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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-025079.R1
Article Type:	Research
Date Submitted by the Author:	26-Oct-2018
Complete List of Authors:	Mhalu, Grace; Ifakara Health Institute Dar es Salaam, Health Intervention; Swiss Tropical and Public Health Institute Hella, Jerry; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Mhimbara, Francis; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Said, Khadija; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Mosabi, Thomas; Ifakara Health Institute Dar es Salaam Tanzania Mlacha, Yeromin; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Schindler, Christian; Swiss Tropical and Public Health Institute; University of Basel Gagneux, Sébastien ; Schweizerisches Tropen- und Public Health-Institut; University of Basel Reither, Klaus; Swiss Tropical and Public Health Institute; University of Basel de Hoogh, Kees; Swiss Tropical and Public Health Institute; University of Basel Weiss, Mitchell; Swiss Tropical and Public Health Institute, Epidemiology and Public Health; University of Basel Zemp, Elisabeth; Swiss Tropical and Public Health Institute, Department of Epidemiology and Public Health; University of Basel, Fenner, Lukas; Universitat Bern; Institute of Social and Preventive medicine
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Infectious diseases, Public health
Keywords:	Tuberculosis < INFECTIOUS DISEASES, Pathways to care, Direct costs, Indirect costs, Health-seeking, Health care



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4 **1 TITLE PAGE:**
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10 **3 Pathways and associated costs of care in confirmed and presumptive**
11 **4 tuberculosis patients in Tanzania: A cross-sectional study**
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20 **Keywords:** Tuberculosis, pathways to care, direct costs, indirect costs, health seeking,
21 Tanzania, healthcare

22 **Word count:**

23 Main text 3999 (max. 4000), abstract 300 (max. 300), references: 46

24 **Inserts:**

25 4 figures and 5 tables, Supplementary File (3 tables)
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27 Abstract

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

30 **Design:** Cross-sectional study.

31 **Setting:** District hospital in Dar es Salaam, Tanzania.

32 **Participants:** Bacteriologically confirmed TB and presumptive TB patients.

33 **Primary and secondary outcome measures:** We calculated distance in meters and
34 visualized pathways to healthcare up to five visits for the current episode of sickness.
35 Costs were described by medians and interquartile ranges (IQR), with comparisons by
36 gender and poverty status.

37 **Results:** Of 100 confirmed and 100 presumptive TB patients, 44% of confirmed patients
38 sought care first at pharmacies after the onset of symptoms, and 42% of presumptive
39 patients did so at hospitals. The median visits made by confirmed patients was 2 (range 1-
40 5), and 2 (range 1-3) by presumptive patients. Patients spent a median of 31% of their
41 monthly household income on health expenditures for all visits. The median total direct
42 costs were higher in confirmed compared to presumptive patients (USD 27.4 [IQR 18.7-
43 48.4] vs. USD 19.8 [IQR 13.8-34.0], $p=0.02$), as were the indirect costs (USD 66.9 [IQR
44 35.5-150.0] vs. USD 46.8 [IQR 20.1-115.3], $p<0.001$). The indirect costs were higher in
45 men compared to women (USD 64.6 [IQR 31.8-159.1] vs. USD 55.6 [IQR 25.1-141.1],
46 $p<0.001$). The median total distance from patients' household to healthcare facilities for
47 confirmed and presumptive TB patients was 2,338 meters (IQR 1,373-4,122) and 2,009
48 meters (IQR 986-2,976) respectively.

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3 49 **Conclusions:** Confirmed TB patients have complex pathways and higher costs of care
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5 50 compared to presumptive TB patients, but their costs are also substantial. Improved
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7 51 access to healthcare is needed for effective patient-centred care. This underscores the
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9 52 need for strengthening the healthcare sector and identifying strategies for diagnostic
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11 53 procedures that are cost-effective and patient-centred, particularly in the light of the
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14 54 introduction of new TB diagnostics.
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55 **Strengths and limitation of the study**

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

62

63 BACKGROUND

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

74 TB is widely regarded as a disease of poverty due to its disproportionate effects on
75 the marginalized populations [7,8]. To help socially and economically marginalized groups
76 fight the disease, healthcare facilities diagnose and treat TB free of charge in countries
77 with a high TB burden [9]. However, patients with symptoms of TB face high direct and
78 indirect costs for diagnosis and treatment [10–13], and these costs are usually higher for
79 patients with confirmed TB than presumptive cases [3,14].

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

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3 85 A national TB prevalence survey indicated that the case detection rate of TB was
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5 86 below 50% [16]. This result may not only be due to the complexity but also the high cost of
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7 87 care [15,17,18]. The recommended pathway to care for TB patients is to present
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9 88 themselves to the appropriate healthcare facilities for TB diagnosis after recognition of TB
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11 89 symptoms [9,19,20].

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14 90 Research has focused predominantly on patients who have already been diagnosed
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16 91 within the healthcare system, rather than costs for presumptive TB cases prior to diagnosis
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18 92 [21]. Costs for presumptive cases are not well understood, especially in sub-Saharan
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20 93 Africa [3,22]. In addition to financial costs, sociocultural and gender-related factors can
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22 94 shape how patients seek healthcare [23], yet such studies of the influence of these factors
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24 95 are scarce [24]. Finally, only few studies have examined pathways and costs of seeking
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26 96 health care by comparing confirmed and presumptive TB patients [3,10,25].

31 97 **Objective**

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33 98 We aimed to assess the pathways to care and associated costs of seeking care from the
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35 99 onset of symptoms until TB diagnosis in confirmed and presumptive TB patients in Dar es
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38 100 Salaam, Tanzania.

101 **METHODS**

102 **Study setting and study population**

103 The study was conducted within the framework of an on-going TB cohort study among the
104 adult population in the Temeke district of Dar es Salaam, Tanzania [4]. The district is
105 densely populated with a population of 1,369,000 persons [26]. It ranks as the poorest in
106 the region with 29% of the households living below the poverty line, resulting in 295 poor
107 persons per square kilometre [27]. The number of health facilities in Temeke district is low
108 compared to other districts in the region. There are six public or private hospitals, eight
109 health centers, and 121 dispensaries [28]. In 2011, a total of 4,112 TB cases of all forms
110 were notified in the Temeke district, of which 1,760 (43%) were smear-positive [29].

111 We included adult, sputum smear-positive TB patients and presumptive TB cases who
112 were consecutively enrolled in the TB-DAR study [4,30] between August 2016 and January
113 2017, until the target sample size of 100 patients in each category was reached (Figure 1).
114 Based on power calculation and previous studies [3,25] we included 100 confirmed TB
115 patients and 100 presumptive TB patients allowing to detect a statistically significant
116 difference in the prevalence of diagnostic delay between the two groups of patients with a
117 power of 80% in case of a true difference of at least 20%. Inclusion criteria were, (i) ≥ 18
118 years of age at recruitment; (ii) bacteriologically confirmed TB diagnosis, or with
119 presumptive TB, and (iii) residency in the Wailes I or II sub-districts of Temeke.
120 Additionally, patients in both groups were screened for TB using sputum smear
121 microscopy and Xpert MTB/RIF. We excluded patients who did not provide consent and
122 those with incomplete data.

123 **Data collection**

124 *Interviews*

125 We interviewed patients, reconstructed retrospectively visits to healthcare facilities and
126 collected data on direct and indirect costs using a standardized questionnaire at the TB
127 clinic. The data collected included patient socio-demographic and socioeconomic
128 characteristics, TB symptoms, the duration of the time from the onset of symptoms until
129 the first help seeking in a healthcare facility, and the number of health care facilities that
130 confirmed and presumptive TB patients had visited. Data were recorded on tablets using
131 the OpenDataKit (ODK) application [31].

132 *Pathways to care*

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

139 *Geographical information system data*

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

144 *Costs of care*

145 We asked patients to estimate direct and indirect costs associated with each visit from the
146 onset of symptoms until TB diagnosis, using a standardized questionnaire [32]. Direct
147 costs included costs for diagnosis (such as costs for X-rays), medical costs (as costs for
148 drugs that excluded TB drugs), food, transport, and other costs that included special
149 supplements and vitamins. Indirect costs included income reduction, decreased
150 production costs, coping costs (including the use of savings or selling of household assets
151 to cater for sickness), and reduced payment for labour. Calculation of patient costs relied
152 upon the 2008 WHO tool [32]. We report costs as US Dollars (USD), converted from
153 Tanzania shillings using the exchange rate from the Bank of Tanzania of USD/TZS
154 2167.84 as of August 2016.

155 **Definitions**

156 A new TB patient was defined by bacteriological confirmation with sputum smear
157 microscopy and/or Xpert MTB/RIF in the absence of prior TB treatment during screening
158 [33]. A presumptive TB patient was defined by presentation with TB symptoms, including
159 coughing for longer than two weeks, fever, night sweats, or unexplained weight loss, and
160 who tested negative on sputum smear or Xpert MTB/RIF [33]. Diagnostic delay was
161 defined according to the framework of WHO (29) and used in previous studies [34,35] as
162 the interval between the onset of any TB-related symptom and the time of TB diagnosis of
163 more than 3 weeks. Healthcare provider was defined as a person or facility that could
164 provide healthcare, this included hospitals, pharmacies, and dispensaries, as well as
165 traditional healers. Prior medication was defined as the use of any prescribed or self-
166 prescribed medication prior to TB diagnosis [4]. We defined patients as poor if their wealth

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3 167 fell in the lowest or second-lowest wealth quintile. The non-poor were defined as persons
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5 168 in the remaining middle, fourth, and highest wealth quintiles [36].
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8 169 **Statistical and geographical analysis**

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10 170 We performed descriptive analyses to summarize the data and used χ^2 or Fisher's test to
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12 171 assess differences between groups in categorical variables. "A cut off point of 300 USD
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14 172 was used as a threshold for the monthly household income as indicated in another similar
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16 173 study [4]. Cost distributions were described by their medians and interquartile ranges
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18 174 (IQR). Costs were further calculated stratifying by gender and poverty status. Wealth
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20 175 quintiles were generated following a principal component analysis of standard household
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22 176 assets as indicated in the Tanzania household survey [26]. To stratify among the poor and
23
24 177 non-poor, we used wealth indicators relating to household characteristics (e.g., roofing
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26 178 type, cooking fuel and nature of flooring) and ownership of assets (e.g., radio and mobile
27
28 179 phone) to create wealth ranking as used in other studies [37,38]. Patients in the first and
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31 180 second quintiles were considered poor and in the remaining quintiles as non-poor. We
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33 181 used the nonparametric Kruskal-Wallis test to assess the statistical significance of the
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35 182 differences in estimated costs between groups. All significance tests were two-sided with a
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37 183 confidence level of 95%. Quintile regression models were performed for median costs to
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39 184 examine the association of patient factors with the different types of costs. Factors
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41 185 considered in these models included male vs female, age in years, unskilled and semi-
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43 186 skilled labour, level of education, and diagnostic delay. Statistical analyses were performed
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45 187 using Stata version 14.0 (Stata Corporation, College Station, TX, USA).
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52 188 We mapped and visualized the pathways of patients to health care providers up to a
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54 189 maximum of five visits for the current episode of sickness as described elsewhere [3,14].
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57 190 We calculated distances in meters as the straight-line distance between the patient's
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3 191 household and the nearest health facility. The resulting distances were imported into Stata
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5 192 for further analyses. All geographical analyses were performed using ArcGIS (version
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7 193 10.5, Esri, Redlands, CA, USA).
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10 194 **Patient involvement**

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12 195 Patients were not involved in the development, design, and analysis of this study.
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16 196 **Ethics approval and consent to participate**

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18 197 The study was approved by Ifakara Health Institute Institutional Review Board
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20 198 (IHI/reference no IHI/IRB /09-2016), the Medical Research Coordinating Committee of the
21
22 199 National Institute for Medical Research in Tanzania (NIMR reference no
23
24 200 NIMR/HQ/R.8c/Vol. I/357), and the Ethics Committee of the Canton of Basel (EKNZ
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26 201 reference no BASEC UBE-2016-00260). Written informed consent was obtained from all
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28 202 study participants.
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33 203 **Availability of data and materials**

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35 204 According to the Institutional Review Board of the Ifakara Health Institute, we are not
36
37 205 allowed to make the data publicly available. Interested researchers should contact the
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39 206 corresponding author.
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43 207 **Competing interest**

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45 208 All authors declare that they have no competing interests.
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210 RESULTS

211 Patient characteristics

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

221 First point of care and diagnostic delay

222 Among confirmed patients, 44% first sought care at pharmacies after the onset of
223 symptoms, whereas 42% of presumptive patients first sought care at hospitals (Table 1).
224 Fewer than 10% of patients in both groups reported visits to traditional healers as the first
225 point of care. Confirmed patients frequently indicated more than 2 visits at health facilities
226 (33% vs. 9%, $p<0.001$).

227 The average time for first seeking healthcare after the onset of symptoms was two
228 weeks. Overall, 45.5% sought care within one week after the onset of TB symptoms. For
229 30%, the diagnostic was established within 2-3 weeks. For around every tenth there was a
230 diagnostic delay of six weeks or more. The diagnostic delay differed significantly between
231 confirmed and presumptive patients, with 41% of confirmed versus 50% of presumptive

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3 232 patients having a short delay (of <1 week). Higher proportion of confirmed patients had a
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5 233 diagnostic delay of 4-5 and of ≥ 6 weeks.
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234 Pathways to care

235 The spatial distribution of healthcare facilities in the study area show pharmacies and
236 dispensaries are distributed over the whole area Figure (2A). Hospitals are situated mainly
237 in the urban centres and traditional healers predominantly in the peripheral area. Figures
238 (2B) and (2C) offer examples of pathways to care until TB diagnosis in confirmed and
239 presumptive patients. Pathways in confirmed patients involved several visits to the
240 healthcare facilities before TB diagnosis. Pathways in presumptive patients were more
241 direct with only one or few visits to healthcare facilities before TB diagnosis.

242 The median total distance from patients' households to healthcare facilities
243 including hospitals, pharmacies, dispensaries, and traditional healers was 2,338 meters
244 (IQR 1,373-4,122) for confirmed patients, and 2,009 meters (IQR 986-2,976) for
245 presumptive patients ($p=0.25$). Among confirmed patients, 37% lived within 500 meters
246 near a pharmacy, as did 42% of presumptive patients. Eighty-three per cent of confirmed
247 patients and 72% of presumptive patients lived within 1,000 meters from the nearest
248 hospital. We did not find an association of the distance from patients' household to the
249 nearest possible healthcare facility with patient characteristics such as being poor (defined
250 as being in the lowest wealth quintile), prior use of medication, or having more than two
251 healthcare visits in multivariate analysis.

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

258 **Costs associated with seeking care**

259 Patients spent a median of 31% (IQR 15.0-56.3%) of their monthly household income for
260 health expenditures for all visits for TB diagnosis. For the first visit confirmed patients had
261 lower median costs than presumptive patients (USD 8.3 [IQR 4.6-17.5] vs. 13.8 [IQR 6.0-
262 20.5]), but their costs were comparatively higher with increasing number of visits
263 (Supplementary Table 1).

264 Overall, indirect costs were considerably higher than direct costs, both in confirmed
265 and presumptive patients from the onset of symptoms until confirmation/exclusion of TB
266 (Table 2). Confirmed patients had higher diagnostic costs than presumptive patients (USD
267 7.0 [IQR 5.8-9.2] and 5.3 [IQR 1.4-7.0]), higher food costs, and higher informal payments.
268 Among the indirect costs, income reduction was considerably higher for confirmed TB
269 patients than presumptive patients. (USD 23.1 [IQR 6.9-55.4] vs. 9.2 [IQR 1.4-25.4]).

270 **Gender, poverty status and costs**

271 Costs for different patients groups differed significantly. Overall, the median total direct
272 costs were similar for men, USD 24.9 (IQR 17.5-41.9), and women, USD 24.6 (IQR 16.1-
273 42.4 p=0.66). Indirect costs for men, USD 64.6 (IQR 31.8-159.1), were significantly higher
274 than those for women, at USD 55.6 (IQR 25.1-141.1, p<0.001).

275 Analyses stratified by sex and poverty status indicate that poor men with confirmed
276 TB had lower total direct costs compared to poor women (USD 24.4 [IQR 18.9-47.9] vs.
277 30.0 [IQR 18.68-49.58.]) (Table 3). For the presumptive TB patients total direct costs for
278 poor men differed slightly from those of poor women (USD 22.6 [IQR 17.5-29.1] vs. 20.5
279 [IQR 14.3-35.1]). Among the non-poor men and women, direct costs varied only little in
280 confirmed and presumptive patients. In confirmed patients, diagnostic costs were lower

281 among poor men compared to poor women (USD 6.91 [IQR 4.61-9.22] vs. 7.61 [IQR 1.38-
282 10.14]), whereas for the presumptive patients, diagnostic costs were the same among poor
283 men and women.

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

289 **Determinants of cost differences**

290 On average, each week of diagnostic delay was associated with an increase in
291 median total costs (direct and indirect costs) among confirmed patients by 1.44 USD
292 (95%CI: (-19.56, -6.63), $p < 0.001$), but no significant association was seen in presumptive
293 patients (Table 5). Diagnostic delay was associated with an increase in total direct costs in
294 confirmed patients (USD 0.52 per week, 95%CI: (0.34, 0.70), $p < 0.001$), but with a
295 decrease in presumptive patients (USD -0.84 per week, 95%CI: (-1.32,-0.35), $p = 0.001$).
296 For total indirect costs, the pattern was similar, but neither of the two associations reached
297 statistical significance.

298 Overall, having a university degree was significantly associated with higher indirect
299 costs (USD 70.14, 95%CI: (9.47, 130.80), $p = 0.02$). None of other factors of the model
300 were significantly associated with median costs. The pattern of positive association
301 between diagnostic delay and total costs among confirmed patients and negative
302 association among presumptive patients was further supported by analyses using linear
303 and quadratic terms (Figure 4). Furthermore, we conducted regression analyses
304 separately for different types of costs (Supplementary table 2 and

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3 305 Supplementary table 3). Medication costs in confirmed patients increased with the number
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5 306 of weeks of delay (USD 0.13 per week, 95%CI: (0.06, 0.19), $p < 0.001$), but not in
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7 307 presumptive patients. Transport costs were significantly lower among men and women
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9 308 with presumptive TB (USD -1.54, 95%CI: (-3.12, -0.03), $p < 0.05$). We further observed an
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11 309 increase in coping costs with the length of diagnostic delay in both confirmed and
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14 310 presumptive patients (Supplementary Table 3). Finally, in patients with presumptive TB,
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16 311 costs due to decreased production were significantly higher among unskilled labourers
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18 312 (USD 8.71, 95%CI: (0.53, 16.89), $p = 0.03$).
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314 **DISCUSSION**

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

326 Almost half of the confirmed TB patients began their search for care at
327 pharmacies, and patients in both groups sought care from more than one healthcare
328 provider before a diagnosis. This highlights a diagnostic shortfall in some healthcare
329 facilities and poor management of patients as documented elsewhere [39], and partially
330 explains the diagnostic delay. Compared to findings of other studies [19,40] the observed
331 diagnostic delay in our study was lower. However, a delay of at least 6 weeks observed in
332 10% of our study population still requires attention. Most patients lived near healthcare
333 facilities, and only 9% of the confirmed TB patients and 6% of the presumptive TB patients
334 reported visiting traditional healers. Living near healthcare facilities might have an impact
335 on treatment seeking [41]. We investigated the impact of geographical distance between
336 household and health facility on health-seeking behaviour, but found no associations
337 between distance and patient characteristics such as being poor, prior use of medication

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3 338 and having more than two visits to the healthcare facility. This is contrary to some other
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5 339 results that found distance to have an impact on patient characteristics such as treatment
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7 340 completion and diagnostic delay [35,42,43]. Diagnostic delay was significantly associated
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9 341 with direct costs, indirect costs (borderline significance) and total costs in confirmed
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11 342 patients. The most likely explanation for this finding is that diagnostic delay worsens
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13 343 patients' morbidity, especially in confirmed TB patients, thus increasing costs of healthcare
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15 344 [42].

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18 345 Patients in both groups spent a median proportion of around 30% of their monthly
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20 346 household income on health expenditures for up to five visits. The economic burden of
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22 347 direct and particularly indirect costs of seeking TB care for patients and their households
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24 348 are high for the marginalized population, which is most at risk of acquiring TB. These
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26 349 findings are consistent with other studies that show patients in low-and-middle income
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28 350 countries face a very high economic burden of seeking TB care [13], and expenditures for
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30 351 seeking healthcare for TB can cause or exacerbate poverty [44]. The total costs for
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32 352 presumptive TB patients were lower compared to confirmed cases in our study. These
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34 353 results are also consistent with those reported in other settings where half of the total costs
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36 354 for seeking healthcare are pre-treatment costs which disproportionately affect poor TB
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38 355 patients [13]

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41 356 While direct costs were relatively low, they may be catastrophic for patients who are
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43 357 semiskilled labourers reporting monthly household income of less than 300 USD. Their
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45 358 situations can further be worsened by employment in the informal sector that lacks
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47 359 sickness benefits [44]. Confirmed TB patients encountered higher indirect costs compared
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49 360 to presumptive patients, which may be due to the prolonged time required for diagnosis
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51 361 leading to their substantially higher income reduction as shown in our study.
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3 362 We found higher indirect costs among poor men compared to poor women. This
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5 363 was mainly due to their more pronounced income reduction and decreased production.
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7 364 Although the direct and indirect costs were higher for men than for women, the costs of ill
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9 365 health are usually more profound for women and their households than for men. When
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11 366 women get sick the impact of the disease on their children and their families is stronger
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14 367 than when men get sick [11]. Furthermore, financial burden may limit access to care for
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16 368 both confirmed and presumptive female TB patients since most of them lack financial
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18 369 autonomy. Moreover, their lower status in households deprioritizes their health.
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371 **ARTICLE SUMMARY**

372 **Strengths and limitations of this study**

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

389 **Conclusions**

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

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3 395 healthcare providers including private, public health practitioners and patients themselves
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5 396 could help not only in reducing the complex pathways during healthcare seeking, but also
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7 397 effective health care utilization [39]. Reducing the direct and indirect costs associated with
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9 398 treatment seeking is likely to support confirmed and presumptive TB patients in timely
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11 399 accessing health care for TB diagnosis and treatment. Decreasing or removing user fees
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14 400 and further decentralization of TB care could reduce diagnostic delay and lower
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16 401 expenditures. Additionally, strengthening of health systems policies including protection of
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18 402 patients against the catastrophic direct and indirect costs, as well as ensuring universal
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21 403 access to healthcare must be interpreted into actions for a better TB control [45]. These
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23 404 interventions are central for reaching the ambitious WHO targets of zero deaths, disease,
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25 405 and suffering due to TB by 2035 [46].
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407 **Funding**

408 This work was supported by funding from the Rudolf Geigy Foundation (Basel,
409 Switzerland). The funder was not involved in any way during study design, data collection,
410 data analysis and interpretation, or in writing the manuscript. The funders had no role in
411 study design, data collection and analysis, decision to publish, or preparation of the
412 manuscript.

