systems as well. All costs were indicated in Ren Min Bi (RMB).

Definitions

Pulmonary TB was diagnosed based on the pathological, clinical, and radiological findings, and confirmed through bacteriological and histological examinations, which were strictly performed according to the Chinese Diagnostic criteria for PTB (WS-288-2008) .[28]

Patient delay is determined as a time interval from the first onset of TB symptoms to the first visit to any health provider; if the time interval lasts for more than 14 days, it is considered as a "delay".[29]

Diagnostic delay is defined as a time interval between a patient's first visit to any health provider and the final diagnosis as TB; if the time interval lasts for more than 14 days, it is considered as a "delay".[29]

Pre-diagnosis is the period from the onset of TB symptoms to the first visit to a local designated TB medical institution. **The period of diagnosis** is from the first visit to a local designated TB medical institution to the diagnosis of TB. **The period of treatment** is the full course of TB treatment.

Direct medical costs are composed of consultation fees, laboratory tests, X-rays, medical tests, and drugs during the period of pre-diagnosis, diagnosis, and treatment.

OOP payments are regarded as the direct medical costs paid by patients themselves.

Measuring the incidence and intensity of catastrophic health expenditure

CHE is usually assessed by incidence and intensity. According to the definition of CHE in several previous studies[11 13 14], we defined 'catastrophic' as the OOP payments of total medical costs for TB care exceeding 10% of the annual household income in this study. Head count (HC) is used to measure the incidence of CHE, while the mean gap (MG) and mean positive gap (MPG) are used to reflect the intensity of CHE. HC means the percentage of households whose OOP payments equal or exceed 10% of their annual income to the total number of households. MG is the average amount by which OOP payments, as a proportion of annual household income, exceeds the threshold. MPG is equal to MG/HC, the excess expenditure per household experiencing CHE. The methods used in measuring HC, MG, and MPG are based on the previous study. [14]

Statistical analysis

Data were double entered and checked using EPI Data Version 3. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 18.0 (SPSS Inc. Chicago, IL, USA). Continuous variables were presented as medians and interquartile (IQR) ranges, while categorical variables were presented as numbers and percentages (%). Pearson's chi-square test was used in univariate analyses to identify factors associated with the CHE and odds ratios with 95% confidence intervals (95% CIs) were computed. All variables with a *P*-value <0.05 in the univariate analysis were included in the multivariate model. A multivariate logistic regression model using a backward elimination method was used to assess the determinants of CHE and to calculate adjusted odds ratios (aOR) and 95% CIs. A two-sided *P*-value of <0.05 was considered statistically significant.

Ethics approval

The study was approved by the Ethical Committee of the Chongqing Institute of Tuberculosis Prevention and Treatment, Chongqing, China. Written informed consent was obtained from each participant prior to inclusion in the survey.

Patient and public involvement

Patients and the public were not involved in the design or planning of the study.

RESULTS

Patient characteristics

The characteristics of these patients with PTB are summarized in Table 1. A total of 1199 patients with PTB were enrolled in the study. The proportion of men to women involved in this study is 2.3:1. More than three-quarters of patients were in their labor age (16–59 years), and the average age of the patients was 43.9 years, with a median age of 44 years. Approximately 30% of patients were migrants. Two-thirds of patients were married and received at least junior high school education. About one-quarter of patients were unemployed, about 30% patients were peasants and

8.0% patients were students. Approximately three-quarters of the households had one to three family members. In the majority, 89.2% of the patients had health insurance and about half of the patients had NCMS. Only 15.9% of patients had been hospitalized in the intensive period. Approximately three-quarters of patients were smearing negative. Of the total participants, 53.0% and 43.0% patients experienced patient and diagnostic delay, with a median (IQR) of 16(3-52) and 9 (3-33) days measured in days, respectively. Patients' average annual household income was 42,200 RMB, with a median (IQR) of 35,000 RMB (20,000–56,000 RMB).

