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Pathways and associated costs of care in patients with confirmed and presumptive tuberculosis in Tanzania: A cross-sectional study

Grace Mhalu,[1,2,3] Jerry Hella,[1,2,3] Francis Mhimbira,[1,2] Khadija Said,[1,2] Thomas Mosabi,[1] Yeromin P Mlacha,[1,2,3] Christian Schindler,[2,3] Sébastien Gagneux,[2,3] Klaus Reither,[2,3] Kees de Hoogh,[2,3] Mitchell G Weiss,[2,3] Elisabeth Zemp,[2,3] Lukas Fenner[4]

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[1]Ifakara Health Institute, Dar es Salaam, Tanzania
[2]Swiss Tropical and Public Health Institute, Basel, Switzerland
[3]University of Basel, Basel, Switzerland
[4]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

Correspondence to
Grace Mhalu; gmhalu@ihi.or.tz

ABSTRACT

Objective To assess pathways and associated costs of seeking care from the onset of symptoms to diagnosis in patients with confirmed and presumptive tuberculosis (TB).

Design Cross-sectional study.

Setting District hospital in Dar es Salaam, Tanzania.

Participants Bacteriologically confirmed TB and presumptive TB patients.

Primary and secondary outcome measures We calculated distance in metres and visualised pathways to healthcare up to five visits for the current episode of sickness. Costs were described by medians and IQRs, with comparisons by gender and poverty status.

Results Of 100 confirmed and 100 presumptive TB patients, 44% of confirmed patients sought care first at pharmacies after the onset of symptoms, and 42% of presumptive patients did so at hospitals. The median visits made by confirmed patients was 2 (range 1–5) and 2 (range 1–3) by presumptive patients. Patients spent a median of 31% of their monthly household income on health expenditures for all visits. The median total direct costs were higher in confirmed compared with presumptive patients (USD 27.4 [IQR 18.7–48.4] vs USD 19.8 [IQR 13.8–34.0], p=0.02), as were the indirect costs (USD 66.9 [IQR 35.5–150.0] vs USD 46.8 [IQR 20.1–115.3], p<0.001). The indirect costs were higher in men compared with women (USD 64.6 [IQR 31.8–159.1] vs USD 55.6 [IQR 25.1–141.1], p<0.001). The median total distance from patients' household to healthcare facilities for patients with confirmed and presumptive TB was 2338 m (IQR 1373–4122) and 2009 m (IQR 986–2976) respectively.

Conclusions Patients with confirmed TB have complex pathways and higher costs of care compared with patients with presumptive TB, but the costs of the latter are also substantial. Improving access to healthcare and ensuring integration of different healthcare providers including private, public health practitioners and patients themselves could help in reducing the complex pathways during healthcare seeking and optimal healthcare utilisation.

Strengths and limitations of this study

- We present data on pathways to care and assess costs of care in patients with confirmed and presumptive tuberculosis (TB) in Tanzania.
- We estimate costs of care by stratifying costs according to poverty status and gender.
- Estimated costs for TB diagnosis did not account for HIV and other comorbidities.
- The accuracy of reported costs may have been compromised by recall bias.

BACKGROUND

Patients with confirmed and presumptive tuberculosis (TB) follow complex pathways to healthcare. Pathways to healthcare are the steps/ways the confirmed and presumptive patients take from the initial point of seeking healthcare to the point of diagnosis and treatment.[1 2] Many patients consult various healthcare providers before being diagnosed with TB.[3 4] These pathways are usually complex and delayed diagnosis and treatment may increase morbidity and mortality.[5] The WHO estimated an incidence of 10.4 million TB cases in 2016, yet only 6.3 million new TB cases were notified to national authorities and reported to WHO.[6] Although many factors contribute to this notification shortfall, the complexity of pathways to TB care may substantially contribute to low notification rates.

TB is widely regarded as a disease of poverty due to its disproportionate effects on the marginalised populations.[7 8] To help socially and economically marginalised groups fight the disease, healthcare facilities diagnose and treat TB free of charge in countries with a high TB burden.[9] However, patients with symptoms of TB face high direct and indirect

costs for diagnosis and treatment,[10–13] and these costs are usually higher for patients with confirmed TB than presumptive cases.[3 14]

Prior to diagnosis, the pathways to care of presumptive TB in Tanzania are complex. They usually involve consultations with more than one healthcare provider with suboptimal or no means for diagnosing TB.[4 15] The complex pathways to care may begin at pharmacies and basic healthcare facilities with no TB diagnostics before reaching healthcare facilities with TB diagnostic capacity.[14]

A national TB prevalence survey in Tanzania indicated that the case detection rate of TB was below 50%.[16] This result may be due to the complexity and the high cost of care.[15 17 18] The recommended pathway to care for patients with TB is to present themselves to the appropriate healthcare facilities for TB diagnosis after recognition of TB symptoms.[9 19 20]

Research has focused predominantly on patients who have already been diagnosed within the healthcare system, rather than costs for presumptive TB cases prior to diagnosis.[21] Costs for presumptive cases are not well understood, especially in sub-Saharan Africa.[3 22] In addition to financial costs, sociocultural and gender-related factors can shape how patients seek healthcare,[23] yet such studies of the influence of these factors are scarce.[24] Finally, only few studies have examined pathways and costs of seeking healthcare by comparing confirmed and presumptive TB patients.[3 10 25]

Objective

We aimed to assess the pathways to care and associated costs of seeking care from the onset of symptoms until TB diagnosis in patients with confirmed and presumptive TB in Dar es Salaam, Tanzania.

METHODS

Study setting and study population

The study was conducted within the framework of an on-going TB cohort (TB-DAR) study among the adult population in the Temeke district of Dar es Salaam, Tanzania.[4] The district is densely populated with a population of 1 369 000 persons.[26] It ranks as the poorest in the region with 29% of the households living below the poverty line, resulting in 295 poor persons per square kilometre.[27] The number of healthcare facilities in Temeke district is low compared with other districts in the region. There are six public and private hospitals, eight health centres and 121 dispensaries.[28] In 2011, a total of 4112 TB cases of all forms were notified in the Temeke district, of which 1760 (43%) were smear positive.[29]

We included adult, sputum smear-positive patients with TB and presumptive TB cases who were consecutively enrolled in the TB-DAR study[4 30] between August 2016 and January 2017, until the target sample size of 100 patients in each category was reached (figure 1). Based on power calculation and previous studies,[3 25] we included 100 patients with confirmed TB and 100 patients with presumptive TB allowing to detect a statistically significant difference in the prevalence of diagnostic delay between the two groups of patients with a power of 80% in case of a true difference of at least 20%. Inclusion criteria were, (i) ≥18 years of age at recruitment; (ii) bacteriologically confirmed TB diagnosis, or with presumptive TB and (iii) residency in the Wailes I or II subdistricts of Temeke. Additionally, patients in both groups were screened for TB using sputum smear microscopy and Xpert MTB/RIF. We excluded patients who did not provide consent and those with incomplete data.

