RESEARCH ARTICLE

Economic costs of accessing tuberculosis (TB) diagnostic services in Malawi: an analysis of patient costs from a randomised controlled trial of computer-aided chest x-ray interpretation [version 1; peer review: awaiting peer review]

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Abstract

Background: Patients with tuberculosis (TB) symptoms in low-resource settings face convoluted diagnostic and treatment linkage pathways, incurring substantial health-seeking costs. In the context of a randomised trial looking at the impact of novel diagnostics such as computer-aided chest x-ray diagnosis (CAD4TB), we aimed to investigate the costs incurred by patients seeking TB diagnosis and whether optimised diagnostic interventions could result in a reduction in the cost faced by households.

Methods: PROSPECT was a three-arm randomised trial conducted in a public primary health clinic in Blantyre, Malawi during 2018-2019 (trial arms: standard of care [SOC]; HIV testing [HIV]; HIV testing and CAD4TB [HIV/TB]). The direct and indirect costs incurred by 219 PROSPECT participants over the 56-day follow-up period were collected. Costs were deemed catastrophic if they exceeded 20% of annual household income. We compared mean costs and used generalised linear regression models to examine whether the interventions could result in a reduction in total costs.

Results: The mean total cost incurred by all 219 participants was US$12.11 (standard error (SE): 1.86). The indirect and direct cost was US$8.47 (SE: 1.66) and US$3.64 (SE: 0.38), respectively. The mean total cost composed of 5.6% of the average annual household income. In total, 5% (9/180) of the participants with complete income data

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incurred catastrophic costs. Compared to SOC, there was no statistically significant difference in the mean total cost faced by those in the HIV (ratio: 0.77, 95% CI: 0.51, 1.19) and HIV/TB arms (ratio: 0.85, 95% CI: 0.53, 1.37).
Conclusions: Despite the absence of user fees, patients seeking healthcare with TB symptoms incurred catastrophic costs. The optimised TB diagnostic interventions that were investigated in the PROSPECT study did not significantly reduce costs. TB diagnosis interventions should be implemented alongside social protection policies whilst ensuring healthcare facilities are accessible by the poor.

Keywords
Tuberculosis, diagnostics and tools, health economics, catastrophic costs

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Introduction

Despite the current achievements made in reducing the burden of tuberculosis (TB), it continues to be a major public health problem and one of the leading causes of death world-wide[1]. During 2019, approximately 10 million new cases of TB and 1.4 million TB-related deaths occurred globally[1]. Low- and middle-income countries (LMICs) carry a substantial proportion of this burden, with at least 25% of all new TB cases occurring in Africa alone[1].

Early diagnosis and treatment can substantially ease the current TB disease burden. Ensuring early diagnosis and prompt initiation of treatment can reduce TB transmission and improve individual health outcomes whilst reducing disability[2–5]. However, the effectiveness of TB diagnostic interventions in health systems are limited as poverty and high out of pocket expenditure are barriers to patients seeking TB diagnosis and treatment in LMICs[6–8].

Malawi is a low-income country and is among the 30 countries listed as having a high TB/HIV burden[9]. The public sector is the largest healthcare provider in Malawi, providing approximately 60% of healthcare services, the rest are provided by the private sector[10]. TB care is provided free of charge through national treatment programmes. However, due to resource constraints and a heavy disease burden, the TB diagnosis and treatment pathways are characterised by suboptimal diagnostic tests and convoluted treatment linkage[11,12]. Not only does this lengthen the time to diagnosis, it leads to substantial care-seeking costs as patients undergo multiple visits to health facilities and endure extensive waiting times[12–15].

Studies conducted in Malawi and other sub-Saharan African countries have shown that the costs incurred from seeking a diagnosis and the cost of treatment can become catastrophic for a substantial proportion of households[9,14,16–19]. Costs are considered catastrophic once they exceed 20% of the patient's annual household income[20]. The elimination of catastrophic costs associated with TB is among the targets set for the year 2020 in the End TB strategy[21]. This, however, is unlikely to have been achieved as by the end of 2019, the average proportion of TB-affected households facing catastrophic costs was 49%[1].

Research efforts towards the identification and development of interventions that can optimise the TB diagnostic and treatment pathways are urgently required[21]. Alongside this, there is a need to investigate whether such interventions can lead to reductions in the costs faced by patients seeking care. The PROSPECT trial (NCT03519425), was an open, three-arm pragmatic randomised trial, recently conducted in Malawi[22]. Its primary aim was to investigate the effectiveness of optimised HIV and TB diagnosis, and linkage to care interventions in reducing time to TB treatment initiation.

By surveying participants recruited to the PROSPECT trial, we aimed to investigate the costs faced by patients when seeking care with TB symptoms in Blantyre, Malawi. As the HIV and TB diagnostic interventions investigated in the PROSPECT trial aimed to reduce time to TB treatment initiation, we hypothesised that these interventions could result in a reduction in the total costs faced by households.