413 **Acknowledgements**

414 We would like to thank all the patients who participated in this study. We thank the District
415 and Regional TB coordinators of Temeke district and the National TB Programme in
416 Tanzania for their support.

417 **Author contributions**

418 Conceived and designed the study: GM, JH, FM, KS, PM, SG, KR, KH, TM, MGW,
419 EZ, and LF. GM, JH, KD, YM and FM analysed the data. GM and LF prepared the
420 first draft of the manuscript. KR, KS, PM, YM, TM, MGW, EM, EZ and LF contributed
421 to the major revision of the manuscript. All authors contributed to final manuscript
422 revisions and approved the final version.

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545 **FIGURE LEGENDS**

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

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

558 **Figure 3.** Spine plots showing distribution of health care facility visits during the pathway of
559 care (first, second, third and fourth/fifth visit) in confirmed and presumptive patients.
560 Numbers on the graph indicate absolute numbers.

562 **Figure 4.** Margin plots showing associations between total costs and diagnostic delay in
563 confirmed TB patients (panel A) and presumptive TB patients (panel B). Associations
564 between median total costs and diagnostic delay were modelled by quadratic polynomials.

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3 565 The p-values are from Wald test of the linear and quadratic terms of the diagnostic delay
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5 566 (p<0.001 for panel A, p=0.08 for panel B).
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567 **Tables and Figures**568 **Table 1.** Socio-demographic characteristics and diagnostic delay for the confirmed and
569 presumptive tuberculosis (TB) patients.

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 (69.0)	63 (63)	75 (75)	
>300 USD per month	62 (31.0)	37 (37)	25 (25)	
Wealth quintile				0.54
Poor -households	47 (23.5)	21 (21)	26 (26)	
Second	33 (16.5)	16 (16)	17.0 (17)	
Middle	41 (20.5)	19 (19)	22 (22)	
Fourth	44 (22.0)	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 (35.0)	28 (28)	42 (42)	
Dispensaries	49 (24.5)	19 (19)	30 (30)	
Pharmacies	66 (33.0)	44 (44)	22 (22)	
Traditional healers	15 (7.5)	9 (9)	6 (6)	
HC facility visits				<0.001
≤2	158 (79.0)	67 (67)	91 (91)	
>2	42 (21.0)	33 (33)	9 (9)	
Transport used for first point of care				<0.001
Car	70 (35.5)	22 (22)	48 (48)	
On foot	95 (47.5)	65 (65)	30 (30)	
Motorcycle/tricycle	35 (17.5)	13 (13)	22 (22)	
Diagnostic delay (weeks)				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)	

570 HC, health facility; IQR, interquartile range; USD, United States Dollar * Wilcoxon-rank sum test

571 P-values provided by Chi-square tests and Fisher's exact test

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

Costs	All (n=200)	Confirmed TB patients (n=100)	Presumptive TB patients (n=100)	P-value
Average number of visits (range)	1.2 (1-5)	1.3 (1-5)	1.1 (1-3)	
Direct costs	Median, (IQR)	Median, (IQR)	Median, (IQR)	
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
Sub-total 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
Sub-total 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

574 IQR, interquartile range; TB, tuberculosis; USD United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016). P-values provided by Wilcoxon rank sum test.
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576 **Table 3.** Direct costs (in USD) of seeking healthcare among confirmed and presumptive TB patients, according sex and poverty status

Variable	All	Confirmed				Presumptive			
		Men		Women		Men		Women	
		Poor ¹ n=21	Non-poor ² n=43	Poor n=16	Non-poor n=20	Poor n=15	Non-poor n=32	Poor n=28	Non-poor n=25
Median (IQR)									
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 (18.68-49.58)	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)

577 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
578 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.

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579 ¹Poor or second lowest wealth quintile

580 ²Non-poor middle, fourth and highest wealth quintile

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582 **Table 4.** Indirect costs (in USD) of seeking health care among confirmed and presumptive TB patients, according to sex and poverty status

Variable	All	Confirmed				Presumptive			
		Men		Women		Men		Women	
		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)

583 IQR, interquartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016)

584 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

585 ¹ Poor or second lowest wealth quintile586 ² Non-poor middle, fourth and highest wealth quintile

587 **Table 5.** Estimates of effects of different factors on median direct, indirect and total costs in USD among confirmed and presumptive TB patients

Variable	All			Confirmed			Presumptive		
	*Difference	95% CI	P-value	*Difference	95% CI	P-value	*Difference	95% CI	P-value
Total direct costs									
Males vs females	-1.71	-11.80, 8.38	0.73	-2.31	-20.29, 15.67	0.79	-3.58	-9.80-2.63	0.25
Age (per year)	-0.01	-0.48, 0.46	0.97	0.28	-0.70, 1.26	0.57	0.06	-0.19, 0.31	0.31
Unskilled labour ¹	1.80	-11.40, 15.01	0.78	-7.55	-33.38, 18.26	0.56	2.20	-5.18, 9.59	0.55
Semi-skilled labour ¹	2.87	-8.75, 14.48	0.62	5.01	-14.66, 24.69	0.61	1.87	-5.49, 9.23	0.61
Poor vs non-poor	-2.34	-12.19, 7.51	0.63	19.73	-56.98, 96.46	0.61	-2.40	-8.07, 3.27	0.40
Primary education ²	3.18	-10.21, 16.56	0.64	8.96	-17.83, 35.76	0.66	0.66	-6.47 7.78	0.85
Secondary education	6.12	-11.16, 23.40	0.48	20.86	-11.40, 53.12	0.20	4.22	-5.88, 14.32	0.40
University ²	9.36	-19.07, 37.84	0.51	10.53	-35.17, 56.25	0.46	-0.59	-21.14, 19.95	0.95
Diagnostic delay	0.04	-0.08, 0.16	0.52	0.52	0.34, 0.70	<0.001	-0.84	-1.32,-0.35	0.001
Total indirect costs									
Males vs females	11.63	-11.37, 34.63	0.32	6.60	-33.93, 47.14	0.74	1.85	-34.74, 38.44	0.92
Age (per year)	0.38	-0.69-1.45	0.48	0.07	-2.14, 2.29	0.94	0.75	-0.74, 2.24	0.32
Unskilled labour	12.68	-17.41, 42.78	0.40	14.47	-43.74, 72.700	0.62	19.13	-24.32, 62.11	0.38
Semi-skilled labour	20.90	-5.58, 47.38	0.12	37.24	-7.11, 81.60	0.09	22.94	-20.38, 66.27	0.29
Poor vs non-poor	6.29	-16.15, 28.75	0.58	6.92	-33.36, 47.20	0.73	5.82	-27.53, 39.18	0.72
Primary education	21.24	-9.27, 51.75	0.17	8.96	-51.46, 69.37	0.76	20.0	-20.34, 60.34	0.32
Secondary/ University	70.14	9.47, 130.80	0.02	56.88	11.71, 125.47	0.10	-38.5	16.52, 93.52	0.16
Diagnostic delay	0.46	0.18-0.74	0.001	0.57	0.16, 0.97	0.07	-1.25	-4.11, 1.60	0.38
Total costs									
Males vs females	9.87	-26.39, 46.14	0.59	-4.98	-58.90, 48.93	0.85	-0.62	-44.96, 43.71	0.97
Age (per year)	0.34	-1.34, 2.03	0.68	-0.56	-3.50, 2.38	0.70	0.74	-1.06, 2.55	0.41
Unskilled labour	11.95	-35.50, 59.40	0.62	8.25	-69.18, 85.69	0.83	16.02	36.64, 68.69	0.54
Semi-skilled labour	30.47	-11.28, 72.23	0.15	58.81	-0.18, 117.81	0.05	26.64	-25.86, 79.14	0.31
Poor vs non-poor	0.89	-34.50, 36.31	0.96	8.39	-45.18, 61.98	0.75	2.39	-38.01, 42.81	0.90
Primary education	24.87	-23.25, 72.98	0.31	19.73	-60.62, 100.09	0.62	18.06	-32.75, 68.88	0.48
Secondary education	69.54	7.43, 131.16	0.02	69.45	-27.29, 166.19	0.15	46.10	-25.86, 79.14	0.20
University	108.89	6.63, 211.16	0.03	69.20	-67.87, 206.28	0.31	-15.74	-162.23, 130.73	0.83
Diagnostic delay	1.29	0.84-1.73	<0.001	1.44	-19.56, -6.63	<0.001	-2.40	-5.86, 1.06	0.17

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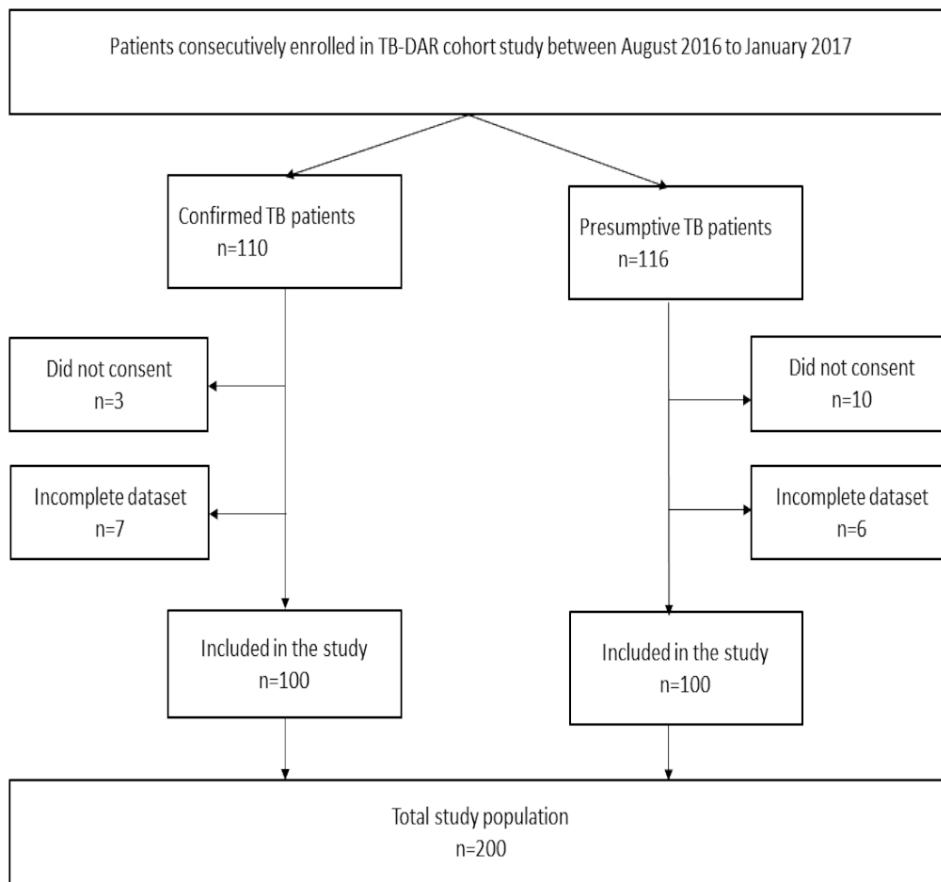
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588 *Estimated differences in median costs are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as a delay in seeking care three weeks or more after the
589 onset of symptoms. Multivariable quintile regression was performed for median costs to examine the association of patient factors with different types of costs. Separate models were run for direct, indirect
590 and total costs.

591 ¹Reference: Unemployed

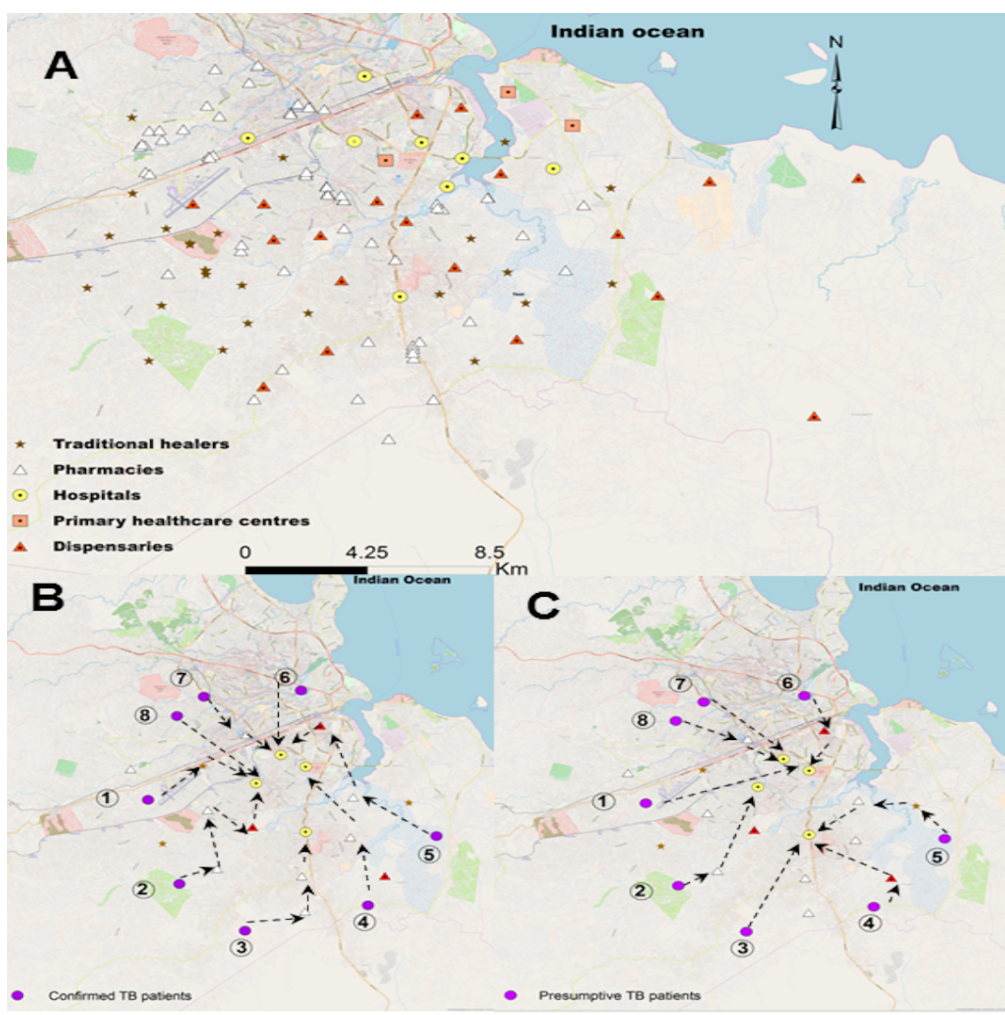
592 ²Reference: no education

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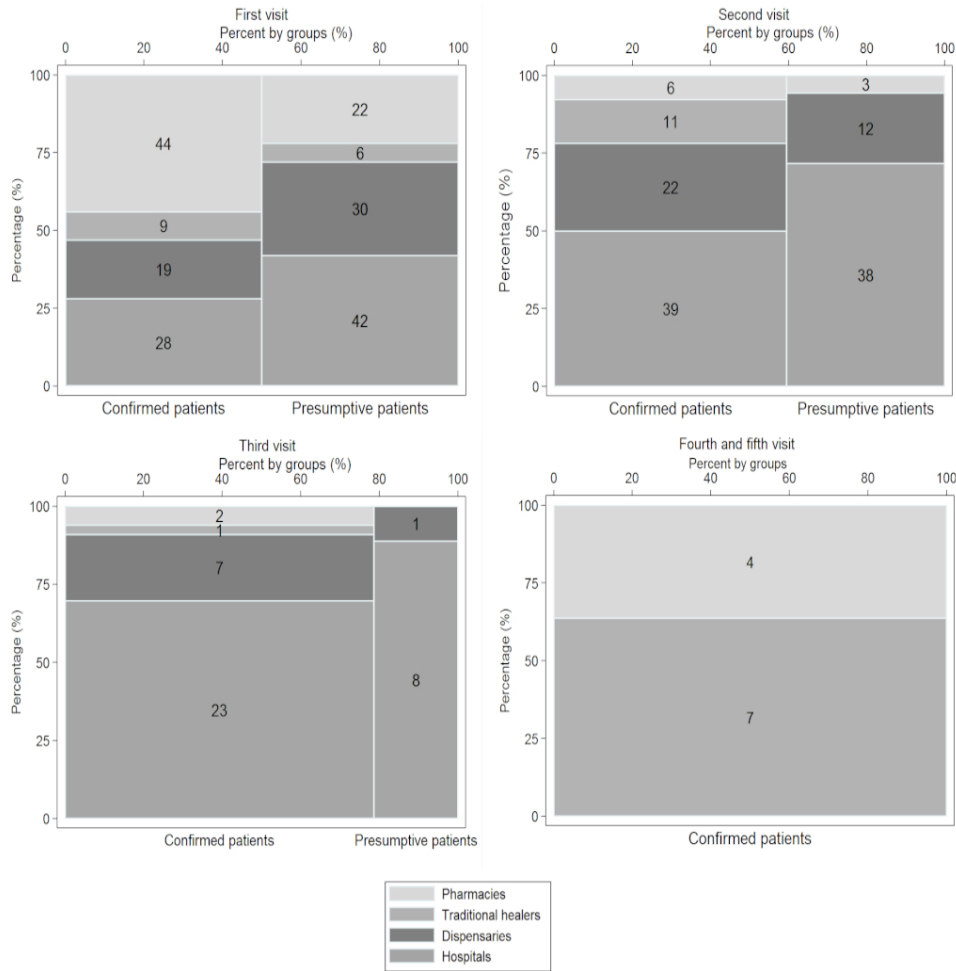
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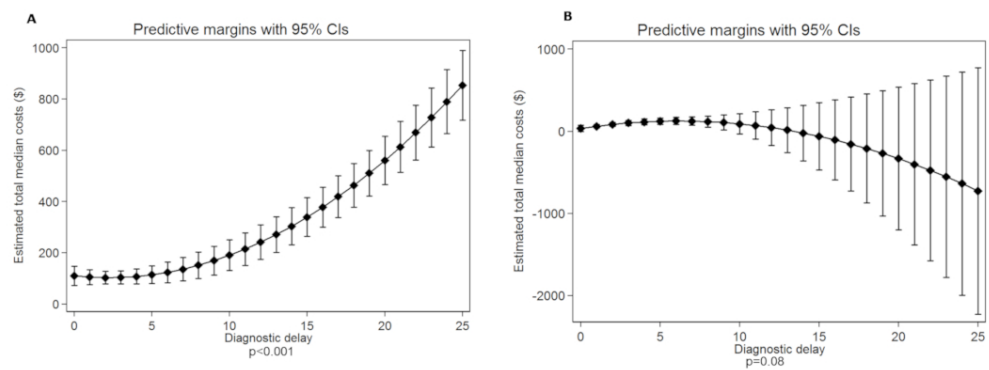
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Supplementary Table 1. Direct costs associated with first, second and >2 visits for patients with confirmed and presumptive TB.

Visit	All n (%)	Cost of visit/patient in USD		Costs as a % of MMHI	
		Median (IQR)		Median (IQR)	
		Confirmed	Presumptive	Confirmed	Presumptive
First visit	200 (100)	8.30 (4.6-17.5)	13.8 (6.0-20.5)	9.1 (3.7-18.3)	15.1 (8.0-34.8)
Second visit	90 (45)	15.2 (11.0-24.0)	14.3 (12.0-22.1)	14.5 (8.7-28.5)	19.7 (10.0-32.0)
Third to fifth visit	42 (21)	27.2 (14.8-38.7)	13.4 (12.9-20.3)	24.6 (13-42)	13.3 (12.0-14.3)
Total direct costs		27.4 (18.7-48.4)	19.8 (13.8-34.0)	30.5 (16.5-53.5)	29.0 (14.1-52.1)

IOR, interquartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016); MMHI, median monthly household income.

Supplementary Table 2. Estimates of effects of different factors on median types of direct costs in USD among confirmed and presumptive TB patients.

