Pretreatment Out-of-Pocket Expenses for Presumptive Multidrug-Resistant Tuberculosis Patients, India, 2016–2017

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In India, under the National Tuberculosis Elimination Programme, the government provides free treatment for multidrug-resistant tuberculosis; however, many patients seek care elsewhere, which is costly. To determine those out-of-pocket expenses, we interviewed 40 presumptive patients and found that they spent more than their median annual income before registering for the government program.

In India, the annual economic loss resulting from tuberculosis (TB) is US $3 billion (*1*). Those in the economically productive age group (15–54 years) account for >70% of the total burden (*1*). Incidence of multidrug-resistant TB (MDR TB) is higher in India than anywhere else in the world; ≈99,000 new cases of MDR TB occur in India each year (*1*). Treatment of MDR TB is more complex, challenging, and costly to manage than that of drug-sensitive TB (*2*–*4*). In India, MDR TB is treated free of cost through programmatic management of drug-resistant TB (PMDT) under the National Tuberculosis Elimination Programme (*5*). However, most patients seek healthcare from the private sector and some resort to alternative forms of medicine, often preferring self-medication and consulting quacks over visiting the PMDT center (*6*,*7*). This behavior not only results in delayed diagnosis but also increases prediagnostic expenses (*7*). Increased expenses accompanied with loss of wages can compel patients and their families affected by TB to borrow money, take loans, or even sell their assets, thereby accentuating any existing financial crises in the family (*6*–*9*). Hence, we estimated the direct and indirect out-of-pocket expenses incurred for diagnosis and pretreatment evaluation by presumptive MDR TB patients in Mangalore, India.

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DOI: https://doi.org/10.3201/eid2605.181992

The Study

Mangalore is a coastal city in the state of Karnataka, India. The state has 6 PMDT centers. Presumptive MDR TB patients, when referred to PMDT centers, are subjected to drug sensitivity testing, preferably by use of a rapid molecular test (cartridge-based nucleic acid amplification assay), line probe assay, or culture, per PMDT guidelines (*10*). Those with an MDR TB diagnosis are admitted to the center for a week for pretreatment evaluation. All services provided under PMDT are free of cost to the patient (*10*).

We included in our study all adults (≥15 years of age) with MDR TB who were registered under PMDT during August 2016–April 2017. By using a valid, pretested, semistructured tool, we interviewed patients about various costs incurred by themselves, their families, or both, from the time they became a presumptive MDR TB patient until they underwent pretreatment evaluation at PMDT. Information about various costs reported by patients was validated with bills, if available. We used the following cost categories: direct medical, direct nonmedical, indirect, and coping. Direct medical costs are expenses incurred during diagnosis and treatment of illness; direct nonmedical costs are costs of food, accommodations, and additional nutrition/supplements; indirect costs are the loss of wages because of illness;

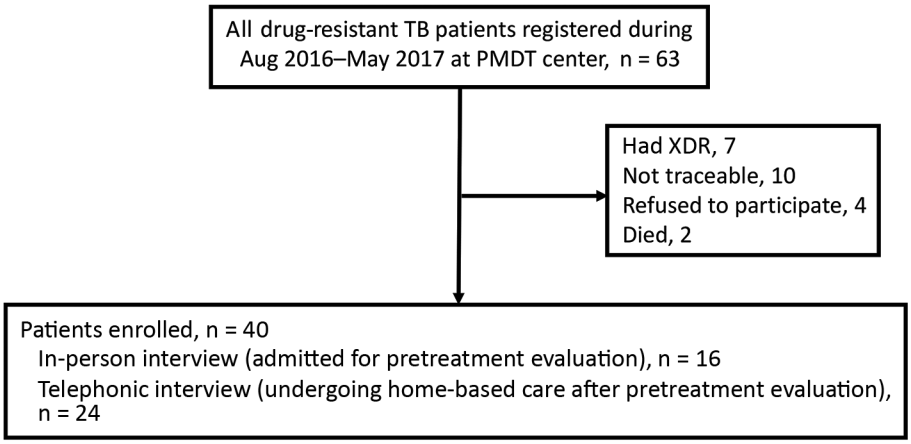

Figure 1. Flow chart showing patient enrollment in study of pretreatment out-of-pocket expenses for presumptive multidrug-resistant tuberculosis patients, India, 2016–2017.

and coping costs are the costs of coping mechanisms (assets sold, school dropouts, loans, and money borrowed) (Appendix, https://wwwnc.cdc.gov/EID/article/26/5/18-1992-App1.pdf). Of the 40 MDR TB patients, the 16 who were admitted during the study period were interviewed in person and the 24 who continued home-based treatment were interviewed by telephone (Figure 1). Ethics approval was obtained from the Institutional Ethics Committee of Kasturba Medical College, Mangalore, and the Ethics Advisory Group of The International Union against Tuberculosis and Lung Disease, Paris, France.