Data collection

Interviews

We interviewed patients, reconstructed retrospectively visits to healthcare facilities and collected data on direct and indirect costs using a standardised questionnaire at the TB clinic. The data collected included patient sociodemographic and socioeconomic characteristics, TB symptoms, the duration of the time from the onset of symptoms until the first help seeking in a healthcare facility and the number of healthcare facilities that patients with confirmed and presumptive TB had visited. Data were recorded on tablets using the OpenDataKit application.[31]

Pathways to care

Visualisation charts were used to reconstruct the pathways to care for each patient from the onset of symptoms until TB diagnosis up to five visits. We assessed all visits to the healthcare facilities made, including transport used and approximate distance from the household to the respective healthcare facilities. Healthcare facilities included pharmacies, dispensaries, health centres, traditional and religious healers and private and government hospitals.

Geographical information system data

We collected geo-coordinates of healthcare facilities, including all pharmacies, dispensaries, private and governmental hospitals, health centres as well as traditional healers identified in the study area. We also collected geo-coordinates of households of all patients who participated in the study.

Costs of care

We asked patients to estimate direct and indirect costs associated with each visit from the onset of symptoms until TB diagnosis, using a standardised questionnaire.[32] Direct costs included costs for diagnosis (such as costs for X-rays), medical costs (as costs for drugs that excluded TB drugs), food, transport and other costs that included special supplements and vitamins. Indirect costs included income reduction, decreased production costs, coping costs (including the use of savings or selling of household assets to cater for sickness) and reduced payment for labour. Calculation of patient costs relied on the 2008 WHO tool.[32] We report costs as US Dollars (USD), converted from Tanzania shillings using the exchange

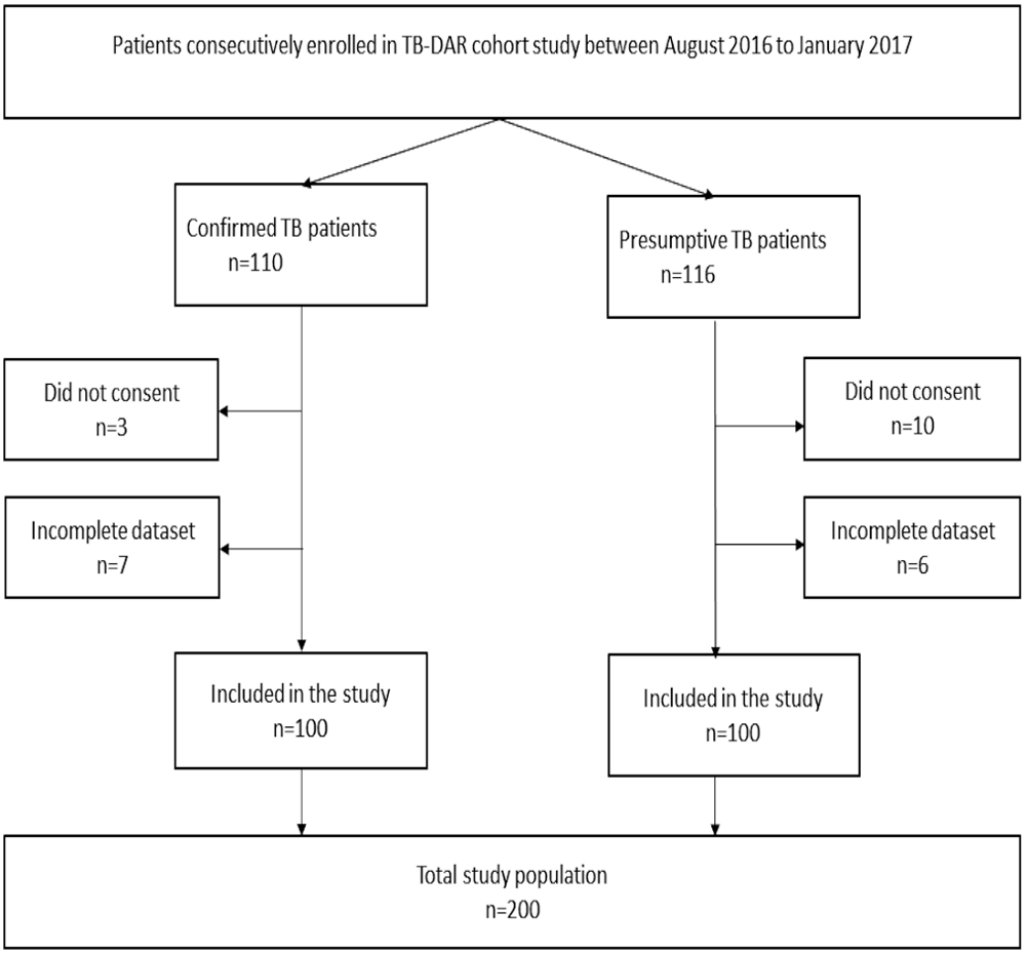

Figure 1 Flowchart of the study population. Participants were enrolled until the final target of 100 patients with confirmed and 100 patients with presumptive TB was reached.

rate from the Bank of Tanzania of USD/TZS 2167.84 as of August 2016.

Definitions

A new patient with TB was defined by bacteriological confirmation with sputum smear microscopy and/or Xpert MTB/RIF in the absence of prior TB treatment during screening.[33] A patient with presumptive TB was defined by presentation with TB symptoms, including coughing for longer than 2 weeks, fever, night sweats or unexplained weight loss, and who tested negative on sputum smear or Xpert MTB/RIF.[33] Diagnostic delay was defined according to the framework of WHO and used in previous studies[34 35] as the interval between the onset of any TB-related symptom and the time of TB diagnosis of more than 3 weeks. Healthcare provider was defined as a person or facility that could provide healthcare, this included hospitals, pharmacies and dispensaries, as well as traditional healers. Prior medication was defined as the use of any prescribed or self-prescribed medication prior to TB diagnosis.[4] We defined patients as poor if their wealth fell in the lowest or second-lowest wealth quantile. The non-poor were defined as persons in the remaining middle, fourth and highest wealth quantiles.[36]