Direct medical costs for TB in different periods of medical treatment

The OOP costs and health insurance reimbursement during the pre-diagnosis, diagnosis, and treatment period are presented in Table 2. Expenses in the pre-diagnosis period were all paid by OOP, accounting for nearly half of the total cost. Excluding the fees covered by free TB service policy, around 7% of costs were reimbursed by health insurance during the treatment period, but no costs were reimbursed during the period of pre-diagnosis and diagnosis. The median total direct medical costs paid by a TB patient were 4085 RMB, about 93% of which was paid by patients themselves.

Incidence and intensity of CHE

Table 3 shows that 52.8% (633/1199) of all TB-related households experienced CHE. On average, healthcare payments for TB were 18.1% higher than the threshold value (10%). For households experiencing CHE, the mean positive gap was 34.2% higher than the threshold. The incidence of CHE in patients experiencing patient delay or diagnostic delay was 11% or 9.7% more than those not suffering patient delay or diagnostic delay, respectively. The intensity measure was also higher for the group of experiencing patient delay or diagnostic delay than the group without delay.

Determinants of CHE

Table 4 shows the influence of different variables on CHE for TB care using a

Pearson's chi-square test. There are many factors associated with CHE, including patient delay, diagnostic delay, sex, age, resident status, marital status, educational level, occupation, health insurance status, and hospitalization. Those factors were included in the multivariate logistic regression.

Logistic regression produced a wide range of determinants related to catastrophic health expenditure (Table 5). Independent determinants of CHE were: patient delay (aOR, 1.342; 95% confidence interval (CI), 1.043–1.726), diagnostic delay (aOR, 1.540; 95% CI, 1.195–1.983), male (aOR, 1.141; 95% CI, 1.066–1.877), age≥60 years (aOR, 2.117; 95% CI, 1.281–3.498), inhabitant (aOR, 1.455; 95% CI, 1.084–1.951), divorced or a widow (aOR, 2.211; 95% CI, 1.093–4.475), peasant (aOR, 2.205; 95% CI, 1.522–3.194), high school and above (aOR, 0.542; 95% CI, 0.356–0.826) and as NCMS membership (aOR, 1.688; 95% CI, 1.071-2.661). However, hospitalization was not related to CHE after controlling for other variables (aOR, 1.342; 95% CI, 0.950-1.897).

DISCUSSION

For the first time, global TB targets aimed to decrease catastrophic costs associated with TB. Evaluating the incidence and intensity of TB-related CHE not only provided insight into the universal health coverage (UHC) but also reflected the economic burden of patients with TB and their families. In this study, the incidence of CHE for TB care was 52.8% after reimbursement, which was lower than the reported rates of 66.8%, 65% and 78.1% in other cities of China, Nigeria, and Benin, respectively, using the same CHE measurement methods. [11 13 17] However, the figure was a little higher than that in Indonesia (50%) when they involved in patients with MDR-TB , [24] and much higher than the rate of CHE incurred by general population or patients with non-communicable chronic disease in China. [19] In that TB inequitably affects poor people and households in poorer economic quintiles are more at risk of suffering CHE and impoverishment.[19 30] The mean gap was 18.1% and the mean positive gap was 34.2% for TB in our study, both were higher than that in Nigeria (6.0%, 9.3%) [11 13] and in Benin (7.8%,14.8%) [13] but lower than that in other cities of China (40.8%, 62.2%) [17] because we did not take non-medical costs into account while other studies did. Although many studies claimed that non-medical costs and indirect costs related to TB care were a severe financial burden for patients with TB and their households, [5 31 32] some studies found that these costs were not high compared with direct medical costs.[18 33 34] Thus, the extent of patients incurring catastrophic costs in this study population may be underestimated but remain reliable.

Although all patients in this study have access to free TB treatment and the majority of them have health insurance, they had a heavy financial burden of out-of-pocket payments and more than half of them incurred catastrophic costs. The phenomena is common in China, [8 18 35] there may be three reasons to explain it: (i) Many associated health-care costs are not covered in the free TB policy, for example, payment for drugs of ancillary and liver protection, and extra diagnostic tests.[2 8 36] (ii) Driven by profits, doctors may prescribe additional medicines and tests.[37] (iii) The reimbursement ratio for outpatient services is low and often ignored, as well as the actual implementation strength of inpatients reimbursement was weak. [38-40] Besides, we also found nearly half of all OOP payments were paid before diagnosis, which was similar to many previous studies. [6 23 41] This cost had aroused particular concern in that it not only reflected the economic burden on families for obtaining a diagnosis, but also may act as an obstacle for poor patients to access timely TB care.