Table 1. Sociodemographic characteristics of 40 MDR TB patients treated at PMDT Centre, Mangalore, India, August 2016–April 2017*

Characteristic	No. (%)
Sex	
M	28 (70)
F	12 (30)
Education	
Illiterate	5 (12.5)
Primary school	15 (37.5)
Secondary school	14 (35.0)
Graduation/professional course	6 (15.0)
Type of occupation	
Salaried job	13 (32.5)
Daily wage	9 (22.5)
Business owner	5 (12.5)
Homemaker	8 (20.0)
Other†	5 (12.5)
Place of residence	
Urban	12 (30.0)
Rural	28 (70.0)
Socioeconomic status†	
Upper class	6 (15.0)
Upper-middle class	14 (35.0)
Middle class	8 (20.0)
Lower-middle class	7 (17.5)
Lower-class	5 (12.5)
Health facility sequence where MDR TB diagnosis made	
First	23 (57.5)
Second	14 (35.0)
Third	3 (7.5)
Fourth	0
Type of healthcare facility visited by patients before PMDT	
Private	24 (60)
Public	16 (40)

*MDR TB, multidrug-resistant TB; PMDT, programmatic management of drug-resistant TB; TB, tuberculosis.
†Modified BG Prasad Classification (https://www.ijcmph.com/index.php/ijcmph/article/view/1242/1005).

Data were double entered in EpiData version 3.1 software (https://www.epidata.dk) and analyzed by using SPSS Statistics 25.0 (https://www.ibm.com) and EpiData analysis 2.2.2.183 software. Direct and indirect costs were summarized as median and interquartile ranges (IQRs). Categorical variables were expressed in proportions. Costs were collected by using Indian rupees (INR) converted to United States dollars (USD) based on the 2016 conversion rate (1 USD = 66.3731 INR). To compare the costs across different countries, we first converted the reported costs (USD) from other studies to local currency for the reported year, then adjusted them for inflation year by year until 2016 (*11*). Then we converted the costs back to USD by using the 2016 conversion rate (Appendix).

We included 40 of the 63 registered patients in the study. Median (IQR) age of participants was 39 (29–50) years. Most patients were male (28, 70%), and most lived in rural areas (28, 70%). Median (IQR) reported patient family income was $608 ($228–$912)/year. Of the 40 patients, 39 (97%) had pulmonary MDR TB and 24 (60%) had approached the private healthcare sector for their first clinical encounter (Table 1; Figure 2).

The median (IQR) pretreatment out-of-pocket expenses incurred by patients were $171 ($72–$432) total, $105 ($49–$306) direct, and $51 ($2–$306) indirect. Within direct costs, direct nonmedical costs ($51) were more than direct medical costs ($37). Of the direct nonmedical costs, most was spent on food ($35). Most of the direct medical costs were for diagnostic investigation ($18) and treatment ($15) (Table 2).

The median total pretreatment out-of-pocket expense incurred by patients in our study is similar to

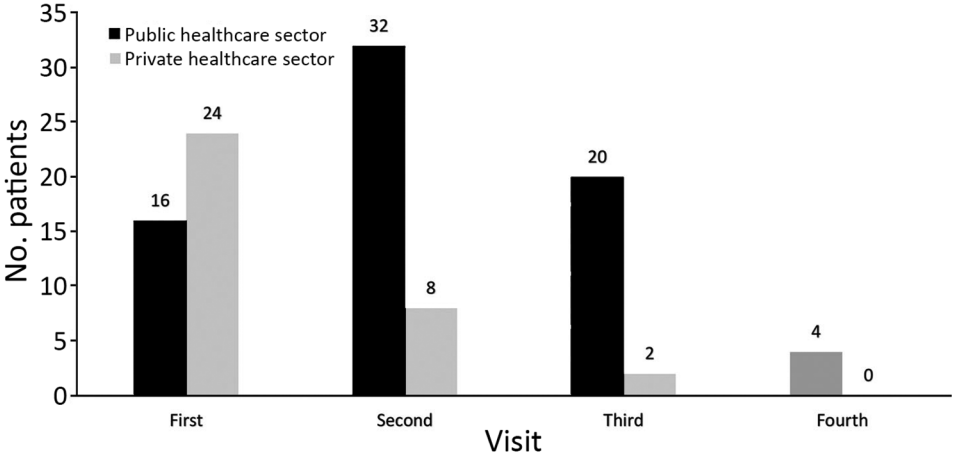

Figure 2. Distribution of visits to healthcare facilities in the public and private sectors by 40 presumptive multidrug-resistant tuberculosis patients before seeking care through programmatic management of drug-resistant tuberculosis, India, 2016–2017.