Methods

Study design

PROSPECT was an open, three-arm, pragmatic randomised trial investigating the impact of novel diagnostic and linkage to care interventions on improving the effectiveness of TB and HIV diagnosis and treatment[22]. We surveyed a consecutive sample of individuals participating in the PROSPECT trial to estimate the direct medical, direct non-medical and indirect costs incurred by those accessing healthcare services with TB symptoms.

Study site and participants

The study took place at the Bangwe Health Centre in Blantyre, Malawi. Bangwe Health Centre is a public primary health care clinic located in a densely populated peri-urban area of Blantyre. Adult TB prevalence in Blantyre is estimated to be 900 per 100,000 adults[23]. TB diagnostic services at the clinic follow standard Malawi Ministry of Health guidelines[24]. TB treatment is provided at the clinic using standard TB regimens. Under routine care conditions, patients with presumptive TB are investigated by sputum smear microscopy and/or GeneXpert MTB/Rif. There are no physicians at the study clinic; all care is provided by clinical officers and nurses. There are no user fees at the clinic.

Patients that were seeking care from Bangwe Health Centre and were at least 18 years old, with a cough of any duration, and not taking TB treatment or isoniazid preventative therapy were eligible for recruitment to the PROSPECT Study. These participants were randomly allocated in a 1:1:1 ratio into one of three trial groups: standard of care (SOC arm); optimised HIV screening and linkage to care (HIV arm); and optimised TB and HIV screening and linkage to care (HIV/TB arm).

Study procedures have been described previously[22]. In brief, participants in the SOC arm underwent clinician-directed TB and HIV screening and linkage to care, without input from the study team. In the HIV arm, participants were offered oral HIV testing, confirmatory study finger-prick HIV testing and linkage to antiretroviral therapy (ART) treatment services, with TB screening directed by the routine clinic system without further input from the study team. In addition to the HIV testing intervention, participants in the HIV/TB arm received TB screening using digital chest x-ray (DCXR), interpreted by computer-aided diagnosis software (CAD4TB v5). Participants with DCXRs showing a high probability of TB (CAD4TB score ≥45) had a sputum sample collected, which was tested at the study clinic using GeneXpert MTB/Rif; those with microbiologically confirmed TB were linked to clinic TB treatment services.

Between 12th February 2019 and 16th September 2019, cost data were collected from 219 consecutive PROSPECT trial participants during their outcome assessment visits at Bangwe

Health Centre, conducted approximately on the 56th day after recruitment. Due to time and resource constraints, this was a convenience sample.

Data collection

An interviewer-administered questionnaire[25], adapted from the STOP TB patients' cost tool[26], was used to estimate the direct medical, direct non-medical and indirect costs incurred by participants and their household members when accessing TB diagnostic and medical services during the 56 day PROSPECT follow-up period. Information was obtained on the direct and indirect costs incurred from accessing healthcare services delivered at the study clinic, any government hospital that they attended and were admitted to, and through any private healthcare provider. Private healthcare providers included private clinics, pharmacies, and traditional healers. For all healthcare provider visits, we recorded the number of visits made, time spent travelling to and waiting at the facility, and any out-of-pocket expenditures (transport costs, food etc). Information on the amount of time the patient and guardian stopped taking part in any income generating activities due to the patient's illness or care-seeking activities was also systematically recorded.

As self-reported expenditure was used, this study was subject to recall bias. However, the extent of this was minimised as the period under evaluation was restricted to the PROSPECT trial's study period, 56 days. Moreover, all questions were delivered in the local language, and care was taken to ensure participants fully understood the question. Additionally, each participant was questioned the same way, regardless of intervention group, to avoid responses being influenced.

Costs and data analysis

Data were analysed using Stata v14 (College Station, Texas, US). All monetary variables were converted from the Malawian Kwacha (MWK) to the United States Dollar (US$) using the market exchange rate as of the 12th of February 2019 as determined by the Reserve Bank of Malawi (MWK739.8089/US$1[27]).

We estimated direct medical, direct non-medical and indirect costs. Direct medical costs consisted of any charges incurred when seeking care from a private healthcare provider. Malawians do not pay to access government health services. Although, it is possible that patients accessing these services may incur informal or under-the-counter medical charges, these costs were not included[28]. Direct non-medical costs included out of pocket costs (e.g. transportation, food) incurred whilst seeking care[29,30]. To estimate the indirect cost, the human capital approach was used. This entailed valuing the patient's or guardian's time with their estimated productive output, based on their pre-illness reported income[29]. Income groups were created by categorising participants into income terciles based on their annual household income (low, middle, and high income).

Descriptive statistics were used to summarise the data and to determine the distribution of key participant characteristics within each trial arm. We used the arithmetic mean and standard error to summarise the direct and indirect costs incurred by participants[31,32]. The mean costs were stratified by patient characteristics and trial arms.

We calculated the mean difference in direct and indirect costs between the intervention arms and the standard of care. As the cost data was skewed, we used non-parametric bootstrap methods to derive 95% confidence intervals for the mean cost differences between categories[31,33]. Additionally, we calculated the percentage of participants whose households' experienced catastrophic care-seeking costs. Participants were considered to have catastrophic costs if their total costs exceeded 20% of their annual household income[20,30,34]. Catastrophic costs were calculated for those with complete household income data. Including those without complete household income data would lead to an overestimation of the proportion of participants facing catastrophic costs, as their household income may have been underestimated. We assumed that the missing data was missing completely at random.