Delay in diagnosis had a massive impact on TB transmission in the community, aggravating the severity and mortality, resulting in an unfavorable treatment outcome and significantly increasing total patient costs.[42-45] This study, we further investigated the relationship between patient/diagnostic delay and CHE for TB care among patients with TB. We found about half patients encountered patient delay or diagnostic delay, who incurred more serious CHE than those without delay. Also, we demonstrated that patient delay and diagnostic delay were crucial determinants of CHE. Consistently, Laokri et al found that patient delay over 1 month was an independent determinant of incurring catastrophic expenditure. [11] In addition, a large number of studies had revealed that patient delay and diagnostic delay were independent factors associated with total out-of-pocket costs. [23 25 34 35 46] Actually, prolonged delays in TB diagnosis are still prevailing problems in many countries in many low- and middle-income countries, such as in Ethiopia，Zambia，Tanzania，Mozambique， Indonesia and so on. [43 47-50] Therefore, it is vital to take measures to shorten the delay in diagnosis.

Patient delay may be related to the fact that patients do not take minor symptoms seriously in its early stage and will pay greater attention to it until symptoms become more severe. [38] In addition, many sociodemographic and economic factors contribute to patient delay. [29] Therefore, we should adopt comprehensive measures to facilitate patients to seek care early, such as strengthening TB health education to the public and adopting a precise poverty alleviation to increase the income of poverty-stricken patients. Early diagnosis is difficult due to the vast percentage of asymptomatic PTB patients and non-availability of rapid, accurate, and cost-effective tests in many settings.[51] In this study, only one-quarter of patients has been confirmed bacteriological and mainly based on traditional methods. Rapid molecular methods were not frequently used in Chongqing in 2013. Hence, more rapid, accurate, and affordable methods are urgently needed to shorten the time of diagnosis.

Multivariate regression analysis indicated that demographic factors such as age, sex, marital status, occupation, resident status, and education level independently affected the risk of catastrophic costs for TB care. Consistent with previous studies in Nigeria and other cities of China, age was an essential determinant of CHE, [11 17] but only patients who were ≥60 years significantly affect CHE after removing the confounding factors in our study. Usually, men were the breadwinner of a family, thus we and Ukwaja et al found male patients were more easily to experience CHE, [11] but Zhou et al showed that gender had no significant associations with CHE.[17] In contrast with a previous study in China, [17] we found marital status was an independent factor related with CHE, but the family size and hospitalization were not determinants of CHE because we grouped different segments of the household population. Besides, only 15.9% of patients had been hospitalized during the treatment, much lower than the figure in a previous study of 55%.[17] Generally, people with low educational level also have less economic income, and thus we all demonstrated patients with less education were more likely to incur CHE.[11 13] Compared with inhabitants, migrants had a smaller proportion of patients being male, elderly, or peasant and a higher proportion of patients with high educational level, thus migrant patients were less likely to experience CHE compared with inhabitant patients.

We found that patients covered by NCMS, compared with those without any type of health insurance, were more likely to experience CHE. A series of studies conducted in China have demonstrated that NCMS could not relieve the financial burden of TB-related medical costs and had a partial effect on protecting TB-related households from CHE. [17 39 52] Compared with patients not covered by NCMS, patients with TB covered by the NCMS only had a 5% higher reimbursement rate regarding outpatient and total medical costs in Zhejiang and Sichuan provinces of

China.[39] NCMS is designed exclusively for rural residents particular for peasants, who are usually in low-income status. Also, the majority of patients without health insurance were migrants. In contrast with the previous study in China, we did not find MIUR or MIUE has any positive effect on reducing CHE.[17] It may be due to the actual reimbursement rate of health insurance is low in China. These three types of health insurances largely cover inpatient services but the benefit package for outpatient care vary widely. In fact, a lot of areas existed to ignore reimbursements to varying degrees in China, especially for outpatient services.[40] In research, there was no reimbursement for medical costs during pre-diagnosis and diagnosis, which further indicated that the actual reimbursement rate is very low. Thus, so far health insurance plan did not actually help to relieve the financial burden for patients with TB in China. Consequently, the health insurance policy should be implemented effectively.