that found in a study in Peru ($210) after adjusting for inflation rate and cost conversion (*12*). The median direct out-of-pocket expenses are higher than the adjusted cost values found in previous comparable studies conducted in Ethiopia ($87), Indonesia ($47), and Peru ($67) and lower than that reported from Cambodia ($144) (*12*–*15*).

The median indirect out-of-pocket expense incurred by patients in India was $51 ($2–$306). This finding contrasts with those of studies in Ethiopia and Indonesia, where indirect pretreatment costs after adjustment for annual inflation were substantially lower (Ethiopia $9, Indonesia $8) (*15*).

In contrast, for patients in Ecuador, the adjusted direct out-of-pocket expenses were 5 times greater than those for patients in India ($105 vs. $549). The adjusted indirect expenses were 10 times greater ($51 vs. $578) (*12*) (Appendix Table).

In addition, 18 (45%) patients in the study lost their job because of the disease and had to borrow money for disease management and daily household needs before receiving accurate diagnosis and appropriate treatment. The percentages of persons with job losses were substantially lower than those reported for Peru (90%) and Ethiopia (72%) but similar to those for Indonesia (53%) (*12*,*15*).

Median coping cost incurred by patients in the study was $640 ($324–$1,360). Wingfield et al. reported a median debt of $435 and a loss of income of $2,450 before diagnosis for patients in Peru (*12*). In the study cohort, total median cost was $171 ($72–$432), which amounted to 28% of median total family income ($608). This expense, when combined with a coping cost of $640, resulted in a financial burden that was 1.25 times greater than the median total family income of the cohort ($608). Also, the cost of disease was $811 (sum of total median cost and median coping cost), and coping costs accounted for 79% of the total. Coping cost in a study conducted in Ecuador was as high as 7 times the average annual income (*14*).

In our study, no patients reported school dropouts or separation in families. None of the patients reported selling assets such as property, gold, and other valuables. A total of 27 (67.5%) of the patients, approximately two thirds, had already incurred catastrophic expenses before they were registered for MDR TB treatment.

Table 2. Median disaggregated costs incurred by 40 patients (households) from the stage of presumptive MDR TB to pre-MDR TB treatment evaluation, India, August 2016–April 2017*

Cost category	Median (IQR), USD
Total income	608.00 (228.00–912.00)
Total direct medical costs†	37.44 (7.10–198.24)
Total diagnosis, n = 38	01.58 (0.30–2.40)
Total investigation, n = 36	17.70 (3.19–60.27)
Total treatment, n = 26	15.07 (11.30–47.08)
Total admission, n = 15	45.20 (30.13–75.34)
Total direct nonmedical costs‡	51.20 (28.00–85.36)
Total food, n = 38	35.41 (18.08–64.97)
Total travel, n = 39	12.84 (5.73–12.84)
Total accommodations, n = 1	36.16 (36.16–36.16)
Additional nutrition, n = 38	01.51 (0.75–3.77)
Total direct costs§	105.12 (48.75–306)
Total indirect costs, n = 18¶	51.20 (1.60–306.00)
Total expenditures#	171.31 (72.00–432.00)
Total coping costs	640.00 (324.00–1,360)

*Because all patients did not incur all categories of costs, n differs for different categories. Median (IQR) is calculated only for those who incurred a given cost. IQR, interquartile range; MDR TB, multidrug-resistant TB; TB, tuberculosis: USD, US dollars.
†Direct medical costs = sum of diagnosis investigation (general investigation and disease-specific investigations), complete blood count, erythrocyte sedimentation rate, liver function testing, renal function testing, spirometry, computed tomography, magnetic resonance imaging. Disease specific cost = sputum-smear microscopy, culture, drug-susceptibility testing, radiography, drugs, and hospitalization.
‡Direct nonmedical costs = sum of food, accommodation, travel by both patient and attendant.
§Direct costs = sum of total direct medical costs and total direct nonmedical costs.
¶Indirect costs = loss of wages for patient and attendant during the visit.
#Total expenditure = sum of total direct and total indirect costs.