Statistical and geographical analysis

We performed descriptive analyses to summarise the data and used χ^2 or Fisher's test to assess differences between groups in categorical variables. 'A cut-off point of 300 USD was used as a threshold for the monthly household income as indicated in another similar study.[4] Cost distributions were described by their medians and IQRs. Costs were further calculated stratifying by gender and poverty status. Wealth quantiles were generated following a principal component analysis of standard household assets as indicated in the Tanzania household survey.[26] To stratify between the poor and non-poor, we used wealth indicators relating to household characteristics (eg, roofing type, cooking fuel and nature of flooring) and ownership of assets (eg, radio and mobile phone) to create wealth ranking as used in other studies.[37 38] Patients in the first and second quantiles were considered poor and in the remaining quantiles as non-poor. We used the non-parametric Kruskal-Wallis test to assess the statistical significance of the differences in estimated costs between groups. All significance tests were two-sided with a confidence level of 95%. Quantile regression models were performed for median costs to examine the association

of patient factors with the different types of costs. Factors considered in these models included male versus female, age in years, unskilled and semi-skilled labour, level of education and diagnostic delay. Statistical analyses were performed using Stata V.14.0 . (Stata Corporation, College Station, TX, USA)

We mapped and visualised the pathways of patients to healthcare providers up to a maximum of five visits for the current episode of sickness as described elsewhere.[3 14] We calculated straight lines distances in metres between the patient's household and the nearest health facility. The resulting distances were imported into Stata for further analyses. All geographical analyses were performed using ArcGIS (V.10.5, Esri Redlands, CA, USAAll maps were obtained from Open Street Maps.

Patient involvement

Patients were not involved in the development, design and analysis of this study.

RESULTS

Patient characteristics

The study population includes 100 patients with confirmed and 100 patients with presumptive TB (table 1). Patients' median age was 34 years, with patients with presumptive TB being slightly older than the confirmed patients. Men slightly predominated (55.5%) and accounted for almost two-thirds of the confirmed patients. Compared with patients with presumptive TB, confirmed patients had a somewhat higher education, were less likely to own a house and more likely to use a car transport for their first point of care. They more frequently used medication after the onset of symptoms and prior to seeking care at the health facilities (71% vs 44%, p<0.001). The proportion of patients with a monthly household income of less than USD 300 was 63% in confirmed and 75% in presumptive patients (p=0.06).

First point of care and diagnostic delay

Among confirmed patients, 44% first sought care at pharmacies after the onset of symptoms, whereas 42% of presumptive patients first sought care at hospitals (table 1). Fewer than 10% of patients in both groups reported visits to traditional healers as the first point of care. Confirmed patients frequently indicated more than two visits at health facilities (33% vs 9%, p<0.001).

The average time for first seeking healthcare after the onset of symptoms was 2 weeks. Overall, 45.5% sought care within 1 week after the onset of TB symptoms. For 30%, the diagnostic was established within 2–3 weeks. For about a tenth, there was a diagnostic delay of 6 weeks or more. The diagnostic delay differed significantly between confirmed and presumptive patients, with 41% of confirmed versus 50% of presumptive patients having a short delay (of <1 week). Higher proportions of confirmed patients had a diagnostic delay of 4–5 and of ≥6 weeks.

Pathways to care

The spatial distribution of healthcare facilities in the study area shows pharmacies and dispensaries are distributed over the whole area (figure 2A). Hospitals are situated mainly in the urban centres and traditional healers predominantly in the peripheral area. Figure 2B,C offer examples of pathways to care until TB diagnosis in confirmed and presumptive patients. Pathways in confirmed patients involved several visits to the healthcare facilities before TB diagnosis. Pathways in presumptive patients were more direct with only one or few visits to healthcare facilities before TB diagnosis.

The median distance from patients' households to healthcare facilities including hospitals, pharmacies, dispensaries, and traditional healers was 2338 m (IQR 1373–4122) for confirmed patients and 2009 m (IQR 986–2976) for presumptive patients (p=0.25). Among confirmed patients, 37% lived within 500 m as did 42% of presumptive patients. Eighty-three per cent of confirmed patients and 72% of presumptive patients lived within 1000 m from the nearest hospital. We did not find an association of the distance from patients' household to the nearest possible healthcare facility with patient characteristics such as being poor (defined as being in the lowest two wealth quantiles), prior use of medication, or having more than two healthcare visits in multivariate analysis.

While seeking care at pharmacies was prominent for the first visit in confirmed patients and also reported by a fifth of the presumptive patients, subsequent visits at pharmacies were mentioned much less (figure 3). The second visit was characterised by a large proportion of patients seeking healthcare at hospitals in both groups. Confirmed patients had more visits to healthcare facilities compared with presumptive patients (none of the presumptive patients indicated a fourth and fifth visit).

Costs associated with seeking care

Patients spent a median of 31% (IQR 15.0%–56.3%) of their monthly household income for health expenditures for all visits for TB diagnosis. For the first visit, confirmed patients had lower median costs than presumptive patients (USD 8.3 [IQR 4.6–17.5] vs 13.8 [IQR 6.0–20.5]), but their costs became comparatively higher with increasing number of visits (see online supplementary table 1).

Overall, indirect costs were considerably higher than direct costs, both in confirmed and presumptive patients from the onset of symptoms until confirmation/exclusion of TB (table 2). Confirmed patients had higher diagnostic costs than presumptive patients (USD 7.0 [IQR 5.8–9.2] and 5.3 [IQR 1.4–7.0]), higher food costs and higher informal payments. Among the indirect costs, income reduction was considerably higher for patients with confirmed TB than presumptive patients (USD 23.1 [IQR 6.9–55.4] vs 9.2 [IQR 1.4–25.4]).

Table 1 Socio-demographic characteristics and diagnostic delay for the patients with confirmed and presumptive tuberculosis (TB).