Variable	All			Confirmed			Presumptive		
	Difference*	95% CI	P-value	Difference*	95% CI	P-value	Difference*	95% CI	P-value
Diagnostic costs									
Males vs females	0.29	-1.33, 1.93	0.71	-0.17	-2.85, 2.52	0.90	-0.95	-3.45, 1.54	0.45
Age (in years)	0.03	-2.67, 0.51	0.18	-0.05	-0.20, 0.01	0.45	0.07	-0.03, 0.17	0.18
Unskilled labour ¹	1.71	-0.42, 1.84	0.11	1.32	-2.53, 5.19	0.49	1.99	-0.97, 4.96	0.18
Semi-skilled ¹	1.22	-0.65, 3.10	0.20	1.77	-1.17, 4.71	0.34	2.66	-0.29, 5.62	0.07
Poor vs non-poor	-1.08	-2.67, 0.51	0.18	-0.16	2.83, 2.50	0.90	-1.80	-4.08, 0.48	0.12
Primary education ²	1.14	-1.03, 3.30	0.30	3.03	-0.98, 7.03	0.13	-0.27	-3.12, 2.59	0.85
Secondary education	2.49	0.29, 5.29	0.08	3.80	-1.02, 8.62	0.12	0.89	-3.17, 4.95	0.85
University ²	6.16	1.56, 10.76	0.09	3.30	-3.53, 10.14	0.34	3.72	-4.54, 11.97	0.37
Diagnostic delay	-0.02	-0.02, 0.19	0.97	0.01	-0.01, 0.04	0.49	-0.07	-0.03, 0.12	0.45
Medication costs									
Males vs females	-0.31	-3.65, 3.09	0.85	-0.69	-7.40, 6.01	0.83	0.45	-2.23-3.13	0.73
Age (in years)	-0.03	0.18, 0.13	0.74	-0.01	-0.38-, 0.35	0.95	-0.05	-0.16, 0.06	0.36
Unskilled labour	0.13	-4.23, 4.49	0.95	-0.03	-9.67, 9.61	0.99	-0.68	-3.86-2.49	0.67
Semi-skilled labour	-0.03	-3.86, 3.81	0.99	0.92	-6.41, 8.27	0.80	-2.01	-5.17, 1.16	0.21
Poor vs non-poor	0.62	-2.64, 3.87	0.71	0.77	-5.90, 7.43	0.82	0.31	-2.12, 2.75	0.80
Primary education	1.26	-3.16-5.68	0.57	2.04	-7.95, 2.04	0.68	0.88	-2.18, 3.95	0.56
Secondary education	1.54	-4.17, 7.25	0.59	4.28	-7.75, 16.32	0.48	0.58	-3.76, 4.93	0.79
University	0.24	9.16, 9.64	0.95	1.98	-15.08, 19.03	0.81	4.24	-4.60, 13.08	0.34
Diagnostic delay	0.06	0.02, 0.10	0.002	0.13	0.06, 0.19	<0.001	-0.17	-0.38, 0.04	0.11
Transport costs									
Males vs females	-1.02	-2.19, 0.13	0.08	-0.52	-2.25, 1.21	0.55	-1.54	-3.12, 0.03	0.05
Age (in years)	0.02	-0.03, 0.74	0.45	0.02	-0.07, 0.12	0.66	-0.01	-0.71, 0.06	0.84
Unskilled labour	1.39	-0.12, 2.90	0.07	-0.29	-2.78, 2.20	0.81	2.36	0.49, 4.24	0.01
Semi-skilled	0.35	-0.98, 1.68	0.60	0.49	-1.41, 2.39	0.61	0.94	-0.92, 2.81	0.31
Poor vs non-poor	-0.36	-1.48-0.76	0.53	0.92	-0.80, 2.64	0.29	-0.32	-1.76, 1.11	0.65

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3	Primary	1.17	-0.36-2.71	0.13	1.16	-1.41, 3.75	0.37	0.84	-0.96, 2.65	0.35
4	Secondary education	1.41	-0.56-3.39	0.16	2.20	-0.91, 5.31	0.16	-0.13	-2.70, 2.42	0.91
5	University	1.48	-1.78-4.74	0.37	0.99	-0.80, 2.64	0.65	0.32	-4.89-5.53	0.90
6	Diagnostic delay	0.01	-0.04-0.24	0.16	0.03	0.01, 0.05	0.002	-0.01	-0.22, 0.30	0.13
7										
8	Total direct costs									
9	Males vs females	-1.71	-11.80, 8.38	0.73	-2.31	-20.29, 15.67	0.79	-3.58	-9.80, 2.63	0.25
10	Age (per year)	-0.01	-0.48, 0.46	0.97	0.28	-0.70, 1.26	0.57	0.06	-0.19	0.31
11	Unskilled labour	1.80	-11.40, 15.01	0.78	-7.55	-33.38, 18.26	0.56	2.20	-5.18, 9.59	0.55
12	Semi-skilled labour	2.87	-8.75, 14.48	0.62	5.01	-14.66, 24.69	0.61	1.87	-5.49, 9.23	0.61
13	Poor vs non-poor	-2.34	-12.19, 7.51	0.63	7.44	-10.42, 25.31	0.41	-2.40	-8.07, 3.27	0.40
14	Primary education	3.18	-10.21, 16.56	0.47	8.96	-17.83, 35.76	0.66	0.66	-6.47, 7.78	0.85
15	Secondary education	6.12	-11.16, 23.40	0.48	20.86	-11.40, 53.12	0.20	4.22	-5.88, 14.32	0.40
16	University	9.36	-19.07, 37.84	0.51	10.53	-35.17, 56.25	0.64	-0.59	-21.14, 19.95	0.95
17	Diagnostic delay	0.04	-0.08, 0.16	0.52	0.52	0.34, 0.70	<0.001	-0.84	-1.32, -0.35	0.001
18										
19	Total costs									
20	Males vs females	9.87	-26.39, 46.14	0.59	-4.98	-58.90, 48.93	0.85	-0.62	-44.96, 43.71	0.97
21	Age (per year)	0.34	-1.34, 2.03	0.68	-0.56	-3.50, 2.38	0.70	0.74	-1.06, 2.55	0.41
22	Unskilled labour	11.95	-35.50, 59.40	0.62	8.25	-69.18, 85.69	0.83	16.02	36.64, 68.69	0.54
23	Semi-skilled labour	30.47	-11.28, 72.23	0.15	58.81	-0.18, 117.81	0.05	26.64	-25.86, 79.14	0.31
24	Poor vs non-poor	0.89	-34.50, 36.31	0.96	8.39	-45.18, 61.98	0.75	2.39	-38.01, 42.81	0.90
25	Primary education	24.87	-23.25-72.98	0.31	19.73	-60.62, 100.09	0.62	18.06	-32.75, 68.88	0.48
26	Secondary education	69.54	7.43-131.65	0.02	69.45	-27.29, 166.19	0.15	46.10	-25.86, 79.14	0.20
27	University	108.89	6.6, 211.16	0.03	69.20	-67.87, 206.28	0.31	-15.74	-162.23, 130.73	0.83
28	Diagnostic delay	1.29	0.84, 1.73	<0.001	1.44	-19.56, -6.63	<0.001	-2.40	-5.86, 1.06	0.17
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33 *Estimated differences in median costs are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the
 34 onset of symptoms

35 Multivariable quintile regression was performed for median costs to examine the association of patient factors with the different types of costs. Separate models were run for direct, indirect and total
 36 costs.

37 ¹ Reference: Unemployed

38 ² Reference: no education.

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Supplementary Table 3 Estimates of effects of different factors on median types of indirect and costs in USD among confirmed and presumptive TB patients.

Variable	All			Confirmed			Presumptive		
	Difference*	95% CI	P-value	Difference*	95% CI	P-value	Difference*	95% CI	P-value
Coping costs									
Males vs females	-0.24	-6.12,5.64	0.93	-3.86	-11.45, 3.71	0.31	-1.39	-12.58, 9.79	0.80
Age (in years)	0.02	-0.25,0.29	0.88	-0.25	-0.66, 0.16	0.23	0.15	-0.30, 0.61	0.51
Unskilled labour ¹	-2.38	-5.71,9.90	0.59	-8.56	-19.45, 2.33	0.12	-0.49	-13.78, 12.79	0.94
Semi-skilled ¹	-4.63	-11.41,2.14	0.17	-2.64	-10.94, 5.66	0.52	-5.01	-18.25, 8.24	0.45
Poor vs non-poor	0.30	-5.43,6.05	0.91	-2.56	-10.09, 4.98	0.50	2.09	-8.10, 12.28	0.68
Primary education ²	2.09	-5.71,9.90	0.59	-2.89	-14.20, 8.40	0.61	5.92	-6.89, 18.74	0.36
Secondary education ²	5.79	-4.28,15.86	0.25	-4.85	-18.46, 8.76	0.48	9.23	-8.94, 27.41	0.31
University ²	-6.65	-23.24, 9.93	0.43	5.09	-14.19-24.37	0.60	-4.09	-41.05, 32.85	0.82
Diagnostic delay	2.47	0.87, 4.07	0.003	-0.04	-0.12, 0.03	0.26	-0.39	-1.27, 0.47	0.36
Less paid labour									
Males vs females	1.32	-2.69,5.33	0.51	3.78	-3.78, 11.35	0.32	0.74	-2.99, 4.46	0.69
Age (in years)	0.17	-0.01,0.35	0.07	0.19	-0.21, 0.60	0.34	0.15	-0.01, 0.30	0.05
Unskilled labour	2.80	-2.45,8.06	0.29	3.16	-7.71, 14.02	0.56	3.59	-0.83, 8.02	0.11
Semi-skilled labour	3.43	-1.18,8.06	0.14	1.44	-6.83, 9.72	0.36	4.63	0.22, 9.05	0.04
Poor vs non-poor	1.54	-2.37,5.57	0.43	-2.33	-9.85, 5.18	0.53	2.10	-1.29, 5.50	0.22
Primary education	3.15	-2.16,8.48	0.24	-2.51	-13.79, 8.77	0.65	4.38	0.11, 8.65	0.04
Secondary education	4.69	-2.17,11.57	0.17	-1.64	-15.22, 11.93	0.80	8.03	1.97, 14.08	0.01
University	3.88	-7.43,15.20	0.49	8.84	-10.40, 28.07	0.36	3.93	-8.37, 16.24	0.52
Diagnostic delay	0.09	0.05,0.15	<0.001	0.09	0.02, 0.17	0.01	-0.27	-0.56, 0.02	0.06
Decreased production									
Males vs females	3.12	-1.67,7.91	0.20	3.31	-4.73, 11.35	0.41	2.48	-4.39, 9.37	0.47
Age (in years)	0.11	-0.11,0.33	0.33	0.18	-0.25, 0.62	0.42	0.09	-0.19, 0.37	0.51
Unskilled labour	7.38	1.11,13.65	0.02	1.37	-10.19, 12.62	0.19	8.71	0.53, 16.89	0.03
Semi-skilled labour	6.40	0.89,11.92	0.02	5.16	-3.64, 13.97	0.24	7.25	-0.90, 15.40	0.08

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1										
2										
3	Poor vs non-poor	-0.07	-4.75-4.60	0.97	0.08	-7.90, 8.09	0.98	-0.79	-7.07, 5.48	0.80
4	Primary education	2.25	-4.10,8.61	0.48	0.63	-11.36, 12.63	0.91	3.40	-4.49, 11.29	0.39
5	Secondary education	6.53	-1.67-,4.73	0.11	5.94	-8.49, 20.38	0.41	5.76	-5.42, 16.95	0.39
6	University	21.51	7.99,35.02	0.002	21.39	0.93,41.85	0.04	-4.33	-27.07, 18.42	18.41
7	Diagnostic delay	0.04	-0.02,0.09	0.20	0.05	-0.02,0.13	0.21	-0.17	-0.71, 0.36	0.51
8										
9	Total indirect costs									
10	Males vs females	11.63	-11.37,34.63	0.32	6.60	-33.93,47.14	0.74	1.85	-34.74, 38.44	0.92
11	Age (per year)	0.38	-0.69,1.45	0.48	0.07	-2.14, 2.29	0.94	0.75	-0.74, 2.24	0.32
12	Unskilled labour	12.68	-17.41,42.78	0.40	14.47	-43.74,72.700	0.62	19.13	-24.32, 62.11	0.38
13	Semi-skilled labour	20.90	-5.58,47.38	0.12	37.24	-7.11, 81.60	0.09	22.94	-20.38, 66.27	0.29
14	Poor vs non-poor	6.29	-16.15,28.75	0.58	6.92	-33.36,47.20	0.73	5.82	-27.53, 39.18	0.72
15	Primary education	21.24	-9.27,51.75	0.17	8.96	-51.46, 69.37	0.76	20.17	-21.76, 62.11	0.34
16	Secondary education	61.52	22.14,100.92	0.002	54.24	-18.48,126.99	0.73	38.79	-20.65, 98.25	0.19
17	University	108.74	43.89,173.60	0.001	85.66	-17-40,188.72	0.10	-7.79	-128.66, 113.09	0.89
18	Diagnostic delay	0.46	0.12,0.74	0.001	0.56	0.16,0.98	0.007	-1.25	-4.09, 1.62	0.39
19										
20	Total costs									
21	Males vs females	9.87	-26.39,46.14	0.59	-4.98	-58.90,48.93	0.85	-0.62	-44.96, 43.71	0.97
22	Age (per year)	0.34	-1.34,2.03	0.68	-0.56	-3.50,2.38	0.70	0.74	-1.06, 2.55	0.41
23	Unskilled labour	11.95	-35.50,59.40	0.62	8.25	-69.18,85.69	0.83	16.02	36.64, 68.69	0.54
24	Semi-skilled labour	30.47	-11.28,72.23	0.15	58.81	-0.18,117.81	0.05	26.64	-25.86-79.14	0.31
25	Poor vs non-poor	0.89	-34.50,36.31	0.96	8.39	-45.18,61.98	0.75	2.39	-38.01, 42.81	0.90
26	Primary education	24.87	-23.25,72.98	0.31	19.73	-60.62,100.09	0.62	18.06	-32.75, 68.88	0.48
27	Secondary education	69.54	7.43,131.65	0.02	69.45	-27.29,166.19	0.15	46.10	-25.86, 79.14	0.20
28	University	108.89	6.63,211.161	0.03	69.20	-67.87,206.28	0.31	-15.74	-162.23, 130.73	0.83
29	Diagnostic delay	1.29	0.84,1.73	<0.001	1.44	-19.56,6.63	<0.001	-2.40	-5.86, 1.06	0.17

*Estimated differences in median costs of are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the onset of symptoms. Multivariable quintile regression was performed for median costs to examine the association of patient factors with the different types of costs. Separate models were run for direct, indirect and total costs.

¹Reference: Unemployed
²Reference: no education

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
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
Methods			
Study design	4	Present key elements of study design early in the paper	Page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
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 7-8
Bias	9	Describe any efforts to address potential sources of bias	Page 9
Study size	10	Explain how the study size was arrived at	Page 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 9
		(b) Describe any methods used to examine subgroups and interactions	Page 9
		(c) Explain how missing data were addressed	-
		(d) If applicable, describe analytical methods taking account of sampling strategy	-
		(e) Describe any sensitivity analyses	-
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 12
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	Page 7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	Page 13
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	-
		(b) Report category boundaries when continuous variables were categorized	-
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17
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 20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17-20
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 22

*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.

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-025079.R1
Article Type:	Research
Date Submitted by the Author:	26-Oct-2018
Complete List of Authors:	Mhalu, Grace; Ifakara Health Institute Dar es Salaam, Health Intervention; Swiss Tropical and Public Health Institute Hella, Jerry; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Mhimbara, Francis; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Said, Khadija; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Mosabi, Thomas; Ifakara Health Institute Dar es Salaam Tanzania Mlacha, Yeromin; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Schindler, Christian; Swiss Tropical and Public Health Institute; University of Basel Gagneux, Sébastien ; Schweizerisches Tropen- und Public Health-Institut; University of Basel Reither, Klaus; Swiss Tropical and Public Health Institute; University of Basel de Hoogh, Kees; Swiss Tropical and Public Health Institute; University of Basel Weiss, Mitchell; Swiss Tropical and Public Health Institute, Epidemiology and Public Health; University of Basel Zemp, Elisabeth; Swiss Tropical and Public Health Institute, Department of Epidemiology and Public Health; University of Basel, Fenner, Lukas; Universitat Bern; Institute of Social and Preventive medicine
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Infectious diseases, Public health
Keywords:	Tuberculosis < INFECTIOUS DISEASES, Pathways to care, Direct costs, Indirect costs, Health-seeking, Health care



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

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20 **Keywords:** Tuberculosis, pathways to care, direct costs, indirect costs, health seeking,
21 Tanzania, healthcare

22 **Word count:**

23 Main text 3999 (max. 4000), abstract 300 (max. 300), references: 46

24 **Inserts:**

25 4 figures and 5 tables, Supplementary File (3 tables)
26

For peer review only

27 Abstract

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

30 **Design:** Cross-sectional study.

31 **Setting:** District hospital in Dar es Salaam, Tanzania.

32 **Participants:** Bacteriologically confirmed TB and presumptive TB patients.

33 **Primary and secondary outcome measures:** We calculated distance in meters and
34 visualized pathways to healthcare up to five visits for the current episode of sickness.
35 Costs were described by medians and interquartile ranges (IQR), with comparisons by
36 gender and poverty status.

37 **Results:** Of 100 confirmed and 100 presumptive TB patients, 44% of confirmed patients
38 sought care first at pharmacies after the onset of symptoms, and 42% of presumptive
39 patients did so at hospitals. The median visits made by confirmed patients was 2 (range 1-
40 5), and 2 (range 1-3) by presumptive patients. Patients spent a median of 31% of their
41 monthly household income on health expenditures for all visits. The median total direct
42 costs were higher in confirmed compared to presumptive patients (USD 27.4 [IQR 18.7-
43 48.4] vs. USD 19.8 [IQR 13.8-34.0], $p=0.02$), as were the indirect costs (USD 66.9 [IQR
44 35.5-150.0] vs. USD 46.8 [IQR 20.1-115.3], $p<0.001$). The indirect costs were higher in
45 men compared to women (USD 64.6 [IQR 31.8-159.1] vs. USD 55.6 [IQR 25.1-141.1],
46 $p<0.001$). The median total distance from patients' household to healthcare facilities for
47 confirmed and presumptive TB patients was 2,338 meters (IQR 1,373-4,122) and 2,009
48 meters (IQR 986-2,976) respectively.

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3 49 **Conclusions:** Confirmed TB patients have complex pathways and higher costs of care
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5 50 compared to presumptive TB patients, but their costs are also substantial. Improved
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7 51 access to healthcare is needed for effective patient-centred care. This underscores the
8
9 52 need for strengthening the healthcare sector and identifying strategies for diagnostic
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11 53 procedures that are cost-effective and patient-centred, particularly in the light of the
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14 54 introduction of new TB diagnostics.
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55 **Strengths and limitation of the study**

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

62

63 BACKGROUND

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

74 TB is widely regarded as a disease of poverty due to its disproportionate effects on
75 the marginalized populations [7,8]. To help socially and economically marginalized groups
76 fight the disease, healthcare facilities diagnose and treat TB free of charge in countries
77 with a high TB burden [9]. However, patients with symptoms of TB face high direct and
78 indirect costs for diagnosis and treatment [10–13], and these costs are usually higher for
79 patients with confirmed TB than presumptive cases [3,14].

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

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3 85 A national TB prevalence survey indicated that the case detection rate of TB was
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5 86 below 50% [16]. This result may not only be due to the complexity but also the high cost of
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7 87 care [15,17,18]. The recommended pathway to care for TB patients is to present
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9 88 themselves to the appropriate healthcare facilities for TB diagnosis after recognition of TB
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11 89 symptoms [9,19,20].

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14 90 Research has focused predominantly on patients who have already been diagnosed
15
16 91 within the healthcare system, rather than costs for presumptive TB cases prior to diagnosis
17
18 92 [21]. Costs for presumptive cases are not well understood, especially in sub-Saharan
19
20 93 Africa [3,22]. In addition to financial costs, sociocultural and gender-related factors can
21
22 94 shape how patients seek healthcare [23], yet such studies of the influence of these factors
23
24 95 are scarce [24]. Finally, only few studies have examined pathways and costs of seeking
25
26 96 health care by comparing confirmed and presumptive TB patients [3,10,25].

31 97 **Objective**

32
33 98 We aimed to assess the pathways to care and associated costs of seeking care from the
34
35 99 onset of symptoms until TB diagnosis in confirmed and presumptive TB patients in Dar es
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37
38 100 Salaam, Tanzania.

101 METHODS

102 Study setting and study population

103 The study was conducted within the framework of an on-going TB cohort study among the
104 adult population in the Temeke district of Dar es Salaam, Tanzania [4]. The district is
105 densely populated with a population of 1,369,000 persons [26]. It ranks as the poorest in
106 the region with 29% of the households living below the poverty line, resulting in 295 poor
107 persons per square kilometre [27]. The number of health facilities in Temeke district is low
108 compared to other districts in the region. There are six public or private hospitals, eight
109 health centers, and 121 dispensaries [28]. In 2011, a total of 4,112 TB cases of all forms
110 were notified in the Temeke district, of which 1,760 (43%) were smear-positive [29].

111 We included adult, sputum smear-positive TB patients and presumptive TB cases who
112 were consecutively enrolled in the TB-DAR study [4,30] between August 2016 and January
113 2017, until the target sample size of 100 patients in each category was reached (Figure 1).
114 Based on power calculation and previous studies [3,25] we included 100 confirmed TB
115 patients and 100 presumptive TB patients allowing to detect a statistically significant
116 difference in the prevalence of diagnostic delay between the two groups of patients with a
117 power of 80% in case of a true difference of at least 20%. Inclusion criteria were, (i) ≥ 18
118 years of age at recruitment; (ii) bacteriologically confirmed TB diagnosis, or with
119 presumptive TB, and (iii) residency in the Wailes I or II sub-districts of Temeke.
120 Additionally, patients in both groups were screened for TB using sputum smear
121 microscopy and Xpert MTB/RIF. We excluded patients who did not provide consent and
122 those with incomplete data.

123 **Data collection**

124 *Interviews*

125 We interviewed patients, reconstructed retrospectively visits to healthcare facilities and
126 collected data on direct and indirect costs using a standardized questionnaire at the TB
127 clinic. The data collected included patient socio-demographic and socioeconomic
128 characteristics, TB symptoms, the duration of the time from the onset of symptoms until
129 the first help seeking in a healthcare facility, and the number of health care facilities that
130 confirmed and presumptive TB patients had visited. Data were recorded on tablets using
131 the OpenDataKit (ODK) application [31].

132 *Pathways to care*

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

139 *Geographical information system data*

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

144 *Costs of care*

145 We asked patients to estimate direct and indirect costs associated with each visit from the
146 onset of symptoms until TB diagnosis, using a standardized questionnaire [32]. Direct
147 costs included costs for diagnosis (such as costs for X-rays), medical costs (as costs for
148 drugs that excluded TB drugs), food, transport, and other costs that included special
149 supplements and vitamins. Indirect costs included income reduction, decreased
150 production costs, coping costs (including the use of savings or selling of household assets
151 to cater for sickness), and reduced payment for labour. Calculation of patient costs relied
152 upon the 2008 WHO tool [32]. We report costs as US Dollars (USD), converted from
153 Tanzania shillings using the exchange rate from the Bank of Tanzania of USD/TZS
154 2167.84 as of August 2016.