Conclusions

Our study appraised the costs expended by MDR TB patients from a single PMDT center. Determination of a complete estimate of costs borne by all MDR TB patients in India would require a comprehensive study conducted at the community level and inclusion of patients receiving treatment from the public and private healthcare sectors.

New strategies that systematically engage private providers are needed to reduce the cost burden surrounding diagnosis for vulnerable patients. The government of India may consider widening the spectrum of free services before patient enrollment in a government-monitored treatment program channeled through the private sector.

Acknowledgments

We acknowledge John E. Oeltmann and Patrick K. Moonan for their valuable input and contributions to the study.

The study was conducted as a part of the TB Operations Research Training Project aimed at building operational research capacity within the India government National Tuberculosis Elimination Programme. This training project was conceived and implemented jointly by Central TB Division (Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India), the National TB Institute (Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, Bangalore, India), the International Union Against Tuberculosis and Lung Diseases (The Union, South-East Asia Regional Office, New Delhi, India), and the US Centers for Disease Control and Prevention (Atlanta, Georgia, USA).

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Article doi: https://doi.org/10.3201/eid2605.181992

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Appendix

Methods and Materials

Healthcare in India is majorly provided by government or public sector and private sector. Also there are alternative forms of medicine (i.e., Ayurveda, Yoga, Unani, Siddha, Homeopathy) and quacks, which people sort to for health related issues. The healthcare providers are majorly public health specialists who provides services under the national programs where they provide free of cost treatment and private practitioners who charge for their services. Health seeking behavior of the Indians are such that they first sort to self-medication, then alternative form of medicines and then to private practitioners (*1*,*2*). Those who can afford to pay continue the treatment in private sector. People in rural area and who cannot afford, avail services from public sector and healthcare programs, where treatment is provided free of cost or with negligible cost (*3*,*4*). RNTCP program is a stand-alone program where presently all forms of tuberculosis are managed by public sector itself. Multi-drug resistant TB is managed under PMDT (Programmatic Management of Drug-resistant Tuberculosis) (*5*,*6*).

Mangalore is a coastal city in the state of Karnataka. There are six PMDT centers in the state, one of them located in Mangalore. It caters to a population of around 100,000 including those from two neighboring districts and is responsible for pre-treatment evaluation and managing treatment for MDR-TB (*6*).

As per national PMDT guidelines, patients experiencing treatment failure or sputum smear positivity while on first-line anti-TB regimen and those previously treated with anti-TB drugs for ≥ 1 month are considered presumptive MDR TB patients (Glossary). They are subjected to drug sensitivity testing, preferably using a rapid molecular test (cartridge-based nucleic amplification assay test (CB-NAAT) or line probe assay (LPA) or culture. Presumptive

MDR TB cases are referred to PMDT centers. Persons with MDR TB are admitted to the PMDT center for a week for pretreatment evaluation at no cost to the patient (*5*,*6*).

This study was conducted as a part of output oriented operational research which was a time bound program. Therefore, we included all cases of adult MDR (≥ 15 years) registered under PMDT between August 2016 and April 2017 (9 months) in the study. The period of data collection was same as period of recruitment of patients in the study.

Assuming that XDR patient's pre-diagnostic and treatment trajectory is more complicated as compared to the MDR patient in India. Their number of visits to other Healthcare facilities prior to reaching PMDT center is more and hence the costs of Pre-diagnosis if included with MDRTB patients, may show an overestimation of expenditure. Hence, we decided to exclude them from study.

Information on various costs incurred was collected during an interview using a pre-tested, semi-structured tool. Costs incurred from the time they were presumptive MDR TB till the time they registered under PMDT and underwent pretreatment evaluation were collected with the help of study tool. The study tool was used to gather information on socio-demographic characteristics, reported income, various healthcare facilities (HCFs) visited, direct and indirect costs of diagnosis and pretreatment evaluation, and any potential coping mechanisms needed to maintain livelihood during this time (e.g., loans, selling off assets, and donations). Information of various costs reported by patients were validated with the bills, if available. Socio-economic status was measured using Modified BG Prasad classification (*7*). Those MDR-TB patients who were admitted during the study period were interviewed face-to-face (n = 16), while patients who continued home-based treatment were interviewed telephonically (n = 24). During face-to-face interview, if the patient was too ill to respond, one of the adult family members were interviewed as a proxy. For personal protection, the principal investigator (PI) wore an N-95 respirator and the patients wore surgical masks. Interviews occurred in an open space outside the PMDT Center with the PI sitting at an angle of 45 degrees from the patient.