Variable n (%)	All n=200	Confirmed n=100	Presumptive n=100	P value
Age in years (median, IQR)	34 (27–41.5)	32.5 (26–39)	34 (29–43)	0.055*
Age groups				0.22
18–27 years	52 (26)	30 (30)	22 (22)	
28–37 years	75 (37.5)	39 (39)	36 (36)	
>38 years	73 (36.5)	31 (31)	42 (42)	
Sex				0.016
Male	111 (55.5)	64 (64)	47 (47)	
Female	89 (44.5)	36 (36)	53 (53)	
Education				0.023
No education	34 (17)	12 (12)	22 (22)	
Primary education	122 (61)	59 (59)	63 (63)	
Secondary/university	44 (22)	29 (29)	15 (15)	
Occupation				0.081
Unemployed/housewife	59 (29.5)	30 (30)	29 (29)	
Unskilled labour	49 (24.5)	18 (18)	31 (31)	
Semiskilled labour	92 (46)	52 (52)	40 (40)	
Household size				0.67
<4	93 (46.5)	45 (45)	48 (48)	
≥4	107 (53.5)	55 (55)	52 (52)	
House ownership				0.050
Rented	135 (67.5)	74 (74)	61 (61)	
Own	65 (32.5)	26 (26)	39 (39)	
Household income				0.067
≤300 USD per month	138 (69)	63 (63)	75 (75)	
>300 USD per month	62 (31.0)	37 (37)	25 (25)	
Wealth quantile				0.54
Poor households	47 (23.5)	21 (21)	26 (26)	
Second	33 (16.5)	16 (16)	17 (17)	
Middle	41 (20.5)	19 (19)	22 (22)	
Fourth	44 (22)	27 (27)	17 (17)	
Non-poor households	35 (17.5)	17 (17)	18 (18)	
Prior medication				<0.001
Yes	115 (57.5)	71 (71)	44 (44)	
No	85 (42.5)	29 (29)	56 (56)	
First point of care				0.004
Hospitals	70 (35)	28 (28)	42 (42)	
Dispensaries	49 (24.5)	19 (19)	30 (30)	
Pharmacies	66 (33)	44 (44)	22 (22)	
Traditional healers	15 (7.5)	9 (9)	6 (6)	
HC facility visits				<0.001
≤2	158 (79)	67 (67)	91 (91)	
>2	42 (21)	33 (33)	9 (9)	
Transport used for first point of care				<0.001
Car	70 (35.5)	22 (22)	48 (48)	

Continued

Table 1 Continued

Variable n (%)	All n=200	Confirmed n=100	Presumptive n=100	P value
On foot	95 (47.5)	65 (65)	30 (30)	
Motorcycle/tricycle	35 (17.5)	13 (13)	22 (22)	
Diagnostic delay				0.04
0–1	91 (45.5)	41 (41)	50 (50)	
2–3	60 (30)	26 (26)	34 (34)	
4–5	27 (13.5)	19 (19)	8 (8)	
6+	22 (11)	14 (14)	8 (8)	

P values provided by χ^2 tests and Fisher's exact test.
*Wilcoxon-rank sum test.
HC, health care facility; USD, United States Dollar.

Gender, poverty status and costs

Costs for different patient groups differed significantly. Overall, the median total direct costs were similar for men, USD 24.9 (IQR 17.5–41.9), and women, USD 24.6 (IQR 16.1–42.4 p=0.66). Indirect costs for men, USD 64.6 (IQR 31.8–159.1), were significantly higher than those for women, at USD 55.6 (IQR 25.1–141.1, p<0.001).

Analyses stratified by sex and poverty status indicate that poor men with confirmed TB had lower total direct costs compared with poor women (USD 24.4 [IQR 18.9–47.9] vs 30.0 [IQR 18.7–49.6]) (table 3). For the patients with presumptive TB, total direct costs for poor men differed slightly from those of poor women (USD 22.6 [IQR 17.5–29.1] vs 20.5 [IQR 14.3–35.1]). Among

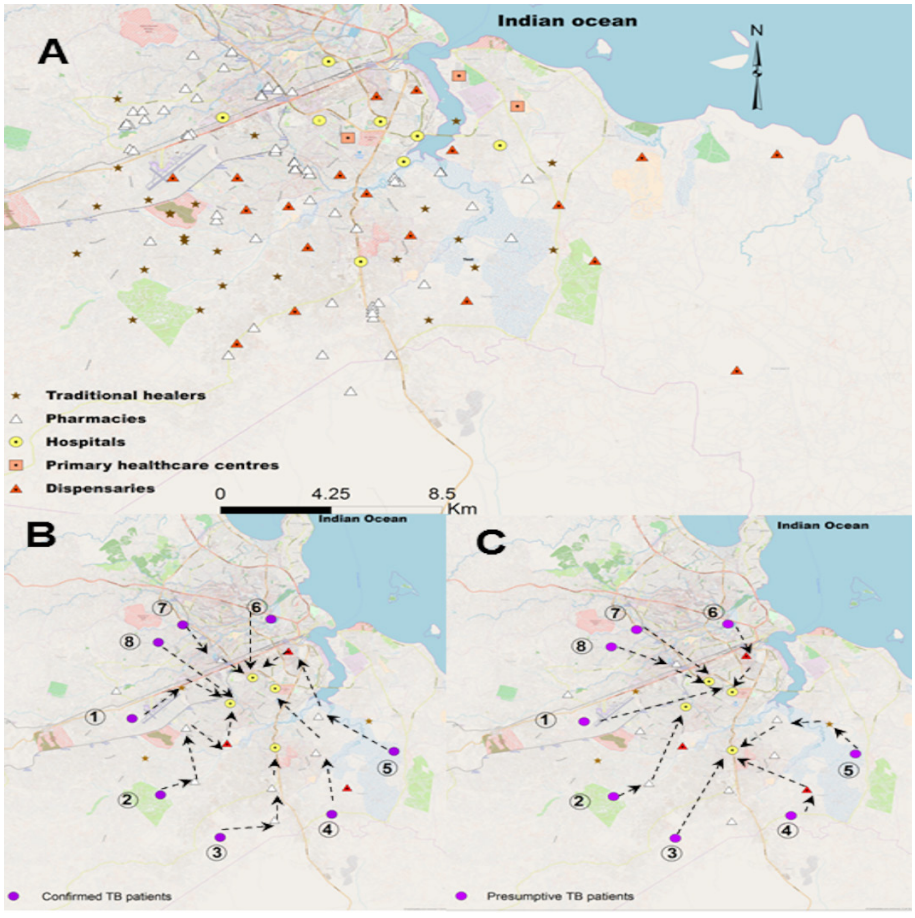

Figure 2 Geographical analyses of healthcare facilities and pathways to care of patients with confirmed and presumptive TB in Temeke District, Dar es Salaam, Tanzania. Various types of healthcare facilities as the entry point into the healthcare system until final diagnosis at the TB clinic are shown.Panel A: Spatial distribution of healthcare facilities in the study area. Panel B: Possible pathways to care of patients with confirmed TB while seeking healthcare. Panel C: Possible pathways to care of patients with presumptive TB while seeking healthcare.