This study has some limitations. Firstly, some data collected based on self-reporting could not be checked, which may be subjected to recall bias. Secondly, the data in this study were collected four years ago, and the per capita income has increased from 2014 to 2017. However, China's free TB service policy has not changed in recent years, and TB inequitably affects poor people. Therefore, the CHE remains a problem for TB now in China. Thirdly, we did not use the new definition of "catastrophic costs due to TB" recommended by WHO, which is the total [direct and indirect] costs exceeding 20% of annual household income recently.[15] Although the threshold (10%) we set was lower than the new definition and we did not take indirect costs into account, it may also be valuable to present the proportion of TB-affected patients (and their households) facing catastrophic costs if direct costs alone are counted.[15] Furthermore, the data about the CHE associated with TB were limited worldwide and correlational research has been conducted only in three cities in China. Consequently, our study may add some new data of CHE for TB care in China.

CONCLUSION

Although all patients have access to free TB service policy and the majority of them have health insurance, patients with TB still shoulder a high burden of OOP payments and experience high incidence and intensity of CHE for TB care in Chongqing, China. Except for social-demographic factors, patient delay and diagnostic delay are essential determinants of CHE for TB care, which highlights the significance of early care seeking and early diagnosis. In addition, NCMS aggravates the catastrophic costs, which implicates that it is essential to improve the actual reimbursement rates of health insurance, especially for outpatients. Furthermore, more fine-tuned interventions such as precise poverty alleviation are essential to taken for vulnerable patients with TB to reduce their catastrophic costs. Overall, our results have provided some baseline data about CHE for TB, which may give some clues for a further prospective study.

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Contributors DH: designed the study and drafted the manuscript; YL: designed the study, implemented the survey and analyzed the data; WD: designed the study, analyzed the data and drafted the manuscript; WZ, CW, QW, and YY: implemented the survey and collected data; HL: analyzed the data and drafted the manuscript. All authors read and approved the final version of the manuscript.

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Competing interests None

Patient consent Obtained

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Table 1 Social-demographic and clinical characteristics of the study participants (n=1199).

Variables	Patients No.	Percent (%)
Sex		
Male	839	70.0
Female	360	30.0
Age		
≤40	532	44.4
41-59	402	33.5
≥60	265	22.1
Residential status		
Inhabitant	848	70.7
Migrant	351	29.3
Marital status		
Single	340	28.4
Married	795	66.3
Divorced/widow	64	5.3
Educational level		
Primary or below	382	31.9
Junior high	356	29.7

High school and above	461	38.4
Occupation		
Unemployed	302	25.2
Employed	327	27.3
Peasant	353	29.4
Student	96	8.0
Retiree	121	10.1
Family size		
1~3	887	74.0
4~8	312	26.0
Health insurance status		
None	130	10.8
NCMS	548	45.7
MIUR	230	19.2
MIUE	249	20.8
Other insurance plan	42	3.5
Hospitalization		
Yes	191	15.9
No	1008	84.1

Forms of TB		
Smear-negative PTB	892	74.4
Smear-positive PTB	307	25.6
Patient delay		
Yes	635	53.0
No	564	47.0
Median (IQR) (days)	16 (3-52)	
Diagnostic delay		
Yes	516	43.0
No	683	57.0
Median (IQR) (days)	9 (3-33)	
Household annual income(RMB)		
Mean	42,200	
Median (IQR) (days)	35,000(20,000-56,000)	

Note: IQR represents interquartile range. TB represents tuberculosis.

NCMS, New Cooperative Medical Scheme; MIUR, Medical Insurance for Urban Residents; MIUE, Medical Insurance for Urban Employees.