155 **Definitions**

156 A new TB patient was defined by bacteriological confirmation with sputum smear
157 microscopy and/or Xpert MTB/RIF in the absence of prior TB treatment during screening
158 [33]. A presumptive TB patient was defined by presentation with TB symptoms, including
159 coughing for longer than two weeks, fever, night sweats, or unexplained weight loss, and
160 who tested negative on sputum smear or Xpert MTB/RIF [33]. Diagnostic delay was
161 defined according to the framework of WHO (29) and used in previous studies [34,35] as
162 the interval between the onset of any TB-related symptom and the time of TB diagnosis of
163 more than 3 weeks. Healthcare provider was defined as a person or facility that could
164 provide healthcare, this included hospitals, pharmacies, and dispensaries, as well as
165 traditional healers. Prior medication was defined as the use of any prescribed or self-
166 prescribed medication prior to TB diagnosis [4]. We defined patients as poor if their wealth

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3 167 fell in the lowest or second-lowest wealth quintile. The non-poor were defined as persons
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5 168 in the remaining middle, fourth, and highest wealth quintiles [36].
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7 8 169 **Statistical and geographical analysis**

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10 170 We performed descriptive analyses to summarize the data and used χ^2 or Fisher's test to
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12 171 assess differences between groups in categorical variables. "A cut off point of 300 USD
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14 172 was used as a threshold for the monthly household income as indicated in another similar
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16 173 study [4]. Cost distributions were described by their medians and interquartile ranges
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18 174 (IQR). Costs were further calculated stratifying by gender and poverty status. Wealth
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20 175 quintiles were generated following a principal component analysis of standard household
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22 176 assets as indicated in the Tanzania household survey [26]. To stratify among the poor and
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24 177 non-poor, we used wealth indicators relating to household characteristics (e.g., roofing
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26 178 type, cooking fuel and nature of flooring) and ownership of assets (e.g., radio and mobile
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28 179 phone) to create wealth ranking as used in other studies [37,38]. Patients in the first and
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33 180 second quintiles were considered poor and in the remaining quintiles as non-poor. We
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35 181 used the nonparametric Kruskal-Wallis test to assess the statistical significance of the
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37 182 differences in estimated costs between groups. All significance tests were two-sided with a
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39 183 confidence level of 95%. Quintile regression models were performed for median costs to
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41 184 examine the association of patient factors with the different types of costs. Factors
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43 185 considered in these models included male vs female, age in years, unskilled and semi-
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45 186 skilled labour, level of education, and diagnostic delay. Statistical analyses were performed
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47 187 using Stata version 14.0 (Stata Corporation, College Station, TX, USA).
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52 188 We mapped and visualized the pathways of patients to health care providers up to a
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54 189 maximum of five visits for the current episode of sickness as described elsewhere [3,14].
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57 190 We calculated distances in meters as the straight-line distance between the patient's
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3 191 household and the nearest health facility. The resulting distances were imported into Stata
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5 192 for further analyses. All geographical analyses were performed using ArcGIS (version
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7 193 10.5, Esri, Redlands, CA, USA).
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10 194 **Patient involvement**

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12 195 Patients were not involved in the development, design, and analysis of this study.
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16 196 **Ethics approval and consent to participate**

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18 197 The study was approved by Ifakara Health Institute Institutional Review Board
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20 198 (IHI/reference no IHI/IRB /09-2016), the Medical Research Coordinating Committee of the
21
22 199 National Institute for Medical Research in Tanzania (NIMR reference no
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24 200 NIMR/HQ/R.8c/Vol. I/357), and the Ethics Committee of the Canton of Basel (EKNZ
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26 201 reference no BASEC UBE-2016-00260). Written informed consent was obtained from all
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28 202 study participants.
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33 203 **Availability of data and materials**

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35 204 According to the Institutional Review Board of the Ifakara Health Institute, we are not
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37 205 allowed to make the data publicly available. Interested researchers should contact the
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39 206 corresponding author.
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43 207 **Competing interest**

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45 208 All authors declare that they have no competing interests.
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210 RESULTS

211 Patient characteristics

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

221 First point of care and diagnostic delay

222 Among confirmed patients, 44% first sought care at pharmacies after the onset of
223 symptoms, whereas 42% of presumptive patients first sought care at hospitals (Table 1).
224 Fewer than 10% of patients in both groups reported visits to traditional healers as the first
225 point of care. Confirmed patients frequently indicated more than 2 visits at health facilities
226 (33% vs. 9%, $p<0.001$).

227 The average time for first seeking healthcare after the onset of symptoms was two
228 weeks. Overall, 45.5% sought care within one week after the onset of TB symptoms. For
229 30%, the diagnostic was established within 2-3 weeks. For around every tenth there was a
230 diagnostic delay of six weeks or more. The diagnostic delay differed significantly between
231 confirmed and presumptive patients, with 41% of confirmed versus 50% of presumptive

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3 232 patients having a short delay (of <1 week). Higher proportion of confirmed patients had a
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5 233 diagnostic delay of 4-5 and of ≥ 6 weeks.
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234 Pathways to care

235 The spatial distribution of healthcare facilities in the study area show pharmacies and
236 dispensaries are distributed over the whole area Figure (2A). Hospitals are situated mainly
237 in the urban centres and traditional healers predominantly in the peripheral area. Figures
238 (2B) and (2C) offer examples of pathways to care until TB diagnosis in confirmed and
239 presumptive patients. Pathways in confirmed patients involved several visits to the
240 healthcare facilities before TB diagnosis. Pathways in presumptive patients were more
241 direct with only one or few visits to healthcare facilities before TB diagnosis.

242 The median total distance from patients' households to healthcare facilities
243 including hospitals, pharmacies, dispensaries, and traditional healers was 2,338 meters
244 (IQR 1,373-4,122) for confirmed patients, and 2,009 meters (IQR 986-2,976) for
245 presumptive patients ($p=0.25$). Among confirmed patients, 37% lived within 500 meters
246 near a pharmacy, as did 42% of presumptive patients. Eighty-three per cent of confirmed
247 patients and 72% of presumptive patients lived within 1,000 meters from the nearest
248 hospital. We did not find an association of the distance from patients' household to the
249 nearest possible healthcare facility with patient characteristics such as being poor (defined
250 as being in the lowest wealth quintile), prior use of medication, or having more than two
251 healthcare visits in multivariate analysis.

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

258 **Costs associated with seeking care**

259 Patients spent a median of 31% (IQR 15.0-56.3%) of their monthly household income for
260 health expenditures for all visits for TB diagnosis. For the first visit confirmed patients had
261 lower median costs than presumptive patients (USD 8.3 [IQR 4.6-17.5] vs. 13.8 [IQR 6.0-
262 20.5]), but their costs were comparatively higher with increasing number of visits
263 (Supplementary Table 1).

264 Overall, indirect costs were considerably higher than direct costs, both in confirmed
265 and presumptive patients from the onset of symptoms until confirmation/exclusion of TB
266 (Table 2). Confirmed patients had higher diagnostic costs than presumptive patients (USD
267 7.0 [IQR 5.8-9.2] and 5.3 [IQR 1.4-7.0]), higher food costs, and higher informal payments.
268 Among the indirect costs, income reduction was considerably higher for confirmed TB
269 patients than presumptive patients. (USD 23.1 [IQR 6.9-55.4] vs. 9.2 [IQR 1.4-25.4]).

270 **Gender, poverty status and costs**

271 Costs for different patients groups differed significantly. Overall, the median total direct
272 costs were similar for men, USD 24.9 (IQR 17.5-41.9), and women, USD 24.6 (IQR 16.1-
273 42.4 p=0.66). Indirect costs for men, USD 64.6 (IQR 31.8-159.1), were significantly higher
274 than those for women, at USD 55.6 (IQR 25.1-141.1, p<0.001).

275 Analyses stratified by sex and poverty status indicate that poor men with confirmed
276 TB had lower total direct costs compared to poor women (USD 24.4 [IQR 18.9-47.9] vs.
277 30.0 [IQR 18.68-49.58.]) (Table 3). For the presumptive TB patients total direct costs for
278 poor men differed slightly from those of poor women (USD 22.6 [IQR 17.5-29.1] vs. 20.5
279 [IQR 14.3-35.1]). Among the non-poor men and women, direct costs varied only little in
280 confirmed and presumptive patients. In confirmed patients, diagnostic costs were lower

281 among poor men compared to poor women (USD 6.91 [IQR 4.61-9.22] vs. 7.61 [IQR 1.38-
282 10.14]), whereas for the presumptive patients, diagnostic costs were the same among poor
283 men and women.

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

289 **Determinants of cost differences**

290 On average, each week of diagnostic delay was associated with an increase in
291 median total costs (direct and indirect costs) among confirmed patients by 1.44 USD
292 (95%CI: (-19.56, -6.63), $p < 0.001$), but no significant association was seen in presumptive
293 patients (Table 5). Diagnostic delay was associated with an increase in total direct costs in
294 confirmed patients (USD 0.52 per week, 95%CI: (0.34, 0.70), $p < 0.001$), but with a
295 decrease in presumptive patients (USD -0.84 per week, 95%CI: (-1.32,-0.35), $p = 0.001$).
296 For total indirect costs, the pattern was similar, but neither of the two associations reached
297 statistical significance.

298 Overall, having a university degree was significantly associated with higher indirect
299 costs (USD 70.14, 95%CI: (9.47, 130.80), $p = 0.02$). None of other factors of the model
300 were significantly associated with median costs. The pattern of positive association
301 between diagnostic delay and total costs among confirmed patients and negative
302 association among presumptive patients was further supported by analyses using linear
303 and quadratic terms (Figure 4). Furthermore, we conducted regression analyses
304 separately for different types of costs (Supplementary table 2 and

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3 305 Supplementary table 3). Medication costs in confirmed patients increased with the number
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5 306 of weeks of delay (USD 0.13 per week, 95%CI: (0.06, 0.19), $p < 0.001$), but not in
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7 307 presumptive patients. Transport costs were significantly lower among men and women
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9 308 with presumptive TB (USD -1.54, 95%CI: (-3.12, -0.03), $p < 0.05$). We further observed an
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11 309 increase in coping costs with the length of diagnostic delay in both confirmed and
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14 310 presumptive patients (Supplementary Table 3). Finally, in patients with presumptive TB,
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16 311 costs due to decreased production were significantly higher among unskilled labourers
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18 312 (USD 8.71, 95%CI: (0.53, 16.89), $p = 0.03$).

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314 **DISCUSSION**

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

326 Almost half of the confirmed TB patients began their search for care at
327 pharmacies, and patients in both groups sought care from more than one healthcare
328 provider before a diagnosis. This highlights a diagnostic shortfall in some healthcare
329 facilities and poor management of patients as documented elsewhere [39], and partially
330 explains the diagnostic delay. Compared to findings of other studies [19,40] the observed
331 diagnostic delay in our study was lower. However, a delay of at least 6 weeks observed in
332 10% of our study population still requires attention. Most patients lived near healthcare
333 facilities, and only 9% of the confirmed TB patients and 6% of the presumptive TB patients
334 reported visiting traditional healers. Living near healthcare facilities might have an impact
335 on treatment seeking [41]. We investigated the impact of geographical distance between
336 household and health facility on health-seeking behaviour, but found no associations
337 between distance and patient characteristics such as being poor, prior use of medication

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3 338 and having more than two visits to the healthcare facility. This is contrary to some other
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5 339 results that found distance to have an impact on patient characteristics such as treatment
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7 340 completion and diagnostic delay [35,42,43]. Diagnostic delay was significantly associated
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9 341 with direct costs, indirect costs (borderline significance) and total costs in confirmed
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11 342 patients. The most likely explanation for this finding is that diagnostic delay worsens
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13 343 patients' morbidity, especially in confirmed TB patients, thus increasing costs of healthcare
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15 344 [42].

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18 345 Patients in both groups spent a median proportion of around 30% of their monthly
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20 346 household income on health expenditures for up to five visits. The economic burden of
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22 347 direct and particularly indirect costs of seeking TB care for patients and their households
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24 348 are high for the marginalized population, which is most at risk of acquiring TB. These
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26 349 findings are consistent with other studies that show patients in low-and-middle income
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28 350 countries face a very high economic burden of seeking TB care [13], and expenditures for
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30 351 seeking healthcare for TB can cause or exacerbate poverty [44]. The total costs for
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32 352 presumptive TB patients were lower compared to confirmed cases in our study. These
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34 353 results are also consistent with those reported in other settings where half of the total costs
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36 354 for seeking healthcare are pre-treatment costs which disproportionately affect poor TB
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38 355 patients [13]

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41 356 While direct costs were relatively low, they may be catastrophic for patients who are
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43 357 semiskilled labourers reporting monthly household income of less than 300 USD. Their
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45 358 situations can further be worsened by employment in the informal sector that lacks
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47 359 sickness benefits [44]. Confirmed TB patients encountered higher indirect costs compared
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49 360 to presumptive patients, which may be due to the prolonged time required for diagnosis
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51 361 leading to their substantially higher income reduction as shown in our study.
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3 362 We found higher indirect costs among poor men compared to poor women. This
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5 363 was mainly due to their more pronounced income reduction and decreased production.
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7 364 Although the direct and indirect costs were higher for men than for women, the costs of ill
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9 365 health are usually more profound for women and their households than for men. When
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11 366 women get sick the impact of the disease on their children and their families is stronger
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14 367 than when men get sick [11]. Furthermore, financial burden may limit access to care for
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16 368 both confirmed and presumptive female TB patients since most of them lack financial
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18 369 autonomy. Moreover, their lower status in households deprioritizes their health.
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371 **ARTICLE SUMMARY**

372 **Strengths and limitations of this study**

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

389 **Conclusions**

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

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3 395 healthcare providers including private, public health practitioners and patients themselves
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5 396 could help not only in reducing the complex pathways during healthcare seeking, but also
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7 397 effective health care utilization [39]. Reducing the direct and indirect costs associated with
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9 398 treatment seeking is likely to support confirmed and presumptive TB patients in timely
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11 399 accessing health care for TB diagnosis and treatment. Decreasing or removing user fees
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14 400 and further decentralization of TB care could reduce diagnostic delay and lower
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16 401 expenditures. Additionally, strengthening of health systems policies including protection of
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18 402 patients against the catastrophic direct and indirect costs, as well as ensuring universal
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21 403 access to healthcare must be interpreted into actions for a better TB control [45]. These
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23 404 interventions are central for reaching the ambitious WHO targets of zero deaths, disease,
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25 405 and suffering due to TB by 2035 [46].
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407 **Funding**

408 This work was supported by funding from the Rudolf Geigy Foundation (Basel,
409 Switzerland). The funder was not involved in any way during study design, data collection,
410 data analysis and interpretation, or in writing the manuscript. The funders had no role in
411 study design, data collection and analysis, decision to publish, or preparation of the
412 manuscript.

413 **Acknowledgements**

414 We would like to thank all the patients who participated in this study. We thank the District
415 and Regional TB coordinators of Temeke district and the National TB Programme in
416 Tanzania for their support.

417 **Author contributions**

418 Conceived and designed the study: GM, JH, FM, KS, PM, SG, KR, KH, TM, MGW,
419 EZ, and LF. GM, JH, KD, YM and FM analysed the data. GM and LF prepared the
420 first draft of the manuscript. KR, KS, PM, YM, TM, MGW, EM, EZ and LF contributed
421 to the major revision of the manuscript. All authors contributed to final manuscript
422 revisions and approved the final version.

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545 **FIGURE LEGENDS**

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

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

558 **Figure 3.** Spine plots showing distribution of health care facility visits during the pathway of
559 care (first, second, third and fourth/fifth visit) in confirmed and presumptive patients.
560 Numbers on the graph indicate absolute numbers.

562 **Figure 4.** Margin plots showing associations between total costs and diagnostic delay in
563 confirmed TB patients (panel A) and presumptive TB patients (panel B). Associations
564 between median total costs and diagnostic delay were modelled by quadratic polynomials.

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3 565 The p-values are from Wald test of the linear and quadratic terms of the diagnostic delay
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5 566 (p<0.001 for panel A, p=0.08 for panel B).
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567 **Tables and Figures**568 **Table 1.** Socio-demographic characteristics and diagnostic delay for the confirmed and
569 presumptive tuberculosis (TB) patients.

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 (69.0)	63 (63)	75 (75)	
>300 USD per month	62 (31.0)	37 (37)	25 (25)	
Wealth quintile				0.54
Poor -households	47 (23.5)	21 (21)	26 (26)	
Second	33 (16.5)	16 (16)	17.0 (17)	
Middle	41 (20.5)	19 (19)	22 (22)	
Fourth	44 (22.0)	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 (35.0)	28 (28)	42 (42)	
Dispensaries	49 (24.5)	19 (19)	30 (30)	
Pharmacies	66 (33.0)	44 (44)	22 (22)	
Traditional healers	15 (7.5)	9 (9)	6 (6)	
HC facility visits				<0.001
≤2	158 (79.0)	67 (67)	91 (91)	
>2	42 (21.0)	33 (33)	9 (9)	
Transport used for first point of care				<0.001
Car	70 (35.5)	22 (22)	48 (48)	
On foot	95 (47.5)	65 (65)	30 (30)	
Motorcycle/tricycle	35 (17.5)	13 (13)	22 (22)	
Diagnostic delay (weeks)				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)	

570 HC, health facility; IQR, interquartile range; USD, United States Dollar * Wilcoxon-rank sum test

571 P-values provided by Chi-square tests and Fisher's exact test

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

Costs	All (n=200)	Confirmed TB patients (n=100)	Presumptive TB patients (n=100)	P-value
Average number of visits (range)	1.2 (1-5)	1.3 (1-5)	1.1 (1-3)	
Direct costs	Median, (IQR)	Median, (IQR)	Median, (IQR)	
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
Sub-total 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
Sub-total 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

574 IQR, interquartile range; TB, tuberculosis; USD United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016). P-values provided by Wilcoxon rank sum test.
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576 **Table 3.** Direct costs (in USD) of seeking healthcare among confirmed and presumptive TB patients, according sex and poverty status

Variable	All	Confirmed				Presumptive			
		Men		Women		Men		Women	
		Poor ¹ n=21	Non-poor ² n=43	Poor n=16	Non-poor n=20	Poor n=15	Non-poor n=32	Poor n=28	Non-poor n=25
Median (IQR)									
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 (18.68-49.58)	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)

577 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
578 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.

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3 579 ¹Poor or second lowest wealth quintile
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582 **Table 4.** Indirect costs (in USD) of seeking health care among confirmed and presumptive TB patients, according to sex and poverty status

Variable	All	Confirmed				Presumptive			
		Men		Women		Men		Women	
		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)

583 IQR, interquartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016)

584 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

585 ¹ Poor or second lowest wealth quintile586 ² Non-poor middle, fourth and highest wealth quintile

587 **Table 5.** Estimates of effects of different factors on median direct, indirect and total costs in USD among confirmed and presumptive TB patients

Variable	All			Confirmed			Presumptive		
	*Difference	95% CI	P-value	*Difference	95% CI	P-value	*Difference	95% CI	P-value
Total direct costs									
Males vs females	-1.71	-11.80, 8.38	0.73	-2.31	-20.29, 15.67	0.79	-3.58	-9.80-2.63	0.25
Age (per year)	-0.01	-0.48, 0.46	0.97	0.28	-0.70, 1.26	0.57	0.06	-0.19, 0.31	0.31
Unskilled labour ¹	1.80	-11.40, 15.01	0.78	-7.55	-33.38, 18.26	0.56	2.20	-5.18, 9.59	0.55
Semi-skilled labour ¹	2.87	-8.75, 14.48	0.62	5.01	-14.66, 24.69	0.61	1.87	-5.49, 9.23	0.61
Poor vs non-poor	-2.34	-12.19, 7.51	0.63	19.73	-56.98, 96.46	0.61	-2.40	-8.07, 3.27	0.40
Primary education ²	3.18	-10.21, 16.56	0.64	8.96	-17.83, 35.76	0.66	0.66	-6.47 7.78	0.85
Secondary education	6.12	-11.16, 23.40	0.48	20.86	-11.40, 53.12	0.20	4.22	-5.88, 14.32	0.40
University ²	9.36	-19.07, 37.84	0.51	10.53	-35.17, 56.25	0.46	-0.59	-21.14, 19.95	0.95
Diagnostic delay	0.04	-0.08, 0.16	0.52	0.52	0.34, 0.70	<0.001	-0.84	-1.32, -0.35	0.001
Total indirect costs									
Males vs females	11.63	-11.37, 34.63	0.32	6.60	-33.93, 47.14	0.74	1.85	-34.74, 38.44	0.92
Age (per year)	0.38	-0.69-1.45	0.48	0.07	-2.14, 2.29	0.94	0.75	-0.74, 2.24	0.32
Unskilled labour	12.68	-17.41, 42.78	0.40	14.47	-43.74, 72.700	0.62	19.13	-24.32, 62.11	0.38
Semi-skilled labour	20.90	-5.58, 47.38	0.12	37.24	-7.11, 81.60	0.09	22.94	-20.38, 66.27	0.29
Poor vs non-poor	6.29	-16.15, 28.75	0.58	6.92	-33.36, 47.20	0.73	5.82	-27.53, 39.18	0.72
Primary education	21.24	-9.27, 51.75	0.17	8.96	-51.46, 69.37	0.76	20.0	-20.34, 60.34	0.32
Secondary/ University	70.14	9.47, 130.80	0.02	56.88	11.71, 125.47	0.10	-38.5	16.52, 93.52	0.16
Diagnostic delay	0.46	0.18-0.74	0.001	0.57	0.16, 0.97	0.07	-1.25	-4.11, 1.60	0.38
Total costs									
Males vs females	9.87	-26.39, 46.14	0.59	-4.98	-58.90, 48.93	0.85	-0.62	-44.96, 43.71	0.97
Age (per year)	0.34	-1.34, 2.03	0.68	-0.56	-3.50, 2.38	0.70	0.74	-1.06, 2.55	0.41
Unskilled labour	11.95	-35.50, 59.40	0.62	8.25	-69.18, 85.69	0.83	16.02	36.64, 68.69	0.54
Semi-skilled labour	30.47	-11.28, 72.23	0.15	58.81	-0.18, 117.81	0.05	26.64	-25.86, 79.14	0.31
Poor vs non-poor	0.89	-34.50, 36.31	0.96	8.39	-45.18, 61.98	0.75	2.39	-38.01, 42.81	0.90
Primary education	24.87	-23.25, 72.98	0.31	19.73	-60.62, 100.09	0.62	18.06	-32.75, 68.88	0.48
Secondary education	69.54	7.43, 131.16	0.02	69.45	-27.29, 166.19	0.15	46.10	-25.86, 79.14	0.20
University	108.89	6.63, 211.16	0.03	69.20	-67.87, 206.28	0.31	-15.74	-162.23, 130.73	0.83
Diagnostic delay	1.29	0.84-1.73	<0.001	1.44	-19.56, -6.63	<0.001	-2.40	-5.86, 1.06	0.17