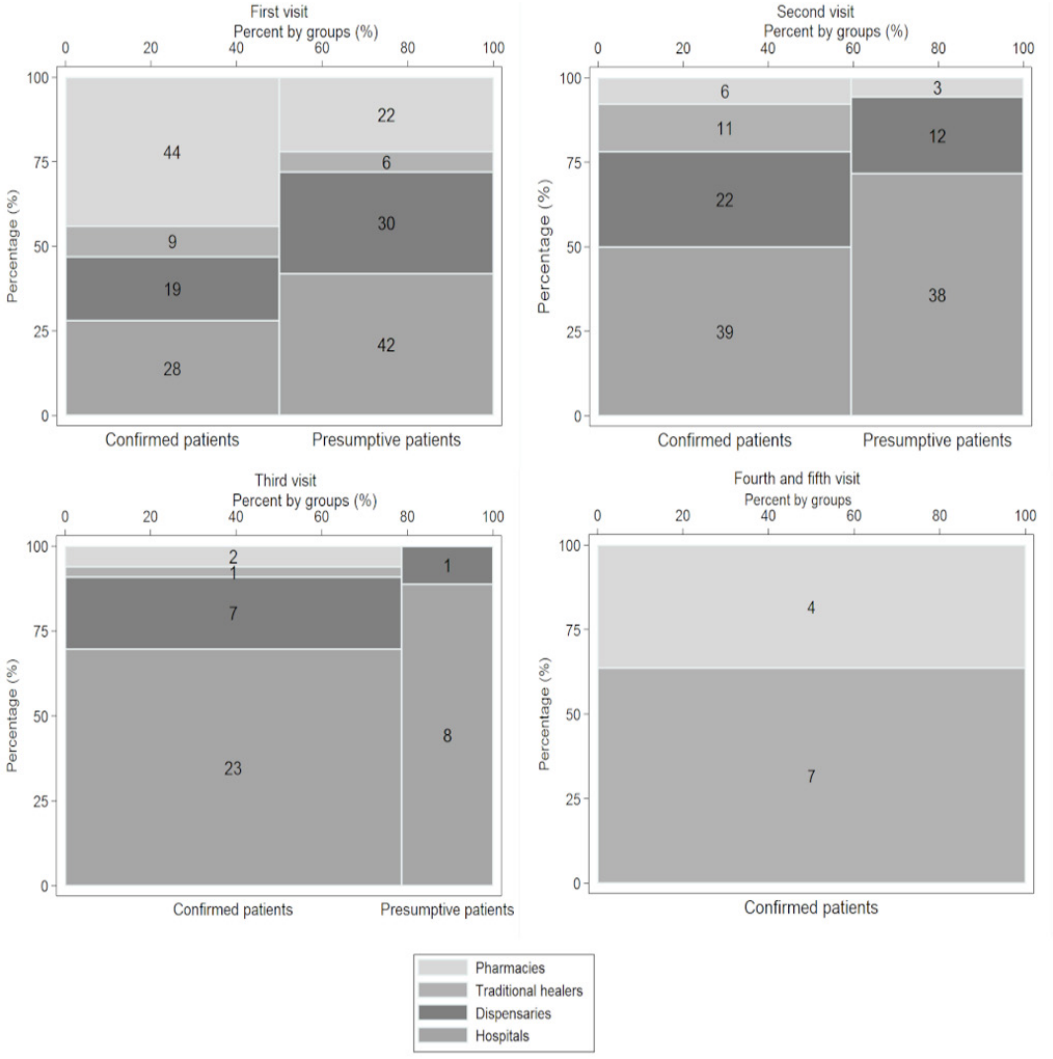

Figure 3 Spine plots showing distribution of healthcare facility visits during the pathway to care (first, second, third and fourth/fifth visit) in confirmed and presumptive patients. Numbers on the graph indicate absolute frequencies.

the non-poor men and women, direct costs differed only little between confirmed and presumptive patients. In confirmed patients, diagnostic costs were lower among poor men compared with poor women (USD 6.91 [IQR 4.61–9.22] vs 7.61 [IQR 1.38–10.14]), whereas for the presumptive patients, diagnostic costs were the same among poor men and women.

Total indirect costs, (table 4) among poor patients with confirmed TB were higher in men than women, (USD 84.4 [IQR 55.3–125] vs 51.7 [IQR 27.6–73.4]), while this gender difference was absent in non-poor confirmed patients. Among patients with presumptive TB, poor men faced higher total indirect costs than poor women (USD 50.2 [IQR 27.6–83.4]) vs 39.2 [IQR 18.6–116.0]).

Determinants of cost differences

On average, each week of diagnostic delay was associated with an increase in median total costs (direct and indirect costs) among confirmed patients by 1.44 USD (95% CI: 0.93,1.96), p<0.001), but no significant association was seen in presumptive patients (table 5). Diagnostic delay was associated with an increase in total direct costs in confirmed patients (USD 0.52 per week, 95% CI: (0.34 to 0.70), p<0.001), but with a decrease in presumptive patients (USD −0.84 per week, 95% CI: (−1.32 to −0.35), p=0.001). For total indirect costs, the pattern was similar, but neither of the two associations reached statistical significance.

Overall, having a university degree was significantly associated with higher indirect costs (USD 70.14, 95% CI: [9.47 to 130.80], p=0.02). None of the other factors of the model were significantly associated with median costs. The pattern of positive association between diagnostic delay and total costs among confirmed patients and negative association among presumptive patients was further supported by analyses using linear and quadratic terms (figure 4). Furthermore, we conducted regression analyses separately for different types of costs (see online supplementary tables 2 and 3). Medication costs in confirmed patients increased with the number of weeks of delay (USD 0.13 per week, 95% CI: [0.06 to 0.19],

Table 2 Direct and indirect costs (in USD) from the onset of symptoms until confirmation/exclusion of TB among patients with confirmed and presumptive TB.