Generalised linear regression models (GLM) with a gamma distribution and log link were used to investigate the association between trial interventions and the total cost incurred. Using GLMs we examined whether the costs varied by patient characteristics with the likelihood ratio test. The modified Park test was used to ensure the models were specified appropriately[35–37].

Ethical approval

Ethical approval was received from the University of Malawi- College of Medicine Research Ethics Committee and from the Ethics Review Board of the Liverpool School of Tropical Medicine. All participants provided written informed consent. If illiterate, participants were asked to provide a witnessed thumbprint.

Results

Of the 1320 participants that completed the PROSPECT trial's 56 day follow up period, 219 participants were recruited to this study[38]. The main reasons for non-participation included the study's time and resource constraints. Aside from age, individuals included in the study did not differ from the PROSPECT participants that did not take part in our study (Table 1).

Table 2 shows participant characteristics stratified by trial arm. Of the 219 participants, just over half were female (52.5%). Across the three arms, most of the participants were below the age of 35 years. A large proportion (71.7%) took part or had taken part in an income generating activity during the 12 months prior to this study. Additionally, 62.6% of the participants' households had more than one income earner. Median household income was US$51.36 (IQR: US$27.03, US$81.10) per month.

During the PROSPECT trial's 56 day follow up period, three (1.4%) out of the 219 participants were admitted into a health facility and five (2.3%) participants had initiated TB treatment.

Table 1. Characteristics of PROSPECT's participants that completed follow up by whether they participated in this study.

Characteristic		Total N=1320	Participated N=219 (16.6%)	Did not participate N=1,101 (83.4%)	P-value
Sex	Male	578 (43.8%)	104 (18.0%)	474 (82.0%)	0.23
	Female	742 (56.2%)	115 (15.5%)	627 (84.5%)	
Age in years	18–24	394 (29.9%)	58 (14.7%)	336 (85.3%)	0.02
	25–34	393 (29.8%)	76 (19.3%)	317 (80.7%)	
	35–44	291 (22.1%)	35 (12.0%)	256 (88.0%)	
	≥45	242 (18.3%)	50 (20.7%)	192 (79.3%)	
Marital status	Single (never married)	205 (15.7%)	32 (15.6%)	173 (84.4%)	0.44
	Married/cohabiting	893 (68.2%)	148 (16.6%)	745 (83.4%)	
	Separated/ divorced	137 (10.5%)	29 (21.2%)	108 (78.8%)	
	Widower/ widow	74 (5.7%)	10 (13.5%)	64 (86.5%)	
Education	Never been to school	157 (11.9%)	20 (12.7%)	137 (87.3%)	0.29
	Primary school	610 (46.2%)	113 (18.5%)	497 (81.5%)	
	Attended secondary school (no MSCE)	357 (27.1%)	56 (15.7%)	301 (84.3%)	
	Has at least an MSCE	196 (14.9%)	30 (15.3%)	166 (84.7%)	
HIV status at baseline	HIV positive	262 (19.9%)	38 (14.5%)	224 (85.5%)	0.34
	HIV negative	968 (73.3%)	162 (16.7%)	806 (83.3%)	
	Never tested	90 (6.8%)	19 (21.1%)	71 (78.9%)	
Trial arm	SOC	420 (31.8%)	73 (17.4%)	347 (82.6%)	0.87
	Optimised HIV screening	450 (34.1%)	73 (16.2%)	377 (83.8%)	
	Optimised HIV & TB screening	450 (34.1%)	73 (16.2%)	377 (83.8%)	

Refers to the participants that completed the PROSPECT trial's 56 day follow up period (N=1320).

SOC: Standard of care

HIV: Human Immunodeficiency Virus

TB: Tuberculosis

On average, participants made 1.63 (SD: 0.91) visits to a healthcare provider.

Patient costs across all trial arms

The mean total cost incurred by all participants seeking diagnostic care for TB symptoms during the PROSPECT study follow-up period was US$12.11 (SE:1.86) (Table 3). Overall, the mean total direct cost was US$3.64 (SE:0.38) and the mean indirect cost was US$8.47 (SE:1.66). On average, men incurred higher total costs (US$14.90, SE:3.34) compared to women (US$9.58, SE:1.83, p=0.001). Costs were also shown to vary with age (p<0.001). Participants aged between 25 and 44 years faced the highest indirect cost (US$14.07, SE:5.84) and total cost (US$16.61, SE:5.97) compared to other age groups. The total cost also varied by education (p<0.001) and income (p<0.001) levels. Participants that have never been to school had the lowest cost (US$8.00, SE:2.46) and costs increased with increasing income group.

Patient costs in the SOC arm

Shown in Table 4 are the mean total cost faced by participants under the SOC arm, which was US$13.18 (SE:2.79). These participants incurred direct costs amounting to US$4.29 (SE:0.74) and an indirect cost of US$8.90 (SE:2.54).

Table 2. Participant characteristics.