Ethical approval was obtained from the Institutional Ethics Committee of Kasturba Medical College, Manipal University, Mangalore, and the Ethics Advisory Group of The International Union against Tuberculosis and Lung Disease, Paris, France.

Data analysis:

The data was double entered in EpiData version 3.1 software (EpiData Association, Odense, Denmark), matched for rectification if required and analyzed using SPSS (version 25.0) and EpiData analysis 2.2.2.183 software (*8*,*9*). The direct cost was further divided into direct medical and direct non-medical. The direct medical cost was calculated by simple addition of cost of consultancy, investigation, treatment. The direct non-medical was costs involved in transport, accommodation, food for both patient and attendant, if any. The indirect cost was summation of loss of wage or salary due to MDRTB. The direct and indirect costs were added to estimate total cost. Apart from these, the various coping mechanisms, adopted by the patients and their family to cover the medical and household expenses (for e.g., borrowing money, taking loan, selling assets, children's school dropouts) were included in calculating coping cost and were presented separately. Detailed definition and formula of calculation of different costs are mentioned in the Glossary. All forms of costs were summarized as median and Inter-Quartile Range (IQR). The socio-demographic characteristics and disease details were expressed in percentages. Costs were collected using Indian Rupees (INR) converted to United States Dollar (USD) amounts based on 2016 conversion rate (1 USD = 66.3731 INR) (*10*). We also compared our results with previously published studies that reported direct and indirect pretreatment expenditures. Because these studies occurred in different years and countries, for comparison, the reported costs were first converted to local currency, then were adjusted to inflation year by year till 2016 using following equation, (E)i = (E)s * n=i-s-1(π)n=0 [{1 + ((R)s+n/100) }] (*11*). The inflated local currency was then converted back to USD using 2016 conversion rate for uniformity (*10*).

The median direct out-of-pocket expenditures (for examinations, laboratory testing, non-TB medications) for our patients was $105($49-306). This was substantially higher than the adjusted cost values of previous comparable studies conducted in Indonesia ($47), Peru ($67), and Ethiopia ($87), but lower than a report from Ecuador ($549) and Cambodia ($144). (*12–15*) The median total pretreatment out-of-pocket expenditure experienced by families in our study was $171($72-432). After adjustment, the total out-of-pocket expenditure costs in Cambodia ($394), and Peru ($210) were slightly lower, suggesting that indirect costs were an important component of overall pretreatment costs (*12*,*13*). Our results were in contrast to studies

conducted by van den Hof *et al.* in Ethiopia and Indonesia. They found substantially lower total median pretreatment costs after adjustment ($171 vs $95, and $55, respectively) (*14*). Variation in results could be due to methodological differences in data collection and analysis. van den Hof *et al.* reported low indirect cost in both country settings, whereas the results of Pichenda *et al.* in Ecuador found more than ten times adjusted indirect costs ($51 vs $578) and overall adjusted pretreatment costs ($171 vs $1126) as compared to our results (*13*,*15*). This could be attributed to steep rise in inflation rates in Ecuador (*16*,*17*).

Health seeking behavior among patients: We also found out the pattern of health seeking behavior of our patient. Majority (n=24, 60%) of the patients approached the private health care sector for the first clinical contact, while subsequently, proportion of patients visiting public health care sector rose.

Glossary of operational definitions used in the study

Presumptive MDR case (*6*): Any of the following: Presumptive DR-TB: It refers to the following patients in order of their risk: TB patients found positive on any follow-up sputum smear examination during treatment with first line drugs including treatment failures; TB patients who are contacts of DR-TB; previously treated TB patients; new TB patients with HIV co-infection; all notified new TB patients.

Quacks: Quacks are those practitioners who did not undergo a formal training in any form of medicine and do not hold any degree for the same.

Costs: All the costs defined below are borne by patients or/and their family members.

Direct Costs: Direct Cost = (direct medical cost + direct non-medical cost)

Direct Medical Cost: Sum of Diagnosis, investigation (general investigation and disease specific investigations), General Complete blood count, Erythrocyte Sedimentation Rate, Liver Function Test, Renal Function Test, spirometry Computer Tomography, Magnetic Resonance Imagine etc, Disease specific like sputum culture and microscopy, Drug Sensitivity Testing, X-ray etc., procedures, drugs and hospitalization prior to starting the treatment at DRTB center, if any).