Costs	All n=200	Confirmed n=100	Presumptive n=100	P value
Average number of visits (range)	1.2 (1–5)	1.3 (1–5)	1.1 (1–3)	
	Median, (IQR)	Median, (IQR)	Median, (IQR)	
Direct costs				
Diagnostic costs	7.0 (2.3–8.8)	7.0 (5.8–9.2)	5.3 (1.4–7.0)	<0.001
Medication costs	2.8 (1.4–8.0)	2.8 (1.4–9.2)	2.8 (1.4–7.4)	0.873
Food costs	2.3 (1.4–4.2)	3.2 (1.8–5.3)	1.8 (1.0–2.5)	<0.001
Transport costs	3.2 (1.8–5.5)	3.2 (1.4–5.5)	3.7 (1.8–6.00)	0.154
Informal payments	2.3 (1.4–4.2)	2.8 (2.3–7.4)	2.1 (1.0–2.8)	<0.001
Other direct costs	4.6 (2.3–9.7)	4.6 (2.3–9.5)	4.4 (2.3–9.7)	0.567
Subtotal direct costs	24.7 (16.1–42.4)	27.4 (18.7–48.4)	19.8 (13.8–33.9)	0.02
Indirect costs (median, [IQR])				
Coping costs	11.3 (4.6–23.1)	11.5 (4.61–20.98)	9.2 (4.6–27.7)	0.765
Income reduction	15.7 (3.7–36.9)	23.1 (6.9–55.4)	9.2 (1.4–25.4)	0.001
Decreased production	9.2 (1.4–23.06)	10.0 (3.2–26.3)	9.2 (0–16.8)	0.137
Less paid labour	4.61 (0–12.0)	5.07 (0–15.22)	4.61 (0–9.2)	0.467
Other indirect costs	8.5 (1.8–19.4)	11.8 (1.4–23.1)	6.5 (2.3–13.8)	0.056
Subtotal indirect costs	60.0 (25.1–141.1)	66.9 (35.1–149.9)	46.8 (20.1–115.3)	0.006
Total costs	83.0 (46.4–173.9)	99.2 (64.3–190.0)	67.11 (37.1–161.0)	0.003

P values provided by Wilcoxon rank sum test.
IQR, Interquartile range, TB, tuberculosis; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016).

p<0.001), but not in presumptive patients. Transport costs were significantly lower among men and women with presumptive TB (USD −1.54, 95% CI: [−3.12 to −0.03], p<0.05). We further observed an increase in coping costs with the length of diagnostic delay in both confirmed and presumptive patients (see online supplementary table 3). Finally, in patients with presumptive TB, costs due to decreased production were significantly higher among unskilled labourers (USD 8.71, 95% CI: [0.53 to 16.89], p=0.03).

DISCUSSION

This study indicates that pathways to care of the patients with confirmed TB are more complex compared with those of presumptive patients, involving visits at several healthcare providers among whom not all have necessary diagnostic equipment. A diagnostic delay of 6 weeks or more after the onset of symptoms was reported by 10% of the patients. Fifty per cent of the patients visited healthcare facilities within 1 week after onset of symptoms. In seeking care, patients incur substantial direct and indirect costs. The costs of care were higher in confirmed patients than in presumptive patients. For half of the confirmed patients, direct costs account for more than 30% of the monthly household income. Total costs were associated with diagnostic delay among confirmed patients only. The indirect costs were higher for men than for women whereas direct costs did not differ. Among the poor, direct costs were higher in women and indirect costs higher in men.

Almost half of the patients with confirmed TB began their search for care at pharmacies, and patients in both groups sought care from more than one healthcare provider before a diagnosis. This highlights a diagnostic shortfall in some healthcare facilities and poor management of patients as documented elsewhere,[39] and partially explains the diagnostic delay. Compared with findings of other studies,[19 40] the observed diagnostic delay in our study was lower. However, a delay of at least 6 weeks observed in 10% of our study population still requires attention. Most patients lived near healthcare facilities, and only 9% of the patients with confirmed TB and 6% of the patients with presumptive TB reported visiting traditional healers. Living near healthcare facilities might have an impact on treatment seeking.[41] We investigated the impact of geographical distance between household and health facility on health-seeking behaviour, but found no associations between distance and patient characteristics such as being poor, prior use of medication and having more than two visits to the healthcare facility. This is contrary to some other results that found distance to have an impact on patient characteristics such as treatment completion and diagnostic delay.[35 42 43] Diagnostic delay was significantly associated with direct costs, indirect costs (borderline significance) and total costs in confirmed patients. The most likely explanation for this finding is

Table 3 Direct costs (in USD) of seeking healthcare among patients with confirmed and presumptive tuberculosis (TB), according sex and poverty status.

Variable		Confirmed				Presumptive			
		Men		Women		Men		Women	
Median (IQR)	All	Poor* n=21	Non-poor† n=43	Poor n=16	Non-poor n=20	Poor n=15	Non-poor n=32	Poor n=28	Non-poor n=25
Diagnostic costs	6.92 (3.22–9.23)	6.91 4.61–9.22	6.91 (6.91–9.22	7.61 (1.38–10.14)	7.61 1.84–11.53	4.61 (0.92–6.91)	6.91 (2.07–9.68)	4.61 (1.84–6.91)	6.91 (3.22–9.22)
Medication costs	3.69 (1.84–8.99)	5.53 (2.30–16.14)	2.30 (1.38–6.91)	3.45 (0.92–8.76)	3.92 (2.07–13.60)	4.15 (1.38–9.22)	5.30 (2.30–8.76)	3.45 (1.84–8.99)	3.69 (2.30–6.91)
Food costs	2.31 (1.38–4.61)	3.22 (1.84–6.45)	4.15 (1.84–5.07)	2.53 (1.84–6.68)	3.45 (2.30–6.22)	1.38 (0.92–2.30)	2.07 (1.15–2.99)	1.84 (0.92–2.53)	2.30 (0.92–2.76)
Transport costs	3.69 (1.84–5.76)	3.69 (1.84–5.53)	2.76 (1.38–5.53)	3.00 (0.69–4.84)	3.69 (2.07–5.53)	3.22 (1.38–5.07)	4.38 (2.53–6.91)	3.69 (2.07–6.45)	4.61 (2.30–6.00)
Informal payments	2.30 (1.38–4.61)	2.30 (2.30–6.45)	2.30 (2.30–9.68)	3.22 (2.30–12.91)	3.92 (1.61–7.38)	1.84 (0.92–2.30)	2.30 (1.61–3.69)	1.16 (0.92–3.22)	2.30 (0.92–2.77)
Other direct costs	5.53 (2.77–10.61)	5.07 (2.30–6.45)	6.45 (3.69–10.60)	6.91 (4.84–8.30)	9.91 (4.84–15.00)	5.07 (1.38–9.68)	5.30 (2.07–12.00)	3.45 (2.30–10.60)	5.53 (3.69–10.60)
Total direct costs	27.21 (18.45–43.12)	24.44 (18.91–47.97)	29.98 (22.60–43.35)	30.00 (18.7–49.6)	32.51 (17.98–55.81)	22.60 (17.52–29.05)	25.13 (15.91–44.28)	20.52 (14.29–35.05)	26.75 (17.98–37.82)

*Poor or second-lowest wealth quantile.
†Non-poor middle, fourth and highest wealth quantile.
IQR, interquartile range, USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016) Other direct costs including costs of special supplements and vitamins required due to illness or additional direct costs due to chronic illness for which patients were receiving treatment for besides the costs for TB diagnosis.