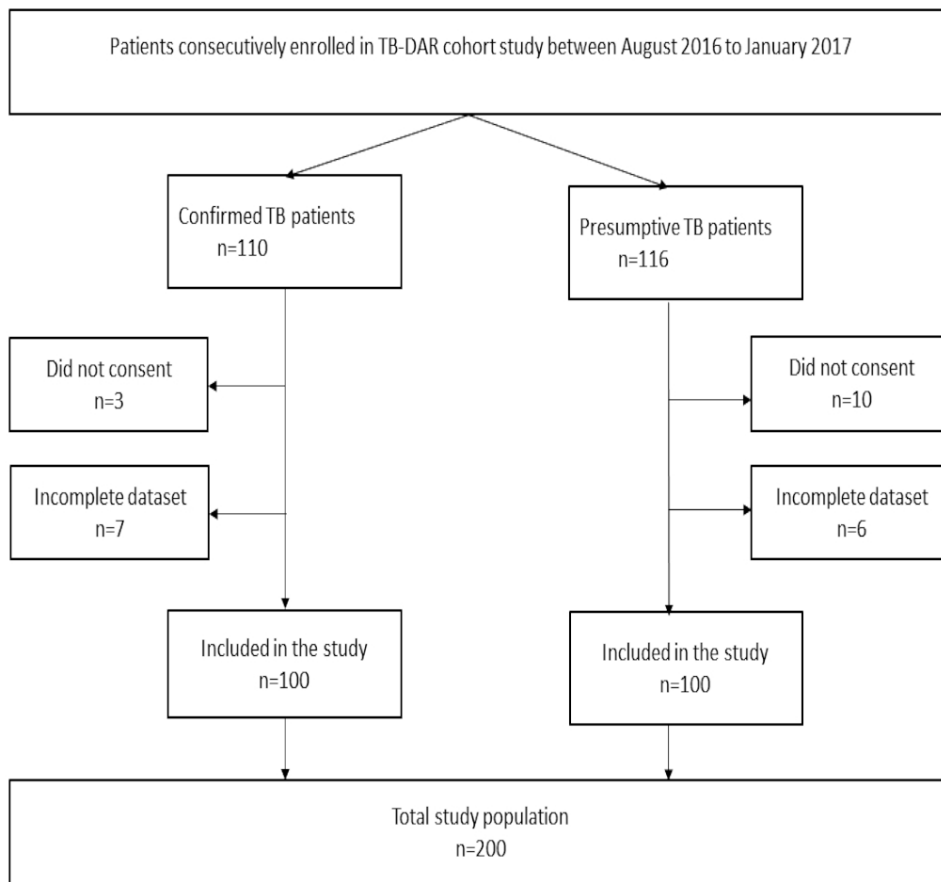
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588 *Estimated differences in median costs are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as a delay in seeking care three weeks or more after the
589 onset of symptoms. Multivariable quintile regression was performed for median costs to examine the association of patient factors with different types of costs. Separate models were run for direct, indirect
590 and total costs.

591 ¹Reference: Unemployed

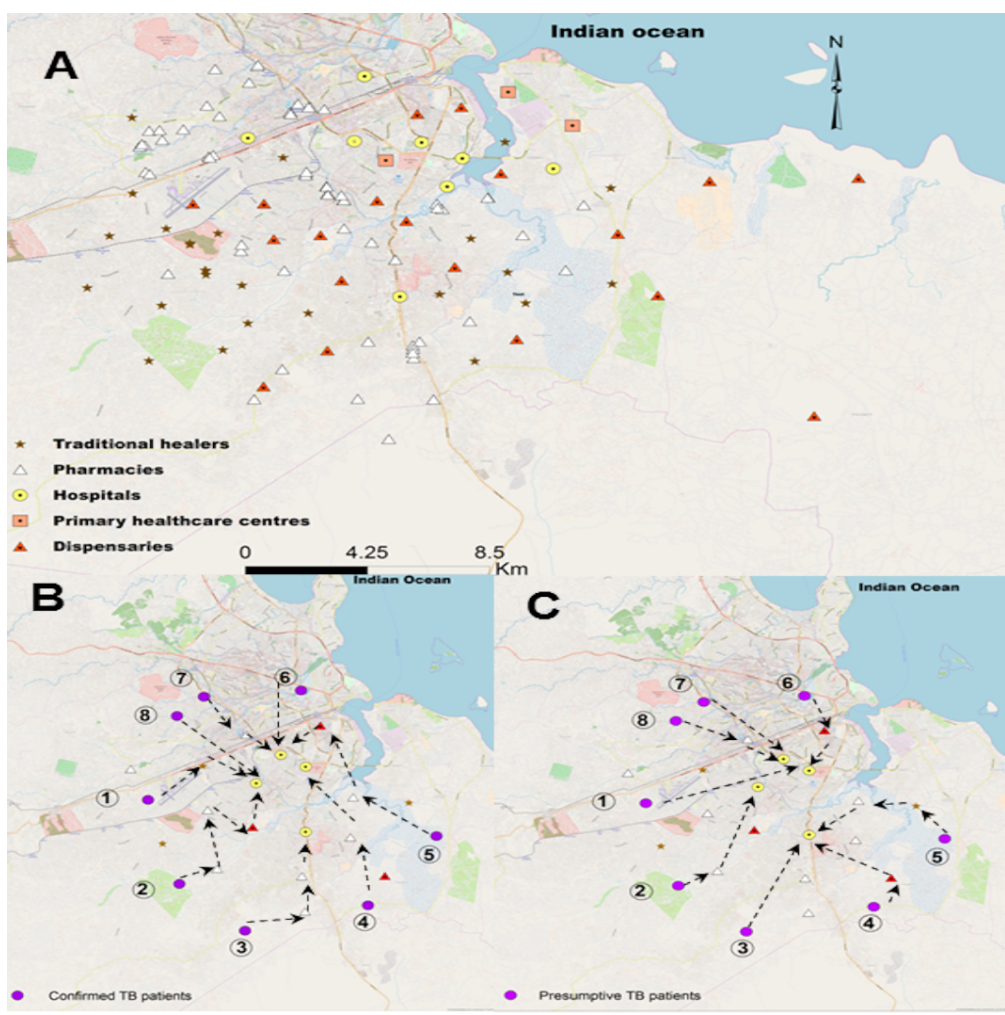
592 ²Reference: no education

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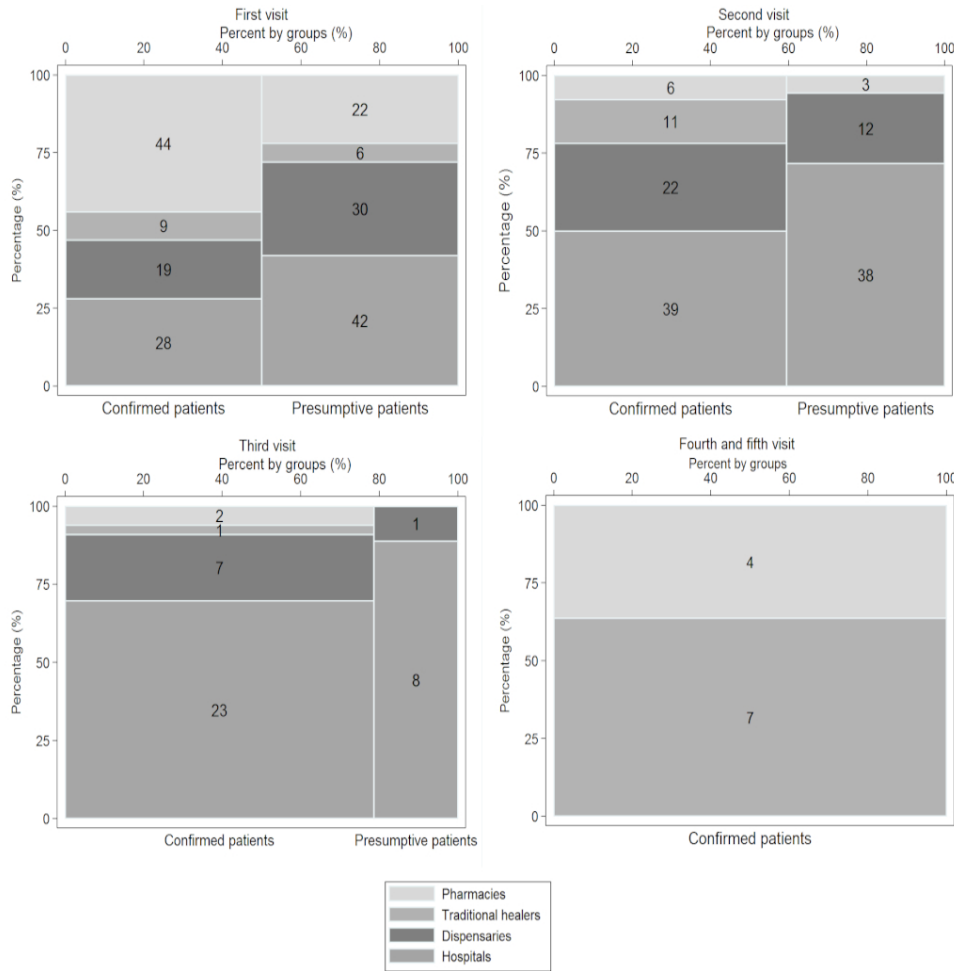
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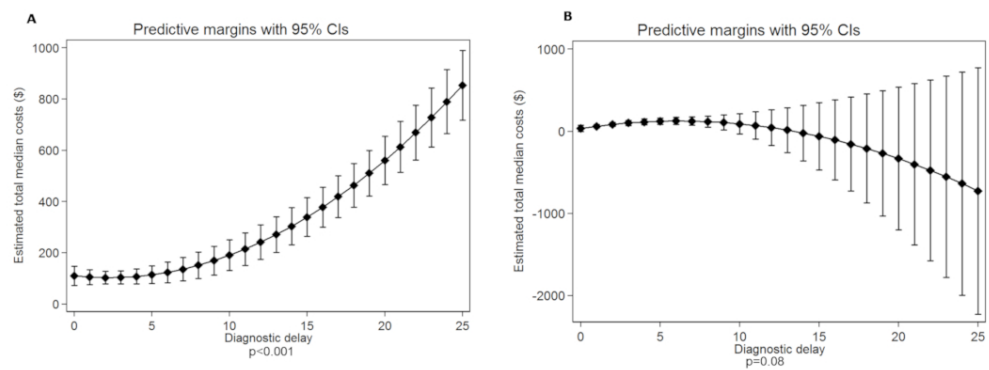
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Supplementary Table 1. Direct costs associated with first, second and >2 visits for patients with confirmed and presumptive TB.

Visit	All n (%)	Cost of visit/patient in USD		Costs as a % of MMHI	
		Median (IQR)		Median (IQR)	
		Confirmed	Presumptive	Confirmed	Presumptive
First visit	200 (100)	8.30 (4.6-17.5)	13.8 (6.0-20.5)	9.1 (3.7-18.3)	15.1 (8.0-34.8)
Second visit	90 (45)	15.2 (11.0-24.0)	14.3 (12.0-22.1)	14.5 (8.7-28.5)	19.7 (10.0-32.0)
Third to fifth visit	42 (21)	27.2 (14.8-38.7)	13.4 (12.9-20.3)	24.6 (13-42)	13.3 (12.0-14.3)
Total direct costs		27.4 (18.7-48.4)	19.8 (13.8-34.0)	30.5 (16.5-53.5)	29.0 (14.1-52.1)

IOR, interquartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016); MMHI, median monthly household income.

Supplementary Table 2. Estimates of effects of different factors on median types of direct costs in USD among confirmed and presumptive TB patients.

Variable	All			Confirmed			Presumptive		
	Difference*	95% CI	P-value	Difference*	95% CI	P-value	Difference*	95% CI	P-value
Diagnostic costs									
Males vs females	0.29	-1.33, 1.93	0.71	-0.17	-2.85, 2.52	0.90	-0.95	-3.45, 1.54	0.45
Age (in years)	0.03	-2.67, 0.51	0.18	-0.05	-0.20, 0.01	0.45	0.07	-0.03, 0.17	0.18
Unskilled labour ¹	1.71	-0.42, 1.84	0.11	1.32	-2.53, 5.19	0.49	1.99	-0.97, 4.96	0.18
Semi-skilled ¹	1.22	-0.65, 3.10	0.20	1.77	-1.17, 4.71	0.34	2.66	-0.29, 5.62	0.07
Poor vs non-poor	-1.08	-2.67, 0.51	0.18	-0.16	2.83, 2.50	0.90	-1.80	-4.08, 0.48	0.12
Primary education ²	1.14	-1.03, 3.30	0.30	3.03	-0.98, 7.03	0.13	-0.27	-3.12, 2.59	0.85
Secondary education	2.49	0.29, 5.29	0.08	3.80	-1.02, 8.62	0.12	0.89	-3.17, 4.95	0.85
University ²	6.16	1.56, 10.76	0.09	3.30	-3.53, 10.14	0.34	3.72	-4.54, 11.97	0.37
Diagnostic delay	-0.02	-0.02, 0.19	0.97	0.01	-0.01, 0.04	0.49	-0.07	-0.03, 0.12	0.45
Medication costs									
Males vs females	-0.31	-3.65, 3.09	0.85	-0.69	-7.40, 6.01	0.83	0.45	-2.23-3.13	0.73
Age (in years)	-0.03	0.18, 0.13	0.74	-0.01	-0.38-, 0.35	0.95	-0.05	-0.16, 0.06	0.36
Unskilled labour	0.13	-4.23, 4.49	0.95	-0.03	-9.67, 9.61	0.99	-0.68	-3.86-2.49	0.67
Semi-skilled labour	-0.03	-3.86, 3.81	0.99	0.92	-6.41, 8.27	0.80	-2.01	-5.17, 1.16	0.21
Poor vs non-poor	0.62	-2.64, 3.87	0.71	0.77	-5.90, 7.43	0.82	0.31	-2.12, 2.75	0.80
Primary education	1.26	-3.16-5.68	0.57	2.04	-7.95, 2.04	0.68	0.88	-2.18, 3.95	0.56
Secondary education	1.54	-4.17, 7.25	0.59	4.28	-7.75, 16.32	0.48	0.58	-3.76, 4.93	0.79
University	0.24	9.16, 9.64	0.95	1.98	-15.08, 19.03	0.81	4.24	-4.60, 13.08	0.34
Diagnostic delay	0.06	0.02, 0.10	0.002	0.13	0.06, 0.19	<0.001	-0.17	-0.38, 0.04	0.11
Transport costs									
Males vs females	-1.02	-2.19, 0.13	0.08	-0.52	-2.25, 1.21	0.55	-1.54	-3.12, 0.03	0.05
Age (in years)	0.02	-0.03, 0.74	0.45	0.02	-0.07, 0.12	0.66	-0.01	-0.71, 0.06	0.84
Unskilled labour	1.39	-0.12, 2.90	0.07	-0.29	-2.78, 2.20	0.81	2.36	0.49, 4.24	0.01
Semi-skilled	0.35	-0.98, 1.68	0.60	0.49	-1.41, 2.39	0.61	0.94	-0.92, 2.81	0.31
Poor vs non-poor	-0.36	-1.48-0.76	0.53	0.92	-0.80, 2.64	0.29	-0.32	-1.76, 1.11	0.65

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3	Primary	1.17	-0.36-2.71	0.13	1.16	-1.41, 3.75	0.37	0.84	-0.96, 2.65	0.35
4	Secondary education	1.41	-0.56-3.39	0.16	2.20	-0.91, 5.31	0.16	-0.13	-2.70, 2.42	0.91
5	University	1.48	-1.78-4.74	0.37	0.99	-0.80, 2.64	0.65	0.32	-4.89-5.53	0.90
6	Diagnostic delay	0.01	-0.04-0.24	0.16	0.03	0.01, 0.05	0.002	-0.01	-0.22, 0.30	0.13
7										
8	Total direct costs									
9	Males vs females	-1.71	-11.80, 8.38	0.73	-2.31	-20.29, 15.67	0.79	-3.58	-9.80, 2.63	0.25
10	Age (per year)	-0.01	-0.48, 0.46	0.97	0.28	-0.70, 1.26	0.57	0.06	-0.19	0.31
11	Unskilled labour	1.80	-11.40, 15.01	0.78	-7.55	-33.38, 18.26	0.56	2.20	-5.18, 9.59	0.55
12	Semi-skilled labour	2.87	-8.75, 14.48	0.62	5.01	-14.66, 24.69	0.61	1.87	-5.49, 9.23	0.61
13	Poor vs non-poor	-2.34	-12.19, 7.51	0.63	7.44	-10.42, 25.31	0.41	-2.40	-8.07, 3.27	0.40
14	Primary education	3.18	-10.21, 16.56	0.47	8.96	-17.83, 35.76	0.66	0.66	-6.47, 7.78	0.85
15	Secondary education	6.12	-11.16, 23.40	0.48	20.86	-11.40, 53.12	0.20	4.22	-5.88, 14.32	0.40
16	University	9.36	-19.07, 37.84	0.51	10.53	-35.17, 56.25	0.64	-0.59	-21.14, 19.95	0.95
17	Diagnostic delay	0.04	-0.08, 0.16	0.52	0.52	0.34, 0.70	<0.001	-0.84	-1.32, -0.35	0.001
18										
19	Total costs									
20	Males vs females	9.87	-26.39, 46.14	0.59	-4.98	-58.90, 48.93	0.85	-0.62	-44.96, 43.71	0.97
21	Age (per year)	0.34	-1.34, 2.03	0.68	-0.56	-3.50, 2.38	0.70	0.74	-1.06, 2.55	0.41
22	Unskilled labour	11.95	-35.50, 59.40	0.62	8.25	-69.18, 85.69	0.83	16.02	36.64, 68.69	0.54
23	Semi-skilled labour	30.47	-11.28, 72.23	0.15	58.81	-0.18, 117.81	0.05	26.64	-25.86, 79.14	0.31
24	Poor vs non-poor	0.89	-34.50, 36.31	0.96	8.39	-45.18, 61.98	0.75	2.39	-38.01, 42.81	0.90
25	Primary education	24.87	-23.25-72.98	0.31	19.73	-60.62, 100.09	0.62	18.06	-32.75, 68.88	0.48
26	Secondary education	69.54	7.43-131.65	0.02	69.45	-27.29, 166.19	0.15	46.10	-25.86, 79.14	0.20
27	University	108.89	6.6, 211.16	0.03	69.20	-67.87, 206.28	0.31	-15.74	-162.23, 130.73	0.83
28	Diagnostic delay	1.29	0.84, 1.73	<0.001	1.44	-19.56, -6.63	<0.001	-2.40	-5.86, 1.06	0.17
29										
30										
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32										

33 *Estimated differences in median costs are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the
 34 onset of symptoms

35 Multivariable quintile regression was performed for median costs to examine the association of patient factors with the different types of costs. Separate models were run for direct, indirect and total
 36 costs.

37 ¹ Reference: Unemployed

38 ² Reference: no education.

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Supplementary Table 3 Estimates of effects of different factors on median types of indirect and costs in USD among confirmed and presumptive TB patients.