Characteristic		Total N=219	Standard of care N=73	Optimised HIV screening N= 73	Optimised HIV & TB screening N=73
Sex	Male	104 (47.5%)	34 (46.6%)	34 (46.6%)	36 (49.3%)
	Female	115 (52.5%)	39 (53.4%)	39 (53.4%)	37 (50.7%)
Age in years	18–24	58 (26.5%)	23 (31.5%)	20 (27.4%)	15 (20.6%)
	25–34	76 (34.7%)	21 (28.8%)	30 (41.1%)	25 (34.3%)
	35–44	35 (16.0%)	13 (17.8%)	9 (12.3%)	13 (17.8%)
	≥45	50 (22.8%)	16 (21.9%)	14 (19.2%)	20 (27.4%)
Marital status	Single (never married)	32 (14.6%)	11 (15.1%)	12 (16.4%)	9 (12.3%)
	Married/cohabiting	148 (67.6%)	51 (69.9%)	47 (64.4%)	50 (68.5%)
	Separated/ divorced	29 (13.2%)	7 (9.6%)	11 (15.1%)	11 (15.1%)
	Widower/ widow	10 (4.6%)	4 (5.5%)	3 (4.1%)	3 (4.1%)
Education	Never been to school	20 (9.1%)	4 (5.5%)	9 (12.3%)	7 (9.6%)
	Primary	113 (51.6%)	37 (50.7%)	33 (45.2%)	43 (58.9%)
	Attended secondary school (no MSCE)	56 (25.6%)	21 (28.8%)	20 (27.4%)	15 (20.6%)
	Has at least an MSCE	30 (13.70%)	11 (15.1%)	11 (15.1%)	8 (11.0%)
Takes part in an income generating activity		157 (71.7%)	50 (68.5%)	57 (78.1%)	50 (68.5%)
Mean household size (SD)		4.4 (2.1)	4.8 (2.2)	4.2 (1.9)	4.3 (2.0)
Households with >1 income earner		137 (62.6%)	48 (65.8%)	41 (56.2%)	48 (65.8%)
Median monthly household income - 2019 US Dollars (IQR)*		51.36 (27.03, 81.10)	51.91 (27.03, 81.10)	54.07 (33.79, 91.92)	40.55 (16.22, 81.10)
HIV status at baseline					
	HIV positive	38 (17.4%)	10 (13.7%)	14 (19.2%)	14 (19.2%)
	HIV negative	162 (74.0%)	57 (78.1%)	52 (71.2%)	53 (72.6%)
	Never tested	19 (8.7%)	6 (8.2%)	7 (9.6%)	6 (8.2%)
Admitted to a health facility during PROSPECT follow up		3 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
Initiated TB treatment during PROSPECT trial follow up		5 (2.3%)	2 (2.7%)	1 (1.4%)	2 (2.7%)

HIV: Human Immunodeficiency Virus

TB: Tuberculosis

SD: Standard deviation

US Dollars: United States Dollars

MSCE: Malawi School Certificate of Education (attained after completing secondary school)

IQR: Interquartile range

*US$1= Malawi Kwacha 739.8089 as of 12/02/19

39 participants had missing income data.

Table 3. Costs associated with seeking TB diagnostic care by participant characteristics (2019 US Dollars).

Characteristic		Mean direct medical cost (SE)	Mean direct non-medical cost (SE)	Mean total direct cost (SE)	Mean indirect cost (SE)	Mean total cost (SE)	P-value* (calculated for mean total cost)
All participants		1.00 (0.13)	2.64 (0.32)	3.64 (0.38)	8.47 (1.66)	12.11 (1.86)	
Sex	Male	0.80 (0.17)	2.44 (0.39)	3.24 (0.44)	11.67 (3.08)	14.90 (3.34)	
	Female	1.18 (0.19)	2.83 (0.50)	4.01 (0.60)	5.57 (1.44)	9.58 (1.83)	0.001
Age (years)	18–24	1.12 (0.25)	2.45 (0.40)	3.57 (0.53)	4.51 (1.13)	8.08 (1.42)	
	25–34	1.11 (0.23)	3.90 (0.81)	5.01 (0.91)	11.24 (3.68)	16.25 (4.30)	
	35–44	1.04 (0.41)	1.49 (0.29)	2.54 (0.53)	14.07 (5.84)	16.61 (5.97)	
	≥45	0.67 (0.21)	1.75 (0.37)	2.42 (0.49)	4.91 (1.50)	7.33 (1.62)	<0.001
Marital status	Single (never married)	0.96 (0.33)	3.55 (1.14)	4.51 (1.37)	8.09 (4.06)	12.59 (5.32)	
	Married/cohabiting	1.07 (0.17)	2.61 (0.39)	3.69 (0.46)	9.13 (2.21)	12.81 (2.43)	
	Separated/ divorced	0.82 (0.31)	2.02 (0.44)	2.84 (0.58)	5.08 (1.81)	7.92 (1.96)	
	Widower/ widow	0.57 (0.35)	1.96 (0.66)	2.53 (0.96)	9.71 (7.39)	12.24 (7.15)	0.16
Education	Never been to school	0.66 (0.35)	2.22 (0.56)	2.88 (0.81)	5.12 (2.31)	8.00 (2.46)	
	Primary school	0.93 (0.18)	1.96 (0.25)	2.90 (0.34)	5.67 (1.27)	8.56 (1.38)	
	Attended secondary school (no MSCE)	1.01 (0.24)	3.82 (0.94)	4.83 (1.01)	13.62 (5.34)	18.46 (5.86)	
	Has at least an MSCE	1.46 (0.44)	3.28 (1.15)	4.73 (1.40)	11.6 (4.52)	16.33 (5.75)	<0.001
Total annual household income	Lowest tertial	0.90 (0.19)	2.35 (0.57)	3.25 (0.64)	2.70 (1.07)	5.96 (1.34)	
	Middle tertial	0.93 (0.22)	2.50 (0.44)	3.43 (0.55)	7.00 (2.41)	10.43 (2.63)	
	Highest tertial	1.19 (0.28)	3.11 (0.65)	4.30 (0.76)	16.44 (4.29)	20.74 (4.84)	<0.001