Table 4 Indirect costs (in USD) of seeking healthcare among patients with confirmed and presumptive tuberculosis (TB), according to sex and poverty status

Variable		Confirmed				Presumptive			
		Men		Women		Men		Women	
Median (IQR)	All	Poor n=21	Non-poor n=43	Poor n=16	Non-poor n=20	Poor n=15	Non-poor n=32	Poor n=28	Non-poor n=25
Coping costs	13.37 (6.91–25.36)	10.60 (4.61–18.45)	13.83 (6.91–20.75)	13.53 (8.53-17-75)	23.06 (9.22–34.59)	9.22 (6.91–13.83)	13.37 (4.61–27.67)	15.91 (6.22–140-35)	9.22 (0–18.45)
Income reduction	18.45 (4.61–35.51)	29.98 (23.06–46.12)	23.06 (11.53–59.96)	14.52 (5.76–28.13)	23.06 (0–53.04)	9.22 (3.69–36.90)	15.22 (6.68–29.98)	4.61 (0.69–11.53)	11.53 (0–23.06)
Decreased production	9.22 (2.30–23.06)	16.14 (7.38–23.06)	12.00 (4.61–31.36)	6.91 (2.30–13.37)	9.45 (0–32.51)	9.22 (4.61–20.75)	13.14 (4.61–31.13)	4.61 (0–13.14)	9.22 (0–14.76)
Less paid labour	4.61 (0–12.0)	6.91 (0–17.52)	6.91 (0–18.45)	0 (0–6.45)	1.61 (0–18.45)	5.53 (0–13.83)	5.75 (0–13.37)	4.61 (0–10.37)	1.38 (0–6.91)
Other indirect costs	8.53 (1.38–19.37)	11.53 (1.38–26.29)	12.0 (0–23.06)	11.53 (2.53–18.45)	11.53 (3.69–26.06)	9.68 (3.22–13.83)	8.53 (4.38–21.90)	5.76 (0.69–11.07)	3.22 (0.92–9.22)
Total indirect costs	61.34 (27.90–128)	84.40 (55.35–125)	71.03 (51.66–156.36)	51.66 (27.67–73.80)	70.80 (31.82–148.52)	50.27 (27.67–83.48)	55.11 (30.21–166.28)	39.20 (18.68–116.00)	39.20 (21.67–65.95)

Other indirect costs including costs that were not treated as direct labour or additional indirect costs due to chronic illness for which patients were receiving treatment for besides the costs for TB diagnosis.
*Poor or second-lowest wealth quantile.
†Non-poor middle, fourth and highest wealth quantile.
IQR, Intequartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016).

Table 5 Estimates of effects of different factors on median direct, indirect and total costs in USD among patients with confirmed and presumptive tuberculosis

	All			Confirmed			Presumptive		
Variable	**Difference***	**95% CI**	**P value**	**Difference***	**95% CI**	**P value**	**Difference***	**95% CI**	**P value**
Total direct costs									
Males versus females	−1.71	−11.80 to 8.38	0.73	−2.31	−20.29 to 15.67	0.79	−3.58	−9.80 to 2.63	0.25
Age (per year)	−0.01	−0.48 to 0.46	0.97	0.28	−0.70 to 1.26	0.57	0.06	−0.19 to 0.31	0.31
Unskilled labour†	1.80	−11.40 to 15.01	0.78	−7.55	−33.38 to 18.26	0.56	2.20	−5.18 to 9.59	0.55
Semiskilled labour	-2.87	−8.75 to 14.48	0.62	5.01	−14.66 to 24.69	0.61	1.87	−5.49 to 9.23	0.61
Poor versus non-poor	−2.34	−12.19 to 7.51	0.63	19.73	−56.98 to 96.46	0.61	−2.40	−8.07 to 3.27	0.40
Primary education‡	3.18	−10.21 to 16.56	0.64	8.96	−17.83 to 35.76	0.66	0.66	−6.47 to 7.78	0.85
Secondary education	6.12	−11.16 to 23.40	0.48	20.86	−11.40 to 53.12	0.20	4.22	−5.88 to 14.32	0.40
University‡	9.36	−19.07 to 37.84	0.51	10.53	−35.17 to 56.25	0.46	−0.59	−21.14 to 19.95	0.95
Diagnostic delay	0.04	−0.08 to 0.16	0.52	0.52	0.34 to 0.70	<0.001	−0.84	−1.32 to 0.35	0.001
Total indirect costs									
Males versus females	11.63	−11.37 to 34.63	0.32	6.60	−33.93 to 47.14	0.74	1.85	−34.74 to 38.44	0.92
Age (per year)	0.38	−0.69 to 1.45	0.48	0.07	−2.14 to 2.29	0.94	0.75	−0.74 to 2.24	0.32
Unskilled labour	12.68	−17.41 to 42.78	0.40	14.47	−43.74 to 72.700	0.62	19.13	−24.32 to 62.11	0.38
Semiskilled labour	20.90	−5.58 to 47.38	0.12	37.24	−7.11 to 81.60	0.09	22.94	−20.38, 66.27	0.29
Poor versus non-poor	6.29	−16.15 to 28.75	0.58	6.92	−33.36 to 47.20	0.73	5.82	−27.53 to 39.18	0.72
Primary education	21.24	−9.27to 51.75	0.17	8.96	−51.46 to 69.37	0.76	20.0	−20.34 to 60.34	0.32
Secondary/university	70.14	9.47 to 130.80	0.02	56.88	11.71 to 125.47	0.10	−38.5	16.52 to 93.52	0.16
Diagnostic delay	0.46	0.18 to 0.74	0.001	0.57	0.16 to 0.97	0.07	−1.25	−4.11 to 1.60	0.38
Total costs									
Males versus females	9.87	−26.39 to 46.14	0.59	−4.98	−58.90 to 48.93	0.85	−0.62	−44.96 to 43.71	0.97
Age (per year)	0.34	−1.34 to 2.03	0.68	−0.56	−3.50 to 2.38	0.70	0.74	−1.06 to 2.55	0.41
Unskilled labour	11.95	−35.50 to 59.40	0.62	8.25	−69.18 to 85.69	0.83	16.02	36.64 to 68.69	0.54
Semiskilled labour	30.47	−11.28 to 72.23	0.15	58.81	−0.18 to 117.81	0.05	26.64	−25.86 to 79.14	0.31
Poor versus non-poor	0.89	−34.50 to 36.31	0.96	8.39	−45.18 to 61.98	0.75	2.39	−38.01 to 42.81	0.90
Primary education	24.87	−23.25 to 72.98	0.31	19.73	−60.62 to 100.09	0.62	18.06	−32.75 to 68.88	0.48
Secondary education	69.54	7.43 to 131.16	0.02	69.45	−27.29 to 166.19	0.15	46.10	−25.86 to 79.14	0.20
University	108.89	6.63 to 211.16	0.03	69.20	−67.87 to 206.28	0.31	−15.74	−162.23 to 130.73	0.83
Diagnostic delay	1.29	0.84 to 1.73	<0.001	1.44	0.93 to 1.96	<0.001	−2.40	−5.86 to 1.06	0.17