Table 2 Direct medical costs for TB care in different periods of services (n=1199). RMB

Costs in different periods (services)	Out-of-pockets		Health insurance reimbursement		Total	
	Median	IQR	Median	IQR	Median	IQR
Pre-diagnosis	750	250-3000	0	0	750	250-3000
Diagnosis*	157	121-250	0	0	157	121-250
Treatment #	1792	834-3050	0	0-501	1966	1000-3723
Total	3789	2106-6645	0	0-501	4085	2222-7371

Note: Expenses excludes the costs of the free-TB policy reduction and exemption. *The expenses excluded the cost of one-time free chest X-ray and sputum smear examination. #The expenses excluded anti-TB drugs (6 months for new patients, 8 months if previously treated), three times sputum smear tests and one time X-ray test during anti-TB treatment. IQR: interquartile range.

Table 3 Incidence and intensity of CHE for TB care stratified by patient and diagnostic delay.

Catastrophic health expenditure	Patient delay		Diagnostic delay		All
	Yes	No	Yes	No	(n=1199)
Head count (%)	58.0	47.0	58.3	48.6	52.8
Mean gap (%)	21.1	14.6	19.3	17.2	18.1
Mean positive gap (%)	36.5	31.1	33.0	35.3	34.2

Table 4 Single factor analysis of catastrophic health expenditure in patients.

Variables	Experiencing CHE (n,%)	Not experiencing CHE(n,%)	OR (95% CI)	Chi-square	*P-value*
Patient delay					
No	265 (47.0)	299(53.0)	1.0		
Yes	368(58.0)	267(42.0)	1.555(1.238-1.954)	14.415	0.000
Diagnostic delay					
No	332(48.6)	351(51.4)	1.0		
Yes	301(58.3)	215(41.7)	1.480(1.175-1.864)	11.153	0.001
Sex					
Female	151(41.9)	209(58.1)	1.0		
Male	482(57.4)	357(42.6)	1.869(1.455-2.400)	24.300	0.000

Age					
≤40	200(37.6)	332(62.4)	1.0		
41-59	242(60.2)	160(39.8)	2.511(1.925-3.275)	46.936	0.000
≥60	191(72.1)	74(27.9)	4.285(3.109-5.904)	84.156	0.000
Resident status					
Migrant	129(36.8)	222(63.2)	1.0		
Inhabitant	504(59.4)	344(40.6)	2.521(1.951-3.259)	51.246	0.000
Marital status					
Single	133(39.1)	207(60.9)	1.0		
Married	450(56.7)	344(43.3)	2.036(1.571-2.638)	29.377	0.000
Divorced/widow	50(76.9)	15(23.1)	5.188(2.800-9.613)	31.488	0.000

Educational level					
Primary or below	277(72.5)	105(27.5)	1.0		
Junior high	190(53.4)	166(46.6)	0.434(0.319-0.589)	29.058	0.000
High school and above	166(36.0)	295(64.0)	0.213(0.159-0.286)	111.600	0.000
Occupation					
Unemployed	139(46.0)	163(54.0)	1.0		
Employed	128(39.1)	199(60.9)	0.754(0.549-1.036)	3.044	0.081
Peasant	261(73.9)	92(26.1)	3.327(2.396-4.519)	53.331	0.000
Student	37(38.5)	59(61.5)	0.735(0.460-1.176)	1.654	0.198
Retiree	68(56.2)	53(43.8)	1.505(0.984-2.300)	3.577	0.059
Family size					

1~3	479(54.0)	408(46.0)	1.0		
4~8	154(49.4)	158(50.6)	0.830(0.641-1.075)	1.997	0.158
Health insurance status					
None	47(36.2)	83(63.8)	1.0		
NCMS	351(64.1)	197(35.9)	3.146(2.113-4.685)	31.853	0.000
MIUR	111(48.3)	119(51.7)	1.647(1.059-2.561)	4.910	0.027
MIUE	109(43.8)	140(56.2)	1.675(0.888-2.128)	2.042	0.153
Other insurance plan	15(35.7)	27(64.3)	0.981(0.475-2.027)	0.003	0.959
Hospitalization					
No	517(51.3)	491(48.7)	1.0		
Yes	116(60.7)	75(39.3)	1.469(1.071-2.014)	5.746	0.017

Forms of TB					
Smear-negative PTB	480(53.8)	412(46.2)	1.0		
Smear-positive PTB	153(49.8)	154(50.2)	0.853(0.658-1.105)	1.448	0.229

Note: PTB, pulmonary tuberculosis. OR, odds ratio. 95% CI, 95% confidence interval for the odds ratio.