Direct medical costs included any charges incurred when seeking care from a private healthcare provider.

Direct non-medical costs consisted of transport, food, and other costs non-related to medical care

US Dollars: United states dollars

US$1= MWK739.8089 as of 12/02/19

SE: Standard error

MSCE: The Malawi School Certificate of Education (attained after completing secondary school)

*likelihood ratio test

39 participants had missing income data.

Patient costs in the intervention arms

Participants in the HIV arm incurred a mean total cost of US$10.76 (SE:2.56). This was composed of a total direct cost amounting to US$3.55 (SE:0.68) and an indirect cost of US$7.21 (SE:2.01). With regards to the HIV/TB arm, the mean total cost was US$12.38 (SE: 4.13). The mean total direct and indirect cost amounted to US$3.09 (SE:0.52) and US$9.28 (SE:3.79) (Table 4).

Composition of costs

Across all intervention groups, a large proportion of the average total cost was composed of indirect costs (69%). The indirect cost composed 67.5%, 67.0%, and 75.0% of the total cost in the SOC, HIV and HIV/TB arms, respectively. Among the direct costs, transportation costs accounted for the greatest share of the total cost (SOC arm: 15.7%; HIV arm: 18.8%; and HIV/TB arm: 13.9%) (Figure 1 & Figure 2).

Table 4. Costs associated with seeking TB diagnostic care by intervention arm (2019 US Dollars).

	Mean (SE)						Mean difference (95% CI) *			
	SOC		HIV		HIV/TB		HIV vs SOC		HIV/TB vs SOC.	
Direct medical cost	$1.34	(0.27)	$0.80	(0.19)	$0.86	(0.21)	-0.54	(-1.17, 0.09)	-0.48	(-1.14, 0.18)
Direct non-medical cost	$2.95	(0.63)	$2.75	(0.55)	$2.23	(0.47)	-0.20	(-1.84, 1.44)	-0.72	(-2.27, 0.84)
Total direct cost	$4.29	(0.74)	$3.55	(0.68)	$3.09	(0.52)	-0.74	(-2.62, 1.14)	-1.20	(-2.87, 0.49)
Indirect cost	$8.90	(2.54)	$7.21	(2.01)	$9.28	(3.79)	-1.69	(-8.15, 4.78)	0.38	(-8.64, 9.41)
Total cost	$13.18	(2.79)	$10.76	(2.56)	$12.38	(4.13)	-2.42	(-9.75, 4.90)	-0.80	(-10.81, 9.20)

Direct medical costs included any charges incurred when seeking care from a private healthcare provider.

Direct non-medical costs consisted of transport, food, and other costs non-related to medical care.

US Dollars: United States DollarsUS$1= Malawi Kwacha 739.8089 as of 12/02/19

SOC: Standard of care arm

HIV: Optimised Human Immunodeficiency Virus (HIV) screening and linkage to care arm.

HIV/TB: Optimised tuberculosis (TB) and HIV screening and linkage to care arm.