*Estimated differences in median costs are presented with the corresponding 95% CIs; diagnostic delay was defined as delay in seeking care 3 weeks or more after the onset of symptoms. Multivariable quintile regression was performed for median costs to examine the association of patient factors with different types of costs. Separate models were run for direct, indirect and total costs.
†Reference: unemployed.
‡Reference: no education.

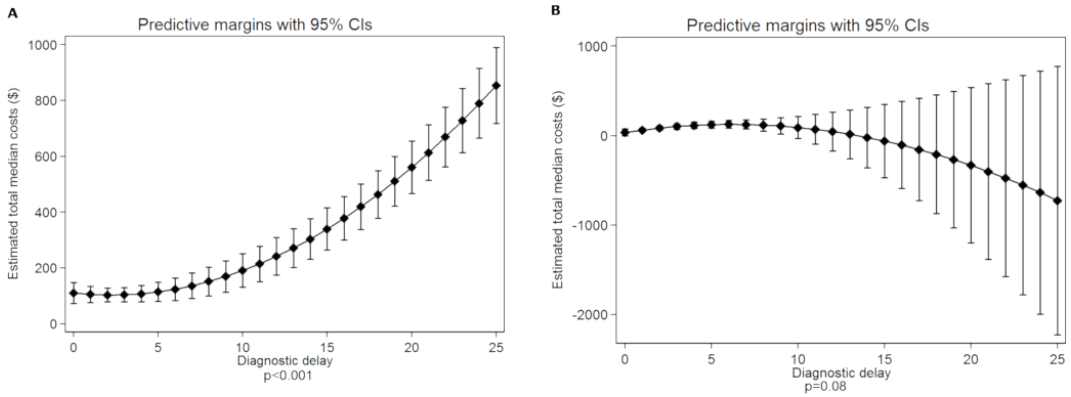

Figure 4 Margin plots showing associations between total costs and diagnostic delay in patients with confirmed TB (panel A) and patients with presumptive TB (panel B). Associations between median total costs and diagnostic delay were modelled by quadratic polynomials. The p values are from Wald test of the linear and quadratic terms of the diagnostic delay (p<0.001 for panel A, p=0.08 for panel B).

that diagnostic delay worsens patients' morbidity, especially in patients with confirmed TB, thus increasing costs of healthcare.[42]

Patients in both groups spent a median proportion of around 30% of their monthly household income on health expenditures for up to five visits. The economic burden of direct and particularly indirect costs of seeking TB care for patients and their households are high for the marginalised population, which is most at risk of acquiring TB. These findings are consistent with other studies that show patients in low-income and middle-income countries face a very high economic burden of seeking TB care[13] and expenditures for seeking healthcare for TB can cause or exacerbate poverty.[44] The total costs for patients with presumptive TB were lower compared with confirmed cases in our study. These results are also consistent with those reported in other settings where half of the total costs for seeking healthcare are pretreatment costs which disproportionately affect poor patients with TB.[13]

While direct costs were relatively low, they may be catastrophic for patients who are semiskilled labourers reporting monthly household income of less than 300 USD. Their situations can further be worsened by employment in the informal sector that lacks sickness benefits.[44] Patients with confirmed TB encountered higher indirect costs compared with presumptive patients, which may be due to the prolonged time required for diagnosis leading to their substantially higher income reduction as shown in our study.

We found higher indirect costs among poor men compared with poor women. This was mainly due to their more pronounced income reduction and decreased production. Although the direct and indirect costs were higher for men than for women, the costs of ill health are usually more profound for women and their households than for men. When women get sick the impact of the disease on their children and their families is stronger than when men get sick.[11] Furthermore, financial burden may limit access to care for both confirmed and presumptive female TB patients since most of them lack financial autonomy. Moreover, their lower status in households deprioritises their health.

Strengths and limitations of this study

Our study is the first to look at pathways to care and assess costs of care before the start of treatment in patients with confirmed and presumptive TB in an urban Tanzania setting. Studies have focused on pathways and costs of care in patients with confirmed TB and ignore the effects on presumptive cases. Furthermore, it's the first study to estimate costs by stratifying according to poverty status and gender in sub-Saharan Africa. However, this study has some limitations. First, recall bias is a concern when inquiring about the costs incurred during healthcare seeking. This might influence the accuracy of the reported costs and pathways to care. However, we attempted to limit the recall bias by linking questions about costs with memorable events such as the onset of symptoms or first care seeking. Our interviews were also conducted by well-trained personnel who spent enough time with the respondents so as to obtain answers that were as accurate as possible. Furthermore, we only addressed pathways and costs of care until TB diagnosis to the public healthcare facilities. Therefore, we might have left out costs of care for the patients who had their final diagnosis at the private and faith-based healthcare facilities. Finally, we only estimated the costs for TB diagnosis. However, comorbidities may have caused higher costs, but this is equally true for confirmed as well as patients with presumptive TB.

CONCLUSIONS

This study demonstrates the complexity of pathways until diagnosis in patients with confirmed TB. It also highlights the high financial burden for the period between symptom onset and diagnosis for patients with confirmed and presumptive TB and points to different direct and indirect costs among poor men and women. This underscores the need to strengthen the healthcare sector to ensure early diagnosis of TB. Ensuring integration of

different healthcare providers including private, public health practitioners and patients themselves could help in reducing the complex pathways during healthcare seeking and optimal healthcare utilisation.[39] Reducing the direct and indirect costs associated with treatment seeking is likely to support patients with confirmed and presumptive TB in timely accessing healthcare for TB diagnosis and treatment. Decreasing or removing user fees and further decentralisation of TB care could reduce diagnostic delay and lower expenditures. Additionally, strengthening of health systems policies including protection of patients against thesubstantial direct and indirect costs, as well as ensuring universal access to healthcare must be interpreted into actions for a better TB control.[45] These interventions are central for reaching the ambitious WHO targets of zero deaths, disease and suffering due to TB by 2035.[46]

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