Variable	All			Confirmed			Presumptive		
	Difference*	95% CI	P-value	Difference*	95% CI	P-value	Difference*	95% CI	P-value
Coping costs									
Males vs females	-0.24	-6.12,5.64	0.93	-3.86	-11.45, 3.71	0.31	-1.39	-12.58, 9.79	0.80
Age (in years)	0.02	-0.25,0.29	0.88	-0.25	-0.66, 0.16	0.23	0.15	-0.30, 0.61	0.51
Unskilled labour ¹	-2.38	-5.71,9.90	0.59	-8.56	-19.45, 2.33	0.12	-0.49	-13.78, 12.79	0.94
Semi-skilled ¹	-4.63	-11.41,2.14	0.17	-2.64	-10.94, 5.66	0.52	-5.01	-18.25, 8.24	0.45
Poor vs non-poor	0.30	-5.43,6.05	0.91	-2.56	-10.09, 4.98	0.50	2.09	-8.10, 12.28	0.68
Primary education ²	2.09	-5.71,9.90	0.59	-2.89	-14.20, 8.40	0.61	5.92	-6.89, 18.74	0.36
Secondary education ²	5.79	-4.28,15.86	0.25	-4.85	-18.46, 8.76	0.48	9.23	-8.94, 27.41	0.31
University ²	-6.65	-23.24, 9.93	0.43	5.09	-14.19-24.37	0.60	-4.09	-41.05, 32.85	0.82
Diagnostic delay	2.47	0.87, 4.07	0.003	-0.04	-0.12, 0.03	0.26	-0.39	-1.27, 0.47	0.36
Less paid labour									
Males vs females	1.32	-2.69,5.33	0.51	3.78	-3.78, 11.35	0.32	0.74	-2.99, 4.46	0.69
Age (in years)	0.17	-0.01,0.35	0.07	0.19	-0.21, 0.60	0.34	0.15	-0.01, 0.30	0.05
Unskilled labour	2.80	-2.45,8.06	0.29	3.16	-7.71, 14.02	0.56	3.59	-0.83, 8.02	0.11
Semi-skilled labour	3.43	-1.18,8.06	0.14	1.44	-6.83, 9.72	0.36	4.63	0.22, 9.05	0.04
Poor vs non-poor	1.54	-2.37,5.57	0.43	-2.33	-9.85, 5.18	0.53	2.10	-1.29, 5.50	0.22
Primary education	3.15	-2.16,8.48	0.24	-2.51	-13.79, 8.77	0.65	4.38	0.11, 8.65	0.04
Secondary education	4.69	-2.17,11.57	0.17	-1.64	-15.22, 11.93	0.80	8.03	1.97, 14.08	0.01
University	3.88	-7.43,15.20	0.49	8.84	-10.40, 28.07	0.36	3.93	-8.37, 16.24	0.52
Diagnostic delay	0.09	0.05,0.15	<0.001	0.09	0.02, 0.17	0.01	-0.27	-0.56, 0.02	0.06
Decreased production									
Males vs females	3.12	-1.67,7.91	0.20	3.31	-4.73, 11.35	0.41	2.48	-4.39, 9.37	0.47
Age (in years)	0.11	-0.11,0.33	0.33	0.18	-0.25, 0.62	0.42	0.09	-0.19, 0.37	0.51
Unskilled labour	7.38	1.11,13.65	0.02	1.37	-10.19, 12.62	0.19	8.71	0.53, 16.89	0.03
Semi-skilled labour	6.40	0.89,11.92	0.02	5.16	-3.64, 13.97	0.24	7.25	-0.90, 15.40	0.08

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1										
2										
3	Poor vs non-poor	-0.07	-4.75-4.60	0.97	0.08	-7.90, 8.09	0.98	-0.79	-7.07, 5.48	0.80
4	Primary education	2.25	-4.10,8.61	0.48	0.63	-11.36, 12.63	0.91	3.40	-4.49, 11.29	0.39
5	Secondary education	6.53	-1.67-,4.73	0.11	5.94	-8.49, 20.38	0.41	5.76	-5.42, 16.95	0.39
6	University	21.51	7.99,35.02	0.002	21.39	0.93,41.85	0.04	-4.33	-27.07, 18.42	18.41
7	Diagnostic delay	0.04	-0.02,0.09	0.20	0.05	-0.02,0.13	0.21	-0.17	-0.71, 0.36	0.51
8										
9	Total indirect costs									
10	Males vs females	11.63	-11.37,34.63	0.32	6.60	-33.93,47.14	0.74	1.85	-34.74, 38.44	0.92
11	Age (per year)	0.38	-0.69,1.45	0.48	0.07	-2.14, 2.29	0.94	0.75	-0.74, 2.24	0.32
12	Unskilled labour	12.68	-17.41,42.78	0.40	14.47	-43.74,72.700	0.62	19.13	-24.32, 62.11	0.38
13	Semi-skilled labour	20.90	-5.58,47.38	0.12	37.24	-7.11, 81.60	0.09	22.94	-20.38, 66.27	0.29
14	Poor vs non-poor	6.29	-16.15,28.75	0.58	6.92	-33.36,47.20	0.73	5.82	-27.53, 39.18	0.72
15	Primary education	21.24	-9.27,51.75	0.17	8.96	-51.46, 69.37	0.76	20.17	-21.76, 62.11	0.34
16	Secondary education	61.52	22.14,100.92	0.002	54.24	-18.48,126.99	0.73	38.79	-20.65, 98.25	0.19
17	University	108.74	43.89,173.60	0.001	85.66	-17-40,188.72	0.10	-7.79	-128.66, 113.09	0.89
18	Diagnostic delay	0.46	0.12,0.74	0.001	0.56	0.16,0.98	0.007	-1.25	-4.09, 1.62	0.39
19										
20	Total costs									
21	Males vs females	9.87	-26.39,46.14	0.59	-4.98	-58.90,48.93	0.85	-0.62	-44.96, 43.71	0.97
22	Age (per year)	0.34	-1.34,2.03	0.68	-0.56	-3.50,2.38	0.70	0.74	-1.06, 2.55	0.41
23	Unskilled labour	11.95	-35.50,59.40	0.62	8.25	-69.18,85.69	0.83	16.02	36.64, 68.69	0.54
24	Semi-skilled labour	30.47	-11.28,72.23	0.15	58.81	-0.18,117.81	0.05	26.64	-25.86-79.14	0.31
25	Poor vs non-poor	0.89	-34.50,36.31	0.96	8.39	-45.18,61.98	0.75	2.39	-38.01, 42.81	0.90
26	Primary education	24.87	-23.25,72.98	0.31	19.73	-60.62,100.09	0.62	18.06	-32.75, 68.88	0.48
27	Secondary education	69.54	7.43,131.65	0.02	69.45	-27.29,166.19	0.15	46.10	-25.86, 79.14	0.20
28	University	108.89	6.63,211.161	0.03	69.20	-67.87,206.28	0.31	-15.74	-162.23, 130.73	0.83
29	Diagnostic delay	1.29	0.84,1.73	<0.001	1.44	-19.56,6.63	<0.001	-2.40	-5.86, 1.06	0.17
30										
31										
32										

*Estimated differences in median costs of are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the onset of symptoms. Multivariable quintile regression was performed for median costs to examine the association of patient factors with the different types of costs. Separate models were run for direct, indirect and total costs.

¹Reference: Unemployed
²Reference: no education

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
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
Methods			
Study design	4	Present key elements of study design early in the paper	Page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
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 7-8
Bias	9	Describe any efforts to address potential sources of bias	Page 9
Study size	10	Explain how the study size was arrived at	Page 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 9
		(b) Describe any methods used to examine subgroups and interactions	Page 9
		(c) Explain how missing data were addressed	-
		(d) If applicable, describe analytical methods taking account of sampling strategy	-
		(e) Describe any sensitivity analyses	-
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 12
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	Page 7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	Page 13
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	-
		(b) Report category boundaries when continuous variables were categorized	-
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17
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 20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17-20
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 22

*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.

BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-025079.R2
Article Type:	Research
Date Submitted by the Author:	18-Jan-2019
Complete List of Authors:	Mhalu, Grace; Ifakara Health Institute Dar es Salaam, Health Intervention; Swiss Tropical and Public Health Institute Hella, Jerry; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Mhimbara, Francis; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Said, Khadija; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Mosabi, Thomas; Ifakara Health Institute Dar es Salaam Tanzania Mlacha, Yeromin; Ifakara Health Institute Bagamoyo Research Training Centre Tanzania; Swiss Tropical and Public Health Institute Schindler, Christian; Swiss Tropical and Public Health Institute; University of Basel Gagneux, Sébastien ; Schweizerisches Tropen- und Public Health-Institut; University of Basel Reither, Klaus; Swiss Tropical and Public Health Institute; University of Basel de Hoogh, Kees; Swiss Tropical and Public Health Institute; University of Basel Weiss, Mitchell; Swiss Tropical and Public Health Institute, Epidemiology and Public Health; University of Basel Zemp, Elisabeth; Swiss Tropical and Public Health Institute, Department of Epidemiology and Public Health; University of Basel, Fenner, Lukas; Universitat Bern; Institute of Social and Preventive medicine
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Infectious diseases, Public health, Epidemiology
Keywords:	Tuberculosis < INFECTIOUS DISEASES, Pathways to care, Direct costs, Indirect costs, Health-seeking, Health care

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4 1 **TITLE PAGE:**
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10 3 **Pathways and associated costs of care in confirmed and presumptive**
11 4 **tuberculosis patients in Tanzania: A cross-sectional study**
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19 6 Grace Mhalu ^{1, 2, 3*}, Jerry Hella ^{1, 2, 3}, Francis Mhimbira ^{1, 2, 3}, Khadija Said ^{1, 2, 3},
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20 **Keywords:** Tuberculosis, pathways to care, direct costs, indirect costs, health seeking,
21 Tanzania, healthcare

22 **Word count:**

23 Main text 4000 (max. 4000), abstract 300 (max. 300), references: 46

24 **Inserts:**

25 4 figures and 5 tables, Supplementary File (3 tables)

26

For peer review only

27 Abstract

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

30 **Design:** Cross-sectional study.

31 **Setting:** District hospital in Dar es Salaam, Tanzania.

32 **Participants:** Bacteriologically confirmed TB and presumptive TB patients.

33 **Primary and secondary outcome measures:** We calculated distance in meters and
34 visualized pathways to healthcare up to five visits for the current episode of sickness.
35 Costs were described by medians and interquartile ranges (IQR), with comparisons by
36 gender and poverty status.

37 **Results:** Of 100 confirmed and 100 presumptive TB patients, 44% of confirmed
38 patients sought care first at pharmacies after the onset of symptoms, and 42% of
39 presumptive patients did so at hospitals. The median visits made by confirmed patients
40 was 2 (range 1-5), and 2 (range 1-3) by presumptive patients. Patients spent a median
41 of 31% of their monthly household income on health expenditures for all visits. The
42 median total direct costs were higher in confirmed compared to presumptive patients
43 (USD 27.4 [IQR 18.7-48.4] vs. USD 19.8 [IQR 13.8-34.0], $p=0.02$), as were the indirect
44 costs (USD 66.9 [IQR 35.5-150.0] vs. USD 46.8 [IQR 20.1-115.3], $p<0.001$). The
45 indirect costs were higher in men compared to women (USD 64.6 [IQR 31.8-159.1] vs.
46 USD 55.6 [IQR 25.1-141.1], $p<0.001$). The median total distance from patients'
47 household to healthcare facilities for confirmed and presumptive TB patients was 2,338
48 meters (IQR 1,373-4,122) and 2,009 meters (IQR 986-2,976) respectively.

49 **Conclusions:** Confirmed TB patients have complex pathways and higher costs of care
50 compared to presumptive TB patients, but their costs are also substantial. Improved

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3 51 access to healthcare is needed for effective patient-centred care. Ensuring integration
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5 52 of different healthcare providers including private, public health practitioners and
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7 53 patients themselves could help not only in reducing the complex pathways during
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9 54 healthcare seeking, but also effective healthcare utilization.
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11 12 55 **Strengths and limitation of the study**

- 13
14 56 • We present data on pathways to care and assess costs of care in confirmed and
15
16 57 presumptive TB patients in Tanzania
- 17
18 58 • We estimate costs of care by stratifying costs according to poverty status and
19
20 59 gender
- 21
22 60 • Estimated costs for TB diagnosis did not account for HIV and other
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24 61 comorbidities.
- 25
26 62 • The accuracy of reported costs may have been compromised by recall bias.
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64 BACKGROUND

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

75 TB is widely regarded as a disease of poverty due to its disproportionate effects
76 on the marginalized populations [7,8]. To help socially and economically marginalized
77 groups fight the disease, healthcare facilities diagnose and treat TB free of charge in
78 countries with a high TB burden [9]. However, patients with symptoms of TB face high
79 direct and indirect costs for diagnosis and treatment [10–13], and these costs are
80 usually higher for patients with confirmed TB than presumptive cases [3,14].

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

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3 86 A national TB prevalence survey indicated that the case detection rate of TB was
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5 87 below 50% [16]. This result may not only be due to the complexity but also the high cost
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7 88 of care [15,17,18]. The recommended pathway to care for TB patients is to present
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9 89 themselves to the appropriate healthcare facilities for TB diagnosis after recognition of
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11 90 TB symptoms [9,19,20].
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14 91 Research has focused predominantly on patients who have already been
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16 92 diagnosed within the healthcare system, rather than costs for presumptive TB cases
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18 93 prior to diagnosis [21]. Costs for presumptive cases are not well understood, especially
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20 94 in sub-Saharan Africa [3,22]. In addition to financial costs, sociocultural and gender-
21
22 95 related factors can shape how patients seek healthcare [23], yet such studies of the
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24 96 influence of these factors are scarce [24]. Finally, only few studies have examined
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26 97 pathways and costs of seeking healthcare by comparing confirmed and presumptive TB
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28 98 patients [3,10,25].
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33 99 **Objective**

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36 100 We aimed to assess the pathways to care and associated costs of seeking care from
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38 101 the onset of symptoms until TB diagnosis in confirmed and presumptive TB patients in
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40 102 Dar es Salaam, Tanzania.
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103 **METHODS**

104 **Study setting and study population**

105 The study was conducted within the framework of an on-going TB cohort study among
106 the adult population in the Temeke district of Dar es Salaam, Tanzania [4]. The district
107 is densely populated with a population of 1,369,000 persons [26]. It ranks as the
108 poorest in the region with 29% of the households living below the poverty line, resulting
109 in 295 poor persons per square kilometre [27]. The number of health facilities in
110 Temeke district is low compared to other districts in the region. There are six public or
111 private hospitals, eight health centers, and 121 dispensaries [28]. In 2011, a total of
112 4,112 TB cases of all forms were notified in the Temeke district, of which 1,760 (43%)
113 were smear-positive [29].

114 We included adult, sputum smear-positive TB patients and presumptive TB cases who
115 were consecutively enrolled in the TB-DAR study [4,30] between August 2016 and
116 January 2017, until the target sample size of 100 patients in each category was
117 reached (Figure 1). Based on power calculation and previous studies [3,25] we included
118 100 confirmed TB patients and 100 presumptive TB patients allowing to detect a
119 statistically significant difference in the prevalence of diagnostic delay between the two
120 groups of patients with a power of 80% in case of a true difference of at least 20%.
121 Inclusion criteria were, (i) ≥ 18 years of age at recruitment; (ii) bacteriologically
122 confirmed TB diagnosis, or with presumptive TB, and (iii) residency in the Wailes I or II
123 sub-districts of Temeke. Additionally, patients in both groups were screened for TB
124 using sputum smear microscopy and Xpert MTB/RIF. We excluded patients who did not
125 provide consent and those with incomplete data.

126 **Data collection**

127 *Interviews*

128 We interviewed patients, reconstructed retrospectively visits to healthcare facilities and
129 collected data on direct and indirect costs using a standardized questionnaire at the TB
130 clinic. The data collected included patient socio-demographic and socioeconomic
131 characteristics, TB symptoms, the duration of the time from the onset of symptoms until
132 the first help seeking in a healthcare facility, and the number of health care facilities that
133 confirmed and presumptive TB patients had visited. Data were recorded on tablets
134 using the OpenDataKit (ODK) application [31].

135 *Pathways to care*

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

142 *Geographical information system data*

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

147 *Costs of care*

148 We asked patients to estimate direct and indirect costs associated with each visit from
149 the onset of symptoms until TB diagnosis, using a standardized questionnaire [32].
150 Direct costs included costs for diagnosis (such as costs for X-rays), medical costs (as
151 costs for drugs that excluded TB drugs), food, transport, and other costs that included
152 special supplements and vitamins. Indirect costs included income reduction, decreased
153 production costs, coping costs (including the use of savings or selling of household
154 assets to cater for sickness), and reduced payment for labour. Calculation of patient
155 costs relied upon the 2008 WHO tool [32]. We report costs as US Dollars (USD),
156 converted from Tanzania shillings using the exchange rate from the Bank of Tanzania
157 of USD/TZS 2167.84 as of August 2016.

158 **Definitions**

159 A new TB patient was defined by bacteriological confirmation with sputum smear
160 microscopy and/or Xpert MTB/RIF in the absence of prior TB treatment during
161 screening [33]. A presumptive TB patient was defined by presentation with TB
162 symptoms, including coughing for longer than two weeks, fever, night sweats, or
163 unexplained weight loss, and who tested negative on sputum smear or Xpert MTB/RIF
164 [33]. Diagnostic delay was defined according to the framework of WHO (29) and used
165 in previous studies [34,35] as the interval between the onset of any TB-related
166 symptom and the time of TB diagnosis of more than 3 weeks. Healthcare provider was
167 defined as a person or facility that could provide healthcare, this included hospitals,
168 pharmacies, and dispensaries, as well as traditional healers. Prior medication was
169 defined as the use of any prescribed or self-prescribed medication prior to TB diagnosis
170 [4]. We defined patients as poor if their wealth fell in the lowest or second-lowest wealth

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3 171 quintile. The non-poor were defined as persons in the remaining middle, fourth, and
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5 172 highest wealth quintiles [36].
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7 8 173 **Statistical and geographical analysis**

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10 174 We performed descriptive analyses to summarize the data and used χ^2 or Fisher's test
11
12 175 to assess differences between groups in categorical variables. "A cut off point of 300
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14 176 USD was used as a threshold for the monthly household income as indicated in another
15
16
17 177 similar study [4]. Cost distributions were described by their medians and interquartile
18
19 178 ranges (IQR). Costs were further calculated stratifying by gender and poverty status.
20
21 179 Wealth quintiles were generated following a principal component analysis of standard
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23 180 household assets as indicated in the Tanzania household survey [26]. To stratify
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26 181 among the poor and non-poor, we used wealth indicators relating to household
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28 182 characteristics (e.g., roofing type, cooking fuel and nature of flooring) and ownership of
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30 183 assets (e.g., radio and mobile phone) to create wealth ranking as used in other studies
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33 184 [37,38]. Patients in the first and second quintiles were considered poor and in the
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35 185 remaining quintiles as non-poor. We used the nonparametric Kruskal-Wallis test to
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37 186 assess the statistical significance of the differences in estimated costs between groups.
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39 187 All significance tests were two-sided with a confidence level of 95%. Quintile regression
40
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42 188 models were performed for median costs to examine the association of patient factors
43
44 189 with the different types of costs. Factors considered in these models included male vs
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46 190 female, age in years, unskilled and semi-skilled labour, level of education, and
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48 191 diagnostic delay. Statistical analyses were performed using Stata version 14.0 (Stata
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50 192 Corporation, College Station, TX, USA).
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54 193 We mapped and visualized the pathways of patients to health care providers up to a
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56 194 maximum of five visits for the current episode of sickness as described elsewhere
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58 195 [3,14]. We calculated distances in meters as the straight-line distance between the
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3 196 patient's household and the nearest health facility. The resulting distances were
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5 197 imported into Stata for further analyses. All geographical analyses were performed
6
7 198 using ArcGIS (version 10.5, Esri, Redlands, CA, USA). All maps were obtained from
8
9 199 Open Street Maps.

10 11 12 13 200 **Patient involvement**

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15 201 Patients were not involved in the development, design, and analysis of this study.

16 17 18 202 **Ethics approval and consent to participate**

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20 203 The study was approved by Ifakara Health Institute Institutional Review Board
21
22
23 204 (IHI/reference no IHI/IRB /09-2016), the Medical Research Coordinating Committee of
24
25 205 the National Institute for Medical Research in Tanzania (NIMR reference no
26
27 206 NIMR/HQ/R.8c/Vol. I/357), and the Ethics Committee of the Canton of Basel (EKNZ
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29 207 reference no BASEC UBE-2016-00260). Written informed consent was obtained from
30
31
32 208 all study participants.

33 34 35 209 **Availability of data and materials**

36
37 210 According to the Institutional Review Board of the Ifakara Health Institute, we are not
38
39
40 211 allowed to make the data publicly available. Interested researchers should contact the
41
42 212 corresponding author.

43 44 45 213 **Competing interest**

46
47 214 All authors declare that they have no competing interests.

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216 RESULTS

217 Patient characteristics

218 The study population includes 100 confirmed and 100 presumptive TB patients (Table
219 1). Patients' median age was 34 years, with presumptive TB patients being slightly
220 older than the confirmed patients. Men slightly predominated (55.5%) and accounted
221 for almost two thirds of the confirmed patients. Compared to presumptive TB patients,
222 confirmed patients had a somewhat higher education, were less likely to own a house
223 and use a car transport for their first point of care. They more frequently used
224 medication after the onset of symptoms and prior to seeking care at the health facilities
225 (71% vs. 44%, $p<0.001$). The proportion of patients with a monthly household income
226 of less than USD 300 was 63% in confirmed and 75% in presumptive patients ($p=0.06$).

227 First point of care and diagnostic delay

228 Among confirmed patients, 44% first sought care at pharmacies after the onset
229 of symptoms, whereas 42% of presumptive patients first sought care at hospitals (Table
230 1). Fewer than 10% of patients in both groups reported visits to traditional healers as
231 the first point of care. Confirmed patients frequently indicated more than 2 visits at
232 health facilities (33% vs. 9%, $p<0.001$).

233 The average time for first seeking healthcare after the onset of symptoms was
234 two weeks. Overall, 45.5% sought care within one week after the onset of TB
235 symptoms. For 30%, the diagnostic was established within 2-3 weeks. For around
236 every tenth there was a diagnostic delay of six weeks or more. The diagnostic delay
237 differed significantly between confirmed and presumptive patients, with 41% of
238 confirmed versus 50% of presumptive patients having a short delay (of <1 week).
239 Higher proportion of confirmed patients had a diagnostic delay of 4-5 and of ≥ 6 weeks.

240 Pathways to care

241 The spatial distribution of healthcare facilities in the study area show pharmacies and
242 dispensaries are distributed over the whole area Figure (2A). Hospitals are situated
243 mainly in the urban centres and traditional healers predominantly in the peripheral area.

244 Figures (2B) and (2C) offer examples of pathways to care until TB diagnosis in
245 confirmed and presumptive patients. Pathways in confirmed patients involved several
246 visits to the healthcare facilities before TB diagnosis. Pathways in presumptive patients
247 were more direct with only one or few visits to healthcare facilities before TB diagnosis.

248 The median total distance from patients' households to healthcare facilities
249 including hospitals, pharmacies, dispensaries, and traditional healers was 2,338 meters
250 (IQR 1,373-4,122) for confirmed patients, and 2,009 meters (IQR 986-2,976) for
251 presumptive patients ($p=0.25$). Among confirmed patients, 37% lived within 500 meters
252 near a pharmacy, as did 42% of presumptive patients. Eighty-three per cent of
253 confirmed patients and 72% of presumptive patients lived within 1,000 meters from the
254 nearest hospital. We did not find an association of the distance from patients'
255 household to the nearest possible healthcare facility with patient characteristics such as
256 being poor (defined as being in the lowest wealth quintile), prior use of medication, or
257 having more than two healthcare visits in multivariate analysis.

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

264 **Costs associated with seeking care**

265 Patients spent a median of 31% (IQR 15.0-56.3%) of their monthly household income
266 for health expenditures for all visits for TB diagnosis. For the first visit confirmed
267 patients had lower median costs than presumptive patients (USD 8.3 [IQR 4.6-17.5] vs.
268 13.8 [IQR 6.0-20.5]), but their costs were comparatively higher with increasing number
269 of visits (Supplementary Table 1).

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

277 **Gender, poverty status and costs**

278 Costs for different patients groups differed significantly. Overall, the median total direct
279 costs were similar for men, USD 24.9 (IQR 17.5-41.9), and women, USD 24.6 (IQR
280 16.1-42.4 $p=0.66$). Indirect costs for men, USD 64.6 (IQR 31.8-159.1), were
281 significantly higher than those for women, at USD 55.6 (IQR 25.1-141.1, $p<0.001$).