SE: Standard error

CI: Confidence interval*Bootstrapped estimate

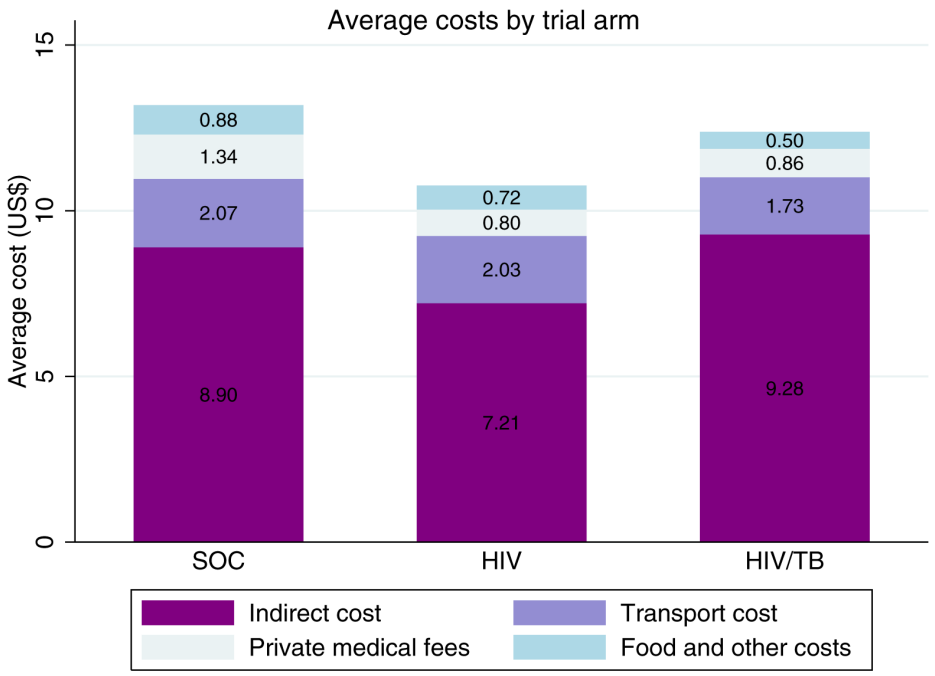

Figure 1. Average costs by trial arm. SOC: Standard of care arm HIV: Optimised Human Immunodeficiency Virus (HIV) screening and linkage to care arm. HIV/TB: Optimised tuberculosis (TB) and HIV screening and linkage to care arm. US$: United States Dollar US$1= Malawi Kwacha 739.8089 as of 12/02/19.

Comparison of costs

Compared to the SOC arm, the total cost faced by participants seeking healthcare for TB related symptoms was US$2.42 lower (95% CI: -US$9.75, US$4.90) in the HIV arm, and US$0.80 lower (95% CI: -US$10.81, US$9.20) in the HIV/TB arm. In comparison to the SOC arm, total direct costs were

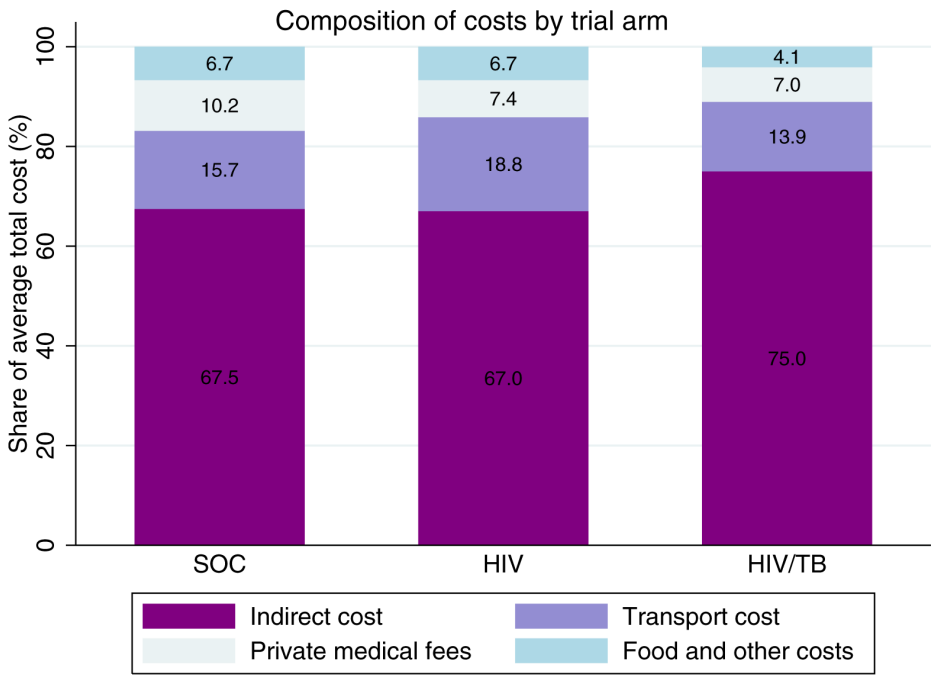

Figure 2. Composition of costs by trial arm. SOC: Standard of care arm HIV: Optimised Human Immunodeficiency Virus (HIV) screening and linkage to care arm. HIV/TB: Optimised tuberculosis (TB) and HIV screening and linkage to care arm. US$: United States Dollar US$1= Malawi Kwacha 739.8089 as of 12/02/19.

US$0.74 (95%CI: -US$2.62, US$1.14) lower in the HIV arm and US$1.20 (95% CI: -US$2.87, US$0.49) lower in the HIV/TB arm. Indirect costs were US$1.69 (95% CI: -US$8.15, US$4.78) lower for those in the HIV arm compared to the SOC arm. The indirect cost faced by participants in the HIV/TB arm was slightly higher (US$0.38, 95% CI: -US$8.64, US$9.41) than the SOC arm (Table 4).

Illustrated in Table 5, both models show that the participants who received optimised diagnostic interventions faced lower costs as compared to the current standard of care. In the fully adjusted model, adjusting for age, sex, marital status, education, income and HIV status, the mean total cost under the HIV arm was 23% (ratio: 0.77, 95% CI: 0.51, 1.19) lower than the SOC arm, although this difference was not statistically significant (p=0.24). The mean total cost incurred by those in the HIV/TB arm was 15% (ratio:0.85, 95%CI: 0.53, 1.37) lower than the SOC arm (p=0.51).