Direct Medical Cost = Cost (diagnosis) + Cost (investigation) + Cost (treatment).

Direct Non-Medical Cost: Extra expenditure by the patient or his family for reasons other than diagnosis and treatment, like transportation, accommodation, purchase of food during visits to health facilities, extra nutrition.

Direct Non-Medical Cost = Cost (travel) + Cost (accommodation) + Cost (food)+ Cost (extra nutrition)

Indirect Cost: loss of wage / lost income /, loss of job for patient and the attendant if any from being labeled as presumptive MDR TB to pre-MDR TB treatment evaluation. This includes loss of wage /income of patient and attendant (if any) during the days where they could not go to work either due to hospital visit or days of incapacitation or for attendant while taking care of patient

Total Cost = Direct Cost + Indirect Cost

Coping Cost (*18*): Cost incurred if important household assets are sold off, children are taken out of school to contribute to household earnings, or loans with high interests are taken and donations

Coping Cost = Cost (assets sold) + Cost (school dropout) + Cost (loans with interest, if any) + Cost (money borrowed)

Disease Cost = Total Cost + Coping Cost

Reported Income: Sum total of household income as informed by the patient.

Catastrophic Cost (*19*): The WHO End TB Strategy suggests that any cost ≥20% of their total family income is considered as catastrophic and is associated with poor outcomes

Costs adjustment (*11,16,17*): Reported costs incurred by MDRTB patients from different countries were first adjusted to inflation within their current currency and then converted to USD for comparison.

Local currency inflation adjustment - Formula used to adjust for inflation in local currency-

$(E)i = (E)start=s * n=i-s-1(\pi)n=0 [\{1 + ((R)s+n/100) \}]$,

where: S is the year of publication of study;(E)s is the reported cost by the study in the year of publication; i: year of current study (2016);(E)i is the cost of the study in current year (2016)

adjusted to inflation rate;(R)x is represents the inflation rate for year x. i.e (R)s+n is the inflation rate for year (s+n);(π): represents product of all values in the range of series.

The source of local inflation rates - World Bank. Official exchange rate. Inflation data . Available at: https://data.worldbank.org/indicator/PA.NUS.FCR.

The source of historical currency conversion - https://data.worldbank.org.

Formula used to adjust for inflation in local currency-

(E)i = (E)start=s * n=i-s-1(π)n=0 [{1 + ((R)s+n/100) }] , where: S is the year of publication of study;(E)s is the reported cost by the study in the year of publication; i: year of current study (2016);(E)i is the cost of the study in current year (2016) adjusted to inflation rate;(R)x is represents the inflation rate for year x. i.e (R)s+n is the inflation rate for year (s+n);(π): represents product of all values in the range of series.

Appendix Table. Adjusted out-of-pocket expenditures incurred by patients prior to anti-tuberculosis treatment in peer-reviewed publications in 2016.

Study	Country	Study Period	Cohort Size	Local currency conversion value for 1USD in the year of study*	Direct Out-of-pocket Pretreatment Expenditures Per Patient		Indirect Out-of-pocket Pretreatment Expenditures Per Patient		Total Out-of-pocket Pretreatment Expenditures per Patient	
					Reported value in USD	Comparable cost adjusted to 2016†	Reported value in USD	Comparable cost adjusted to 2016†	Reported value in USD	Comparable cost adjusted to 2016†
Wingfield T. et al, 2014	Peru	2002–2009	93	3.16	46	67	103	150	144	210
Pichenda K. et al, 2012	Cambodia	2008–2009	8	4000	95	144	144	218	260	394
Rouzier V. et al, 2010	Ecuador	2007	14	25000	374	549	394	578	768	1,126
van den Hof S. et al, 2016	Ethiopia	2013	169	18.28	68	87	7‡	9	75	95
van den Hof S. et al, 2016	Indonesia	2013	143	9636	39	47	7‡	8	46	55
Rathi P. et al, 2018 (Current Study)	India	2016–2017	40		105	105	51	51	171	171

*https://fxtop.com/en/historical-currency-converter.php,

†Adjusted for annual inflation rate of local currency for year 2016 and converted later to USD for comparison between countries. (Reference: †Inflation data from World Bank (http://api.worldbank.org/v2/en/indicator/FP.CPI.TOTL.ZG?downloadformat=excel).

‡Calculated as the median difference from the total out-of-pocket expenditures minus the direct out-of-pocket expenditures.

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