282 Analyses stratified by sex and poverty status indicate that poor men with
283 confirmed TB had lower total direct costs compared to poor women (USD 24.4 [IQR
284 18.9-47.9] vs. 30.0 [IQR 18.68.5-49.58.]) (Table 3). For the presumptive TB patients
285 total direct costs for poor men differed slightly from those of poor women (USD 22.6
286 [IQR 17.5-29.1] vs. 20.5 [IQR 14.3-35.1]). Among the non-poor men and women, direct
287 costs varied only little in confirmed and presumptive patients. In confirmed patients,
288 diagnostic costs were lower among poor men compared to poor women (USD 6.91

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3 289 [IQR 4.61-9.22] vs. 7.61 [IQR 1.38-10.14]), whereas for the presumptive patients,
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5 290 diagnostic costs were the same among poor men and women.

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7 291 Total indirect costs, (Table 4) among poor confirmed TB patients were higher in
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9 292 men than women, (USD 84.4 [IQR 55.3-125] vs. 51.7 [IQR 27.6-73.4]), while this
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11 293 gender difference was absent in non-poor confirmed patients. Among presumptive TB
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13 294 patients, poor men faced higher total indirect costs than poor women (USD 50.2 [IQR
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15 295 27.6-83.4]) vs. 39.2 [IQR 18.6-116.0]).

18 296 **Determinants of cost differences**

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21 297 On average, each week of diagnostic delay was associated with an increase in
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23 298 median total costs (direct and indirect costs) among confirmed patients by 1.44 USD
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25 299 (95%CI: (-19.56, -6.63), $p < 0.001$), but no significant association was seen in
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27 300 presumptive patients (Table 5). Diagnostic delay was associated with an increase in
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29 301 total direct costs in confirmed patients (USD 0.52 per week, 95%CI: (0.34, 0.70),
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31 302 $p < 0.001$), but with a decrease in presumptive patients (USD -0.84 per week, 95%CI: (-
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33 303 1.32,-0.35), $p = 0.001$). For total indirect costs, the pattern was similar, but neither of the
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35 304 two associations reached statistical significance.

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39 305 Overall, having a university degree was significantly associated with higher
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41 306 indirect costs (USD 70.14, 95%CI: (9.47, 130.80), $p = 0.02$). None of other factors of the
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43 307 model were significantly associated with median costs. The pattern of positive
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45 308 association between diagnostic delay and total costs among confirmed patients and
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47 309 negative association among presumptive patients was further supported by analyses
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49 310 using linear and quadratic terms (Figure 4). Furthermore, we conducted regression
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51 311 analyses separately for different types of costs (Supplementary table 2 and
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53 312 Supplementary table 3). Medication costs in confirmed patients increased with the
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55 313 number of weeks of delay (USD 0.13 per week, 95%CI: (0.06, 0.19), $p < 0.001$), but not
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57 314 in presumptive patients. Transport costs were significantly lower among men and

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3 315 women with presumptive TB (USD -1.54, 95%CI: (-3.12, -0.03), $p < 0.05$). We further
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5 316 observed an increase in coping costs with the length of diagnostic delay in both
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7 317 confirmed and presumptive patients (Supplementary Table 3). Finally, in patients with
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9 318 presumptive TB, costs due to decreased production were significantly higher among
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11 319 unskilled labourers (USD 8.71, 95%CI: (0.53, 16.89), $p=0.03$).

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For peer review only

DISCUSSION

This study indicates that pathways to care of the confirmed TB patients are more complex compared to those of presumptive patients, involving visits at several healthcare providers among whom not all have necessary diagnostic equipment. A diagnostic delay of six weeks or more after the onset of symptoms was reported by 10% of the patients. Fifty percent of the patients visited healthcare facilities within one 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 confirmed TB patients 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 to 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 confirmed TB patients and 6% of the presumptive TB patients 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

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3 347 facility. This is contrary to some other results that found distance to have an impact on
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5 348 patient characteristics such as treatment completion and diagnostic delay [35,42,43].
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7 349 Diagnostic delay was significantly associated with direct costs, indirect costs (borderline
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9 350 significance) and total costs in confirmed patients. The most likely explanation for this
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11 351 finding is that diagnostic delay worsens patients' morbidity, especially in confirmed TB
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14 352 patients, thus increasing costs of healthcare [42].

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16 353 Patients in both groups spent a median proportion of around 30% of their
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18 354 monthly household income on health expenditures for up to five visits. The economic
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20 355 burden of direct and particularly indirect costs of seeking TB care for patients and their
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22 356 households are high for the marginalized population, which is most at risk of acquiring
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24 357 TB. These findings are consistent with other studies that show patients in low-and-
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26 358 middle income countries face a very high economic burden of seeking TB care [13],
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28 359 and expenditures for seeking healthcare for TB can cause or exacerbate poverty [44].
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30 360 The total costs for presumptive TB patients were lower compared to confirmed cases in
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32 361 our study. These results are also consistent with those reported in other settings where
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34 362 half of the total costs for seeking healthcare are pre-treatment costs which
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36 363 disproportionately affect poor TB patients [13]

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39 364 While direct costs were relatively low, they may be catastrophic for patients who
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41 365 are semiskilled labourers reporting monthly household income of less than 300 USD.
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43 366 Their situations can further be worsened by employment in the informal sector that
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45 367 lacks sickness benefits [44]. Confirmed TB patients encountered higher indirect costs
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47 368 compared to presumptive patients, which may be due to the prolonged time required for
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49 369 diagnosis leading to their substantially higher income reduction as shown in our study.

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51 370 We found higher indirect costs among poor men compared to poor women. This
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53 371 was mainly due to their more pronounced income reduction and decreased production.
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55 372 Although the direct and indirect costs were higher for men than for women, the costs of

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3 373 ill health are usually more profound for women and their households than for men.
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5 374 When women get sick the impact of the disease on their children and their families is
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7 375 stronger than when men get sick [11]. Furthermore, financial burden may limit access to
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9 376 care for both confirmed and presumptive female TB patients since most of them lack
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11 377 financial autonomy. Moreover, their lower status in households deprioritizes their
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14 378 health.

16 379 **Strengths and limitations of this study**

17 380
18 381 Our study is the first to look at pathways to care and assess costs of care before
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21 382 the start of treatment in confirmed and presumptive TB patients in an urban Tanzania
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23 383 setting. Studies have focused on pathways and costs of care in confirmed TB patients
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25 384 and ignore the effects on presumptive cases. Furthermore, it's the first study to
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27 385 estimate costs by stratifying according to poverty status and gender in sub-Saharan
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29 386 Africa. However, this study has some limitations. First, recall bias is a concern when
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31 387 inquiring about the costs incurred during health-care seeking. This might influence the
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33 388 accuracy of the reported costs and pathways to care. However, we attempted to limit
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35 389 the recall bias by linking questions about costs with memorable events such as the
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37 390 onset of symptoms or first care seeking. Our interviews were also conducted by well-
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39 391 trained personnel who spent enough time with the respondents so as to obtain answers
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41 392 that were as accurate as possible. Furthermore, we only addressed pathways and
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43 393 costs of care until TB diagnosis to the public healthcare facilities. Therefore, we might
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45 394 have left out costs of care for the patients who had their final diagnosis at the private
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47 395 and faith based healthcare facilities. Finally, we only estimated the costs for TB
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49 396 diagnosis. However, comorbidities may have caused higher costs, but this is equally
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51 397 true for confirmed as well as presumptive TB patients.
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398 **Conclusions**

399 This study demonstrates the complexity of pathways until diagnosis in confirmed TB
400 patients. It also highlights the high financial burden for the period between symptom
401 onset and diagnosis for confirmed and presumptive TB patients, and points to different
402 direct and indirect costs among poor men and women. This underscores the need to
403 strengthen the healthcare sector to ensure early diagnosis of TB. Ensuring integration
404 of different healthcare providers including private, public health practitioners and
405 patients themselves could help not only in reducing the complex pathways during
406 healthcare seeking, but also effective healthcare utilization [39]. Reducing the direct
407 and indirect costs associated with treatment seeking is likely to support confirmed and
408 presumptive TB patients in timely accessing healthcare for TB diagnosis and treatment.
409 Decreasing or removing user fees and further decentralization of TB care could reduce
410 diagnostic delay and lower expenditures. Additionally, strengthening of health systems
411 policies including protection of patients against the catastrophic direct and indirect
412 costs, as well as ensuring universal access to healthcare must be interpreted into
413 actions for a better TB control [45]. These interventions are central for reaching the
414 ambitious WHO targets of zero deaths, disease, and suffering due to TB by 2035 [46].

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3 416 **Funding**

4
5 417 This work was supported by funding from the Rudolf Geigy Foundation (Basel,
6
7 418 Switzerland). The funder was not involved in any way during study design, data
8
9 419 collection, data analysis and interpretation, or in writing the manuscript. The funders
10
11 420 had no role in study design, data collection and analysis, decision to publish, or
12
13
14 421 preparation of the manuscript.

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16
17 422 **Acknowledgements**

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19 423 We would like to thank all the patients who participated in this study. We thank the
20
21 424 District and Regional TB coordinators of Temeke district and the National TB
22
23
24 425 Programme in Tanzania for their support.

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26
27 426 **Author contributions**

28
29 427 Conceived and designed the study: GM, JH, FM, KS, PM, SG, KR, KH, TM,
30
31 428 MGW, EZ, and LF. GM, JH, KD, CS, YPM and FM analysed the data. GM and LF
32
33 429 prepared the first draft of the manuscript. KR, KS, PM, YPM, TM, MGW, EM, EZ,
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36 430 CS and LF contributed to the major revision of the manuscript. All authors
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38 431 contributed to final manuscript revisions and approved the final version.

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FIGURE LEGENDS

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

Figure 2. Geographical analyses of health care facilities and pathways to care of confirmed and presumptive TB patients in Temeke District Dar es Salaam Tanzania.

Panel A: Spatial distribution of healthcare facilities in the study area. **Panel B:** Possible pathways to care of confirmed TB patients while seeking healthcare. Various types of healthcare facilities as the entry point into the healthcare system until final diagnosis at the TB clinic are shown. **Panel C:** Possible pathways to care of presumptive TB patients while seeking healthcare. Various types of healthcare facilities as the entry point into the healthcare system until final diagnosis at the TB clinic are shown.

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

Figure 4. Margin plots showing associations between total costs and diagnostic delay in confirmed TB patients (panel A) and presumptive TB patients (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).

581 **Tables and Figures**582 **Table 1.** Socio-demographic characteristics and diagnostic delay for the confirmed and
583 presumptive tuberculosis (TB) patients.

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 (69.0)	63 (63)	75 (75)	
>300 USD per month	62 (31.0)	37 (37)	25 (25)	
Wealth quintile				0.54
Poor -households	47 (23.5)	21 (21)	26 (26)	
Second	33 (16.5)	16 (16)	17.0 (17)	
Middle	41 (20.5)	19 (19)	22 (22)	
Fourth	44 (22.0)	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 (35.0)	28 (28)	42 (42)	
Dispensaries	49 (24.5)	19 (19)	30 (30)	
Pharmacies	66 (33.0)	44 (44)	22 (22)	
Traditional healers	15 (7.5)	9 (9)	6 (6)	
HC facility visits				<0.001
≤2	158 (79.0)	67 (67)	91 (91)	
>2	42 (21.0)	33 (33)	9 (9)	
Transport used for first point of care				<0.001
Car	70 (35.5)	22 (22)	48 (48)	
On foot	95 (47.5)	65 (65)	30 (30)	
Motorcycle/tricycle	35 (17.5)	13 (13)	22 (22)	
Diagnostic delay (weeks)				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)	

584 HC, health facility; IQR, interquartile range; USD, United States Dollar * Wilcoxon-rank sum test

585 P-values provided by Chi-square tests and Fisher's exact test

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

Costs	All (n=200)	Confirmed TB patients (n=100)	Presumptive TB patients (n=100)	P-value
Average number of visits (range)	1.2 (1-5)	1.3 (1-5)	1.1 (1-3)	
Direct costs	Median, (IQR)	Median, (IQR)	Median, (IQR)	
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
Sub-total 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
Sub-total 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 (37.1-161.4)	0.003

588 IQR, interquartile range; TB, tuberculosis; USD United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016). P-values provided by Wilcoxon rank sum test.
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590 **Table 3.** Direct costs (in USD) of seeking healthcare among confirmed and presumptive TB patients, according sex and poverty status

Variable	All	Confirmed				Presumptive			
		Men		Women		Men		Women	
		Poor ¹ n=21	Non-poor ² 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 0.07-12.00	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 (18.68-49.58)	32.51 (17.98-55.81)	22.60 (17.52-29.05)	25.13 (5.91-44.28)	20.52 (14.29-35.05)	26.75 (17.98-37.82)

591 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
592 due to illness or additional direct costs due to chronic illness for which patients were receiving treatment for besides the costs for TB diagnosis.

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593 ¹Poor or second lowest wealth quintile
594 ²Non-poor middle, fourth and highest wealth quintile
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596 **Table 4.** Indirect costs (in USD) of seeking health care among confirmed and presumptive TB patients, according to sex and poverty status

Variable	All	Confirmed				Presumptive			
		Men		Women		Men		Women	
		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)

597 IQR, interquartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016)

598 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

599 ¹Poor or second lowest wealth quintile600 ²Non-poor middle, fourth and highest wealth quintile

601 **Table 5.** Estimates of effects of different factors on median direct, indirect and total costs in USD among confirmed and presumptive TB patients

Variable	All			Confirmed			Presumptive		
	*Difference	95% CI	P-value	*Difference	95% CI	P-value	*Difference	95% CI	P-value
Total direct costs									
Males vs females	-1.71	-11.80, 8.38	0.73	-2.31	-20.29, 15.67	0.79	-3.58	-9.80-2.63	0.25
Age (per year)	-0.01	-0.48, 0.46	0.97	0.28	-0.70, 1.26	0.57	0.06	-0.19, 0.31	0.31
Unskilled labour ¹	1.80	-11.40, 15.01	0.78	-7.55	-33.38, 18.26	0.56	2.20	-5.18, 9.59	0.55
Semi-skilled labour ¹	2.87	-8.75, 14.48	0.62	5.01	-14.66, 24.69	0.61	1.87	-5.49, 9.23	0.61
Poor vs non-poor	-2.34	-12.19, 7.51	0.63	19.73	-56.98, 96.46	0.61	-2.40	-8.07, 3.27	0.40
Primary education ²	3.18	-10.21, 16.56	0.64	8.96	-17.83, 35.76	0.66	0.66	-6.47, 7.78	0.85
Secondary education	6.12	-11.16, 23.40	0.48	20.86	-11.40, 53.12	0.20	4.22	-5.88, 14.32	0.40
University ²	9.36	-19.07, 37.84	0.51	10.53	-35.17, 56.25	0.46	-0.59	-21.14, 19.95	0.95
Diagnostic delay	0.04	-0.08, 0.16	0.52	0.52	0.34, 0.70	<0.001	-0.84	-1.32,-0.35	0.001
Total indirect costs									
Males vs females	11.63	-11.37, 34.63	0.32	6.60	-33.93, 47.14	0.74	1.85	-34.74, 38.44	0.92
Age (per year)	0.38	-0.69-1.45	0.48	0.07	-2.14, 2.29	0.94	0.75	-0.74, 2.24	0.32
Unskilled labour	12.68	-17.41, 42.78	0.40	14.47	-43.74, 72.700	0.62	19.13	-24.32, 62.11	0.38
Semi-skilled labour	20.90	-5.58, 47.38	0.12	37.24	-7.11, 81.60	0.09	22.94	-20.38, 66.27	0.29
Poor vs non-poor	6.29	-16.15, 28.75	0.58	6.92	-33.36, 47.20	0.73	5.82	-27.53, 39.18	0.72
Primary education	21.24	-9.27, 51.75	0.17	8.96	-51.46, 69.37	0.76	20.0	-20.34, 60.34	0.32
Secondary/ University	70.14	9.47, 130.80	0.02	56.88	11.71, 125.47	0.10	-38.5	16.52, 93.52	0.16
Diagnostic delay	0.46	0.18-0.74	0.001	0.57	0.16, 0.97	0.07	-1.25	-4.11, 1.60	0.38
Total costs									
Males vs females	9.87	-26.39, 46.14	0.59	-4.98	-58.90, 48.93	0.85	-0.62	-44.96, 43.71	0.97
Age (per year)	0.34	-1.34, 2.03	0.68	-0.56	-3.50, 2.38	0.70	0.74	-1.06, 2.55	0.41
Unskilled labour	11.95	-35.50, 59.40	0.62	8.25	-69.18, 85.69	0.83	16.02	36.64, 68.69	0.54
Semi-skilled labour	30.47	-11.28, 72.23	0.15	58.81	-0.18, 117.81	0.05	26.64	-25.86, 79.14	0.31
Poor vs non-poor	0.89	-34.50, 36.31	0.96	8.39	-45.18, 61.98	0.75	2.39	-38.01, 42.81	0.90
Primary education	24.87	-23.25, 72.98	0.31	19.73	-60.62, 100.09	0.62	18.06	-32.75, 68.88	0.48
Secondary education	69.54	7.43, 131.16	0.02	69.45	-27.29, 166.19	0.15	46.10	-25.86, 79.14	0.20
University	108.89	6.63, 211.16	0.03	69.20	-67.87, 206.28	0.31	-15.74	-162.23, 130.73	0.83
Diagnostic delay	1.29	0.84-1.73	<0.001	1.44	-19.56, -6.63	<0.001	-2.40	-5.86, 1.06	0.17

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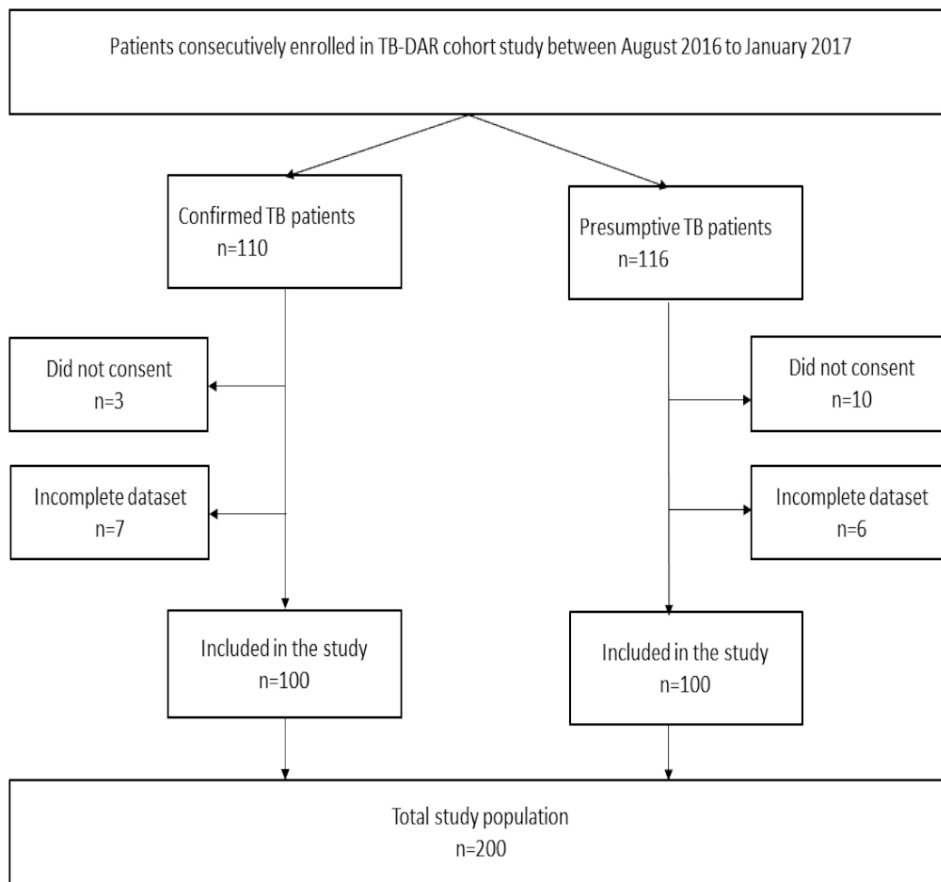
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602 *Estimated differences in median costs are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the onset of
603 symptoms. Multivariable quintile regression 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.