Economic burden and catastrophic costs

Of the 180 participants with complete household income data, the total cost comprised 5.6% of participants' average annual household income. In this study, nine (5.0%) participants incurred catastrophic costs (Table 6). Within each group, three (4.8%), three (5.1%), and three (5.1%) participants in the SOC arm, HIV arm and HIV/TB arm experienced catastrophic costs, respectively. Women carried a higher economic burden as 8.3% of their income was taken up by care-seeking costs, for men this was 3.0%. The economic burden was also higher among those aged 45 years and over (11.1%) as compared to other age groups. Those with a primary education faced a higher burden with costs being 7.7% of annual household income. The economic burden faced by patients decreased with increasing income, with the lowest income group facing the greatest burden (15.1%).

Discussion

Within the context of a three-arm randomised trial of novel TB diagnostics in Malawi, we set out to investigate the costs faced by patients when seeking care with TB symptoms and whether optimising the diagnostic pathway would reduce these costs. The main finding was that participants seeking diagnosis and care with TB symptoms incurred substantial costs, with 5.0% of participants incurring catastrophic costs. Within the SOC arm, 4.8% of participants had costs that were catastrophic. This is despite the absence of user fees and healthcare services being provided for free in primary healthcare facilities in Malawi. Although the costs incurred under the optimised diagnostic interventions were slightly lower than the current standard of care, the differences were not statistically significant.

According to existing literature, optimising the diagnostic pathway to reduce the time to diagnosis and treatment

Table 5. Multivariable analysis exploring the relationship between trial arm and mean total cost.

	Model 1			Model 2		
Trial arm	**Ratio of mean total cost (95% CI)**		**P-value**	**Ratio of mean total cost (95% CI)**		**P-value**
SOC	Ref	-	-	Ref	-	-
HIV	0.82	(0.50, 1.35)	0.44	0.77	(0.51, 1.19)	0.24
HIV/TB	0.82	(0.47, 1.45)	0.50	0.85	(0.53, 1.37)	0.51

Model 1: adjusted for age and sex.

Model 2: additionally, adjusted for marital status, educational attainment, total household income tertial and HIV status at baseline.

SOC: Standard of care arm

HIV: Optimised Human Immunodeficiency Virus (HIV) screening and linkage to care arm.

HIV/TB: Optimised tuberculosis (TB) and HIV screening and linkage to care arm.

CI: Confidence interval; Ref: reference category

Findings from generalized linear models with gamma distribution and log link.

initiation should lead to a reduction in the costs faced by patients as the number of visits required to obtain a diagnosis reduces[13–15,39]. The lack of evidence for this association in this study may be due to the participants making approximately two visits to a healthcare provider, on average. This is further compounded by most of the participants not being diagnosed with TB (97.7%), as these patients do not require multiple visits to healthcare providers as compared to those diagnosed with TB disease. Altogether, this meant that the interventions examined in this study had a limited impact on the income loss from spending time seeking healthcare, and the cost of transport of which were the main cost drivers found in this study.

However, given that most patients did not have TB disease, the substantial care-seeking costs further substantiates the need for optimised diagnostic interventions to reduce the time and healthcare visits taken to obtain a diagnosis and initiate treatment In line with previous studies conducted in sub-Saharan Africa[14–16,40–42], this study found that a large proportion (69.9%) of the total cost was due to income loss. For patients with TB disease, these costs can be detrimental as they often undergo extensive waiting times and multiple visits to healthcare providers when seeking diagnosis and treatment. The direct medical expenses that can be incurred have been minimised by the public health services in Malawi being provided free of charge; and most patients not seeking additional healthcare from private health facilities. Therefore, efforts should be made towards minimising the income losses by patients with TB disease through reducing the time and number of visits needed to obtain a diagnosis.

A large share of the direct cost was the cost of transport. This has also been shown in previous studies and is seen as an indication of TB diagnostic services not being easily accesible[13,14,39]. Although optimising the TB diagnostic and treatment pathways may reduce the costs incurred from transportation as fewer visits are made before receiving a diagnosis, the effectiveness of these interventions may be limited if healthcare services are inaccessible to most Malawians. This implies that alongside optimising the TB diagnostic pathway, efforts towards ensuring universal access to healthcare should be put in place. Such solutions can include community-based interventions. Aside from increasing coverage of TB health services, previous studies have shown that such interventions can reduce the costs faced by patients[43,44]. This is primarily due to these interventions bringing services closer to the community therefore inducing savings on transportation costs and possible user from private health facilities[44].

Alongside optimised diagnosis pathways, social protection interventions should be put in place. The findings of this study show that similar proportions (4.8% to 6.8%) of patients incurred catastrophic costs regardless of intervention group. Additionally, the economic burden faced by patients varied by socio-demographic characteristics revealing that certain groups are more vulnerable to impoverishment. Of importance, it was demonstrated that despite having lower costs, those in the lowest income group faced the highest economic burden. Moreover, this group had the highest proportion of individuals facing catastrophic costs. This has also been demonstrated in previous studies conducted in Malawi's rural areas as the proportion of income consumed by care-seeking costs rose with decreasing wealth[16]. This is similarly shown among women, as although having lower costs as compared to men, their economic burden was much higher. The high economic burden experienced by these groups is regardless of healthcare being provided free of charge and costs being comparably lower. This signifies the need for social protection policies that can ease

Table 6. Average economic burden and catastrophic costs by trial arm and patient characteristics.