NCMS, New Cooperative Medical Scheme; MIUR, Medical Insurance for Urban Residents; MIUE, Medical Insurance for Urban Employees.

Table 5 Independent determinants of CHE for TB care using a logistic regression model.

Variables	β	Standard error	Wald	*P-value*	OR(95% CI)
Patient delay (Ref: Without delay)	0.294	0.128	5.251	0.022	1.342(1.043-1.726)
Diagnostic delay (Ref: Without delay)	0.431	0.129	11.145	0.001	1.540(1.195-1.983)

Sex (Ref: Female)	0.347	0.144	5.764	0.016	1.141(1.066-1.877)
Age (Ref: ≤40)			8.557	0.014	
41-59	0.336	0.187	3.216	0.073	1.399(0.969-2.019)
≥60	0.75	0.256	8.554	0.003	2.117(1.281-3.498)
Resident status (Ref: Migrant)	0.375	0.15	6.247	0.012	1.455(1.084-1.951)
Marital status (Ref: Single)			6.239	0.044	
Married	-0.005	0.192	0.001	0.977	0.995(0.683-1.448)
Divorced/widow	0.794	0.36	4.87	0.027	2.211(1.093-4.475)
Educational level (Ref: Primary or below)			8.224	0.016	
Junior high	-0.294	0.187	2.485	0.115	0.745(0.517-1.074)
High school and above	-0.612	0.215	8.114	0.004	0.542(0.356-0.826)

Occupation (Ref: Unemployed)			28.975	0.000	
Employed	0.025	0.176	0.02	0.887	1.025(0.726-1.448)
Peasant	0.791	0.189	17.475	0.000	2.205(1.522-3.194)
Student	0.368	0.279	1.745	0.187	1.446(0.837-2.497)
Retiree	-0.318	0.257	1.53	0.216	0.727(0.439-1.204)
Health insurance (Ref: none)			6.355	0.174	
NCMS	0.524	0.232	5.087	0.024	1.688(1.071-2.661)
MIUR	0.358	0.248	2.085	0.149	1.431(0.880-2.327)
MIUE	0.158	0.266	0.353	0.553	1.171(0.695-1.974)
Other insurance plan	0.169	0.398	0.181	0.671	1.184(0.543-2.583)
Hospitalization (Ref: not hospitalization)	0.294	0.176	2.784	0.095	1.342(0.950-1.897)

Note: The variables that showed association with CHE ($p<0.05$) in the univariate analysis were included in the multivariate model. OR, odds ratio. 95% CI,95%

confidence interval for the odds ratio. Ref, reference group.

NCMS, New Cooperative Medical Scheme; MIUR, Medical Insurance for Urban Residents; MIUE, Medical Insurance for Urban Employees.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6 line 38-54
Methods			
Study design	4	Present key elements of study design early in the paper	Page 7 line 9-11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7 line 9-41
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 7 line 43-59
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 8 line 49-58 Page 9 line 3-58
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 8-9

Bias	9	Describe any efforts to address potential sources of bias	Page 8 line 11-46
Study size	10	Explain how the study size was arrived at	Page 7 line 43-59
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 10 line 6-26
		(*b*) Describe any methods used to examine subgroups and interactions	Page 10 line 6-26
		(*c*) Explain how missing data were addressed	No missing data
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	None
		(*e*) Describe any sensitivity analyses	None
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 7 line 43-60
		(b) Give reasons for non-participation at each stage	Page 7 line 55-60
		(c) Consider use of a flow diagram	None
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 Page 11
		(b) Indicate number of participants with missing data for each variable of interest	No participant with missing data
Outcome data	15*	Report numbers of outcome events or summary measures	Table 2-5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Table 4 and 5

		interval). Make clear which confounders were adjusted for and why they were included	Page 12 line 18-47
		(*b*) Report category boundaries when continuous variables were categorized	Table 4 and 5
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	None
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17 line4-25
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 16 line 30-57
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 17 line 51-54

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.