604 ¹Reference: Unemployed

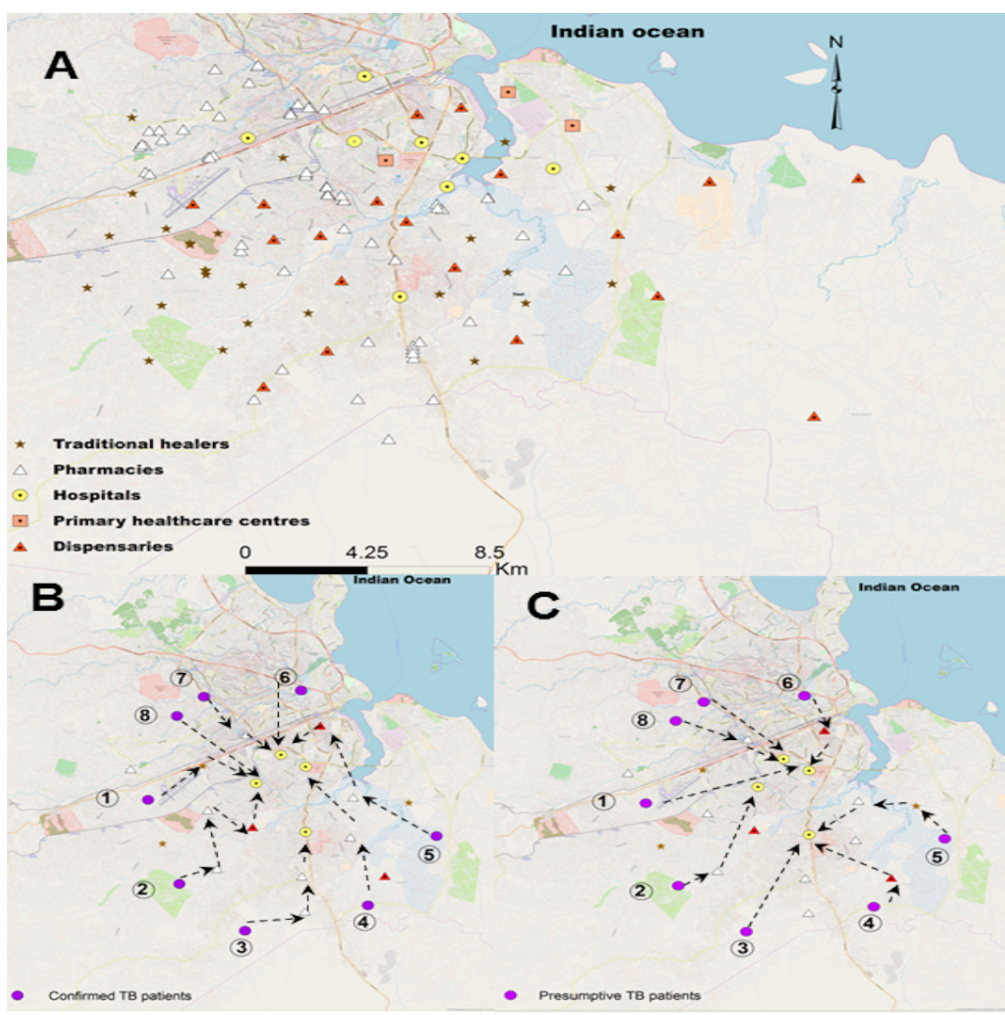
605 ²Reference: no education

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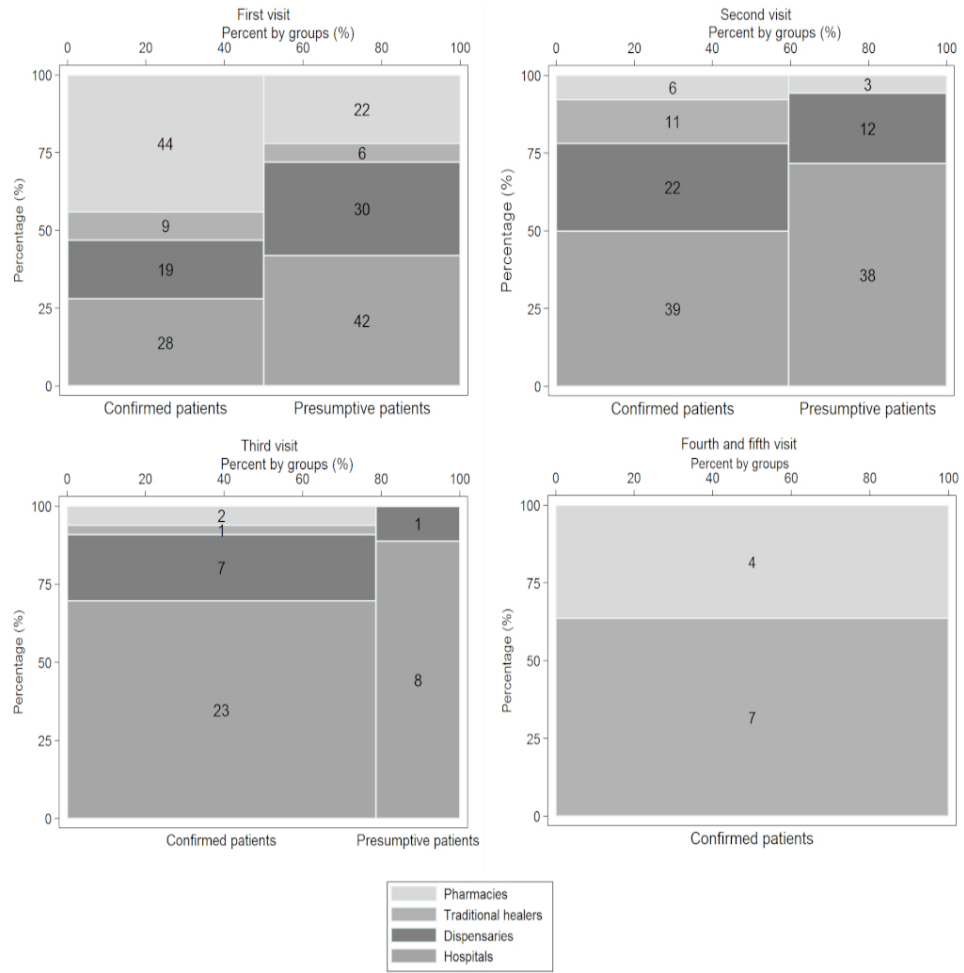
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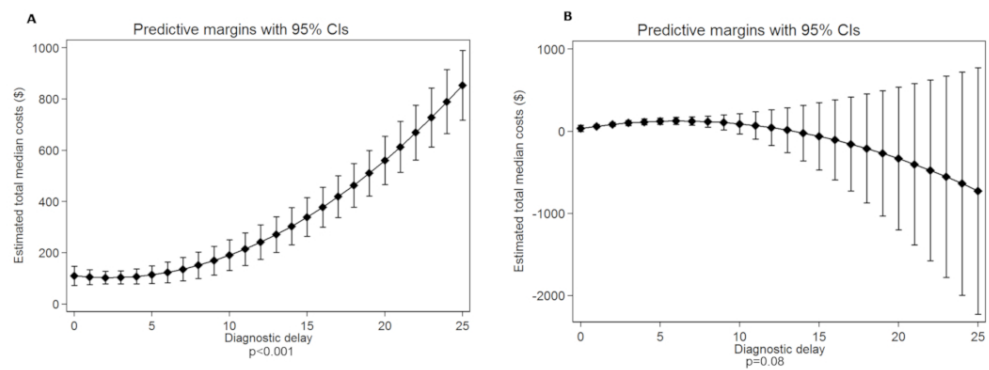
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Supplementary Table 1. Direct costs associated with first, second and >2 visits for patients with confirmed and presumptive TB.

Visit	All n (%)	Cost of visit/patient in USD		Costs as a % of MMHI	
		Median (IQR)		Median (IQR)	
		Confirmed	Presumptive	Confirmed	Presumptive
First visit	200 (100)	8.30 (4.6-17.5)	13.8 (6.0-20.5)	9.1 (3.7-18.3)	15.1 (8.0-34.8)
Second visit	90 (45)	15.2 (11.0-24.0)	14.3 (12.0-22.1)	14.5 (8.7-28.5)	19.7 (10.0-32.0)
Third to fifth visit	42 (21)	27.2 (14.8-38.7)	13.4 (12.9-20.3)	24.6 (13-42)	13.3 (12.0-14.3)
Total direct costs		27.4 (18.7-48.4)	19.8 (13.8-34.0)	30.5 (16.5-53.5)	29.0 (14.1-52.1)

IOR, interquartile range; USD, United States Dollar (1 USD=2168 Tanzania shillings, exchange rates as of August 2016); MMHI, median monthly household income.

Supplementary Table 2. Estimates of effects of different factors on median types of direct costs in USD among confirmed and presumptive TB patients.

Variable	All			Confirmed			Presumptive		
	Difference*	95% CI	P-value	Difference*	95% CI	P-value	Difference*	95% CI	P-value
Diagnostic costs									
Males vs females	0.29	-1.33, 1.93	0.71	-0.17	-2.85, 2.52	0.90	-0.95	-3.45, 1.54	0.45
Age (in years)	0.03	-2.67, 0.51	0.18	-0.05	-0.20, 0.01	0.45	0.07	-0.03, 0.17	0.18
Unskilled labour ¹	1.71	-0.42, 8.4	0.11	1.32	-2.53, 5.19	0.49	1.99	-0.97, 4.96	0.18
Semi-skilled ¹	1.22	-0.65, 3.10	0.20	1.77	-1.17, 4.71	0.34	2.66	-0.29, 5.62	0.07
Poor vs non-poor	-1.08	-2.67, 0.51	0.18	-0.16	2.83, 2.50	0.90	-1.80	-4.08, 0.48	0.12
Primary education ²	1.14	-1.03, 3.30	0.30	3.03	-0.98, 7.03	0.13	-0.27	-3.12, 2.59	0.85
Secondary education	2.49	0.29, 5.29	0.08	3.80	-1.02, 8.62	0.12	0.89	-3.17, 4.95	0.85
University ²	6.16	1.56, 10.76	0.09	3.30	-3.53, 10.14	0.34	3.72	-4.54, 11.97	0.37
Diagnostic delay	-0.02	-0.02, 0.19	0.97	0.01	-0.01, 0.04	0.49	-0.07	-0.03, 0.12	0.45
Medication costs									
Males vs females	-0.31	-3.65, 3.09	0.85	-0.69	-7.40, 6.01	0.83	0.45	-2.23-3.13	0.73
Age (in years)	-0.03	0.18, 0.13	0.74	-0.01	-0.38-, 0.35	0.95	-0.05	-0.16, 0.06	0.36
Unskilled labour	0.13	-4.23, 4.49	0.95	-0.03	-9.67, 9.61	0.99	-0.68	-3.86-2.49	0.67
Semi-skilled labour	-0.03	-3.86, 3.81	0.99	0.92	-6.41, 8.27	0.80	-2.01	-5.17, 1.16	0.21
Poor vs non-poor	0.62	-2.64, 3.87	0.71	0.77	-5.90, 7.43	0.82	0.31	-2.12, 2.75	0.80
Primary education	1.26	-3.16-5.68	0.57	2.04	-7.95, 2.04	0.68	0.88	-2.18, 3.95	0.56
Secondary education	1.54	-4.17, 7.25	0.59	4.28	-7.75, 16.32	0.48	0.58	-3.76, 4.93	0.79
University	0.24	9.16, 9.64	0.95	1.98	-15.08, 19.03	0.81	4.24	-4.60, 13.08	0.34
Diagnostic delay	0.06	0.02, 0.10	0.002	0.13	0.06, 0.19	<0.001	-0.17	-0.38, 0.04	0.11
Transport costs									
Males vs females	-1.02	-2.19, 0.13	0.08	-0.52	-2.25, 1.21	0.55	-1.54	-3.12, 0.03	0.05
Age (in years)	0.02	-0.03, 0.74	0.45	0.02	-0.07, 0.12	0.66	-0.01	-0.71, 0.06	0.84
Unskilled labour	1.39	-0.12, 2.90	0.07	-0.29	-2.78, 2.20	0.81	2.36	0.49, 4.24	0.01
Semi-skilled	0.35	-0.98, 1.68	0.60	0.49	-1.41, 2.39	0.61	0.94	-0.92, 2.81	0.31
Poor vs non-poor	-0.36	-1.48-0.76	0.53	0.92	-0.80, 2.64	0.29	-0.32	-1.76, 1.11	0.65

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Primary	1.17	-0.36-2.71	0.13	1.16	-1.41, 3.75	0.37	0.84	-0.96, 2.65	0.35	
Secondary education	1.41	-0.56-3.39	0.16	2.20	-0.91, 5.31	0.16	-0.13	-2.70, 2.42	0.91	
University	1.48	-1.78-4.74	0.37	0.99	-0.80, 2.64	0.65	0.32	-4.89-5.53	0.90	
Diagnostic delay	0.01	-0.04-0.24	0.16	0.03	0.01, 0.05	0.002	-0.01	-0.22, 0.30	0.13	
Total direct costs										
Males vs females	-1.71	-11.80, 8.38	0.73	-2.31	-20.29, 15.67	0.79	-3.58	-9.80, 2.63	0.25	
Age (per year)	-0.01	-0.48, 0.46	0.97	0.28	-0.70, 1.26	0.57	0.06	-0.19	0.31	
Unskilled labour	1.80	-11.40, 15.01	0.78	-7.55	-33.38, 18.26	0.56	2.20	-5.18, 9.59	0.55	
Semi-skilled labour	2.87	-8.75, 14.48	0.62	5.01	-14.66, 24.69	0.61	1.87	-5.49, 9.23	0.61	
Poor vs non-poor	-2.34	-12.19, 7.51	0.63	7.44	-10.42, 25.31	0.41	-2.40	-8.07, 3.27	0.40	
Primary education	3.18	-10.21, 16.56	0.47	8.96	-17.83, 35.76	0.66	0.66	-6.47, 7.78	0.85	
Secondary education	6.12	-11.16, 23.40	0.48	20.86	-11.40, 53.12	0.20	4.22	-5.88, 14.32	0.40	
University	9.36	-19.07, 37.84	0.51	10.53	-35.17, 56.25	0.64	-0.59	-21.14, 19.95	0.95	
Diagnostic delay	0.04	-0.08, 0.16	0.52	0.52	0.34, 0.70	<0.001	-0.84	-1.32, -0.35	0.001	
Total costs										
Males vs females	9.87	-26.39, 46.14	0.59	-4.98	-58.90, 48.93	0.85	-0.62	-44.96, 43.71	0.97	
Age (per year)	0.34	-1.34, 2.03	0.68	-0.56	-3.50, 2.38	0.70	0.74	-1.06, 2.55	0.41	
Unskilled labour	11.95	-35.50, 59.40	0.62	8.25	-69.18, 85.69	0.83	16.02	36.64, 68.69	0.54	
Semi-skilled labour	30.47	-11.28, 72.23	0.15	58.81	-0.18, 117.81	0.05	26.64	-25.86, 79.14	0.31	
Poor vs non-poor	0.89	-34.50, 36.31	0.96	8.39	-45.18, 61.98	0.75	2.39	-38.01, 42.81	0.90	
Primary education	24.87	-23.25-72.98	0.31	19.73	-60.62, 100.09	0.62	18.06	-32.75, 68.88	0.48	
Secondary education	69.54	7.43-131.65	0.02	69.45	-27.29, 166.19	0.15	46.10	-25.86, 79.14	0.20	
University	108.89	6.6, 211.16	0.03	69.20	-67.87, 206.28	0.31	-15.74	-162.23, 130.73	0.83	
Diagnostic delay	1.29	0.84, 1.73	<0.001	1.44	-19.56, -6.63	<0.001	-2.40	-5.86, 1.06	0.17	

*Estimated differences in median costs are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the onset of symptoms

Multivariable quintile regression was performed for median costs to examine the association of patient factors with the different types of costs. Separate models were run for direct, indirect and total costs.

¹ Reference: Unemployed

² Reference: no education.

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Supplementary Table 3 Estimates of effects of different factors on median types of indirect and costs in USD among confirmed and presumptive TB patients.

Variable	All			Confirmed			Presumptive		
	Difference*	95% CI	P-value	Difference*	95% CI	P-value	Difference*	95% CI	P-value
Coping costs									
Males vs females	-0.24	-6.12,5.64	0.93	-3.86	-11.45, 3.71	0.31	-1.39	-12.58, 9.79	0.80
Age (in years)	0.02	-0.25,0.29	0.88	-0.25	-0.66, 0.16	0.23	0.15	-0.30, 0.61	0.51
Unskilled labour ¹	-2.38	-5.71,9.90	0.59	-8.56	-19.45, 2.33	0.12	-0.49	-13.78, 12.79	0.94
Semi-skilled ¹	-4.63	-11.41,2.14	0.17	-2.64	-10.94, 5.66	0.52	-5.01	-18.25, 8.24	0.45
Poor vs non-poor	0.30	-5.43,6.05	0.91	-2.56	-10.09, 4.98	0.50	2.09	-8.10, 12.28	0.68
Primary education ²	2.09	-5.71,9.90	0.59	-2.89	-14.20, 8.40	0.61	5.92	-6.89, 18.74	0.36
Secondary education ²	5.79	-4.28,15.86	0.25	-4.85	-18.46, 8.76	0.48	9.23	-8.94, 27.41	0.31
University ²	-6.65	-23.24, 9.93	0.43	5.09	-14.19-24.37	0.60	-4.09	-41.05, 32.85	0.82
Diagnostic delay	2.47	0.87, 4.07	0.003	-0.04	-0.12, 0.03	0.26	-0.39	-1.27, 0.47	0.36
Less paid labour									
Males vs females	1.32	-2.69,5.33	0.51	3.78	-3.78, 11.35	0.32	0.74	-2.99, 4.46	0.69
Age (in years)	0.17	-0.01,0.35	0.07	0.19	-0.21, 0.60	0.34	0.15	-0.01, 0.30	0.05
Unskilled labour	2.80	-2.45,8.06	0.29	3.16	-7.71, 14.02	0.56	3.59	-0.83, 8.02	0.11
Semi-skilled labour	3.43	-1.18,8.06	0.14	1.44	-6.83, 9.72	0.36	4.63	0.22, 9.05	0.04
Poor vs non-poor	1.54	-2.37,5.57	0.43	-2.33	-9.85, 5.18	0.53	2.10	-1.29, 5.50	0.22
Primary education	3.15	-2.16,8.48	0.24	-2.51	-13.79, 8.77	0.65	4.38	0.11, 8.65	0.04
Secondary education	4.69	-2.17,11.57	0.17	-1.64	-15.22, 11.93	0.80	8.03	1.97, 14.08	0.01
University	3.88	-7.43,15.20	0.49	8.84	-10.40, 28.07	0.36	3.93	-8.37, 16.24	0.52
Diagnostic delay	0.09	0.05,0.15	<0.001	0.09	0.02, 0.17	0.01	-0.27	-0.56, 0.02	0.06
Decreased production									
Males vs females	3.12	-1.67,7.91	0.20	3.31	-4.73, 11.35	0.41	2.48	-4.39, 9.37	0.47
Age (in years)	0.11	-0.11,0.33	0.33	0.18	-0.25, 0.62	0.42	0.09	-0.19, 0.37	0.51
Unskilled labour	7.38	1.11,13.65	0.02	1.37	-10.19, 12.62	0.19	8.71	0.53, 16.89	0.03
Semi-skilled labour	6.40	0.89,11.92	0.02	5.16	-3.64, 13.97	0.24	7.25	-0.90, 15.40	0.08

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Poor vs non-poor	-0.07	-4.75-4.60	0.97	0.08	-7.90, 8.09	0.98	-0.79	-7.07, 5.48	0.80	
Primary education	2.25	-4.10,8.61	0.48	0.63	-11.36, 12.63	0.91	3.40	-4.49, 11.29	0.39	
Secondary education	6.53	-1.67-,4.73	0.11	5.94	-8.49, 20.38	0.41	5.76	-5.42, 16.95	0.39	
University	21.51	7.99,35.02	0.002	21.39	0.93,41.85	0.04	-4.33	-27.07, 18.42	18.41	
Diagnostic delay	0.04	-0.02,0.09	0.20	0.05	-0.02,0.13	0.21	-0.17	-0.71, 0.36	0.51	
Total indirect costs										
Males vs females	11.63	-11.37,34.63	0.32	6.60	-33.93,47.14	0.74	1.85	-34.74, 38.44	0.92	
Age (per year)	0.38	-0.69,1.45	0.48	0.07	-2.14, 2.29	0.94	0.75	-0.74, 2.24	0.32	
Unskilled labour	12.68	-17.41,42.78	0.40	14.47	-43.74,72.700	0.62	19.13	-24.32, 62.11	0.38	
Semi-skilled labour	20.90	-5.58,47.38	0.12	37.24	-7.11, 81.60	0.09	22.94	-20.38, 66.27	0.29	
Poor vs non-poor	6.29	-16.15,28.75	0.58	6.92	-33.36,47.20	0.73	5.82	-27.53, 39.18	0.72	
Primary education	21.24	-9.27,51.75	0.17	8.96	-51.46, 69.37	0.76	20.17	-21.76, 62.11	0.34	
Secondary education	61.52	22.14,100.92	0.002	54.24	-18.48,126.99	0.73	38.79	-20.65, 98.25	0.19	
University	108.74	43.89,173.60	0.001	85.66	-17-40,188.72	0.10	-7.79	-128.66, 113.09	0.89	
Diagnostic delay	0.46	0.12,0.74	0.001	0.56	0.16,0.98	0.007	-1.25	-4.09, 1.62	0.39	
Total costs										
Males vs females	9.87	-26.39,46.14	0.59	-4.98	-58.90,48.93	0.85	-0.62	-44.96, 43.71	0.97	
Age (per year)	0.34	-1.34,2.03	0.68	-0.56	-3.50,2.38	0.70	0.74	-1.06, 2.55	0.41	
Unskilled labour	11.95	-35.50,59.40	0.62	8.25	-69.18,85.69	0.83	16.02	36.64, 68.69	0.54	
Semi-skilled labour	30.47	-11.28,72.23	0.15	58.81	-0.18,117.81	0.05	26.64	-25.86-79.14	0.31	
Poor vs non-poor	0.89	-34.50,36.31	0.96	8.39	-45.18,61.98	0.75	2.39	-38.01, 42.81	0.90	
Primary education	24.87	-23.25,72.98	0.31	19.73	-60.62,100.09	0.62	18.06	-32.75, 68.88	0.48	
Secondary education	69.54	7.43,131.65	0.02	69.45	-27.29,166.19	0.15	46.10	-25.86, 79.14	0.20	
University	108.89	6.63,211.161	0.03	69.20	-67.87,206.28	0.31	-15.74	-162.23, 130.73	0.83	
Diagnostic delay	1.29	0.84,1.73	<0.001	1.44	-19.56,6.63	<0.001	-2.40	-5.86, 1.06	0.17	

*Estimated differences in median costs of are presented with the corresponding 95% confidence intervals (95% CI); Diagnostic delay was defined as delay in seeking care three weeks or more after the onset of symptoms. Multivariable quintile regression was performed for median costs to examine the association of patient factors with the different types of costs. Separate models were run for direct, indirect and total costs.

¹Reference: Unemployed
²Reference: no education

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
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
Methods			
Study design	4	Present key elements of study design early in the paper	Page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
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 7-8
Bias	9	Describe any efforts to address potential sources of bias	Page 9
Study size	10	Explain how the study size was arrived at	Page 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 9
		(b) Describe any methods used to examine subgroups and interactions	Page 9
		(c) Explain how missing data were addressed	-
		(d) If applicable, describe analytical methods taking account of sampling strategy	-
		(e) Describe any sensitivity analyses	-
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 12
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	Page 7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	Page 13
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	-
		(b) Report category boundaries when continuous variables were categorized	-
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 17
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 20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 17-20
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17-20
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 22

*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.