		Number of participants	*Annual household income (SE)	Average Economic burden	Catastrophic costs
All participants		180 (100%)	801.52 (53.92)	5.6%	9 (5.0%)
Trial arm	SOC	62 (34.4%)	833.69 (82.87)	4.0%	3 (4.8%)
	HIV	59 (32.8%)	781.28 (93.14)	6.3%	3 (5.1%)
	HIV/TB	59 (32.8%)	787.98 (105.25)	6.7%	3 (5.1%)
Sex	Male	90 (50%)	921.11 (70.18)	3.0%	2 (2.2%)
	Female	90 (50%)	681.94 (80.30)	8.3%	7 (7.8.%)
Age (years)	18–24	41 (22.8%)	927.19 (131.64)	1.0%	0
	25–34	69 (38.3%)	892.83 (95.97)	3.3%	1 (1.5%)
	35–44	29 (16.1%)	724.87 (107.86)	10.0%	4 (13.8%)
	≥45	41 (22.8%)	576.42 (74.57)	11.1%	4 (9.8%)
Marital status	Single (never married)	19 (10.6%)	1266.25 (267.36)	0.8%	0
	Married/cohabiting	129 (71.7%)	830.52 (57.31)	2.6%	2 (1.6%)
	Separated/ divorced	23 (12.8%)	382.45 (84.98)	19.0%	4 (17.4%)
	Widower/ widow	9 (5.0%)	475.80 (172.0)	26.1%	3 (33.3%)
Education	Never been to school	16 (8.9%)	560.11 (111.78)	7.6%	1 (6.3%)
	Primary	97 (53.9%)	686.34 (56.47)	7.7%	6 (6.2%)
	Attended secondary school (no MSCE)	43 (23.9%)	932.79 (146.62)	2.7%	2 (4.7%)
	Has at least an MSCE	24 (13.3%)	1192.81 (167.68)	1.2%	0
Total annual household income	Lowest tertial	55 (30.6%)	226.97 (19.24)	15.1%	8 (14.5%)
	Middle tertial	69 (38.3%)	620.63 (14.14)	1.6%	1 (1.5%)
	Highest tertial	56 (31.1%)	1588.70 (108.89)	1.3%	0

* US$1= MWK739.8089 as of 12/02/19

SOC: Standard of care arm

HIV: Optimised Human Immunodeficiency Virus (HIV) screening and linkage to care arm.

HIV/TB: Optimised tuberculosis (TB) and HIV screening and linkage to care arm.

SE: Standard Error

MSCE: Malawi Secondary Certificate of Education

the financial burden faced by vulnerable households in Malawi when seeking healthcare.

We also found that the most economically active groups incurred the highest care-seeking costs. Firstly, men are shown to have higher costs. This is also true in studies conducted in other urban and rural areas of Malawi[14,45]. Individuals aged between 25 and 44 years experienced higher costs compared to other age groups. In rural Malawi however, people aged 65 years and over incurred the highest direct cost when seeking care for a chronic cough[45]. It is possible that the individuals from that study may have had a relatively lower cost as compared to other groups if income loss were considered. In settings such as Malawi, males and those aged between 25 and 44 years are relatively more economically active. As a result, these groups will often have a greater loss of income when seeking healthcare[14,46]. This can deter such individuals from seeking healthcare. This can lead to adverse

health outcomes and have a negative impact on the strides made towards reducing the incidence of TB in Malawi. This further suggests that optimised TB diagnosis interventions are likely to be more effective alongside social protection policies that ensure such groups are compensated for the time lost when seeking healthcare.

A limitation of this study was the use of self-reported income for the estimation of total indirect cost. The use of self-reported income in settings where the informal employment sector dominates is often unreliable and subject to non-response[29,47]. However, this approach was used because recent national income data was unavailable, and the calculation of consumption expenditure was beyond the scope of this study. Moreover, there is uncertainty around which method provides the most accurate estimates in such settings[47]. This indicates the necessity for further research on comparing and determining appropriate methods for measuring household income in facility-based surveys taking place in such settings. Additionally, findings of this study may have been subjected to recall bias. This can lead to inaccurate estimates of the costs faced by the patients. However, this method was the only feasible way of obtaining information that would lead to the estimation of the total cost faced by patients seeking diagnosis for acute symptoms of TB.

Although it can be assumed that the findings of this study can be generalised across Malawi, caution must be taken as the participants in this study may not fully be representative of Malawi. This is particularly true with regards to the costs faced by patients seeking care as the extent of these costs can vary geographically. Nonetheless, the study highlights that patients face costs that can be catastrophic when seeking care.

In conclusion, individuals seeking diagnostic care for TB symptoms in Blantyre, Malawi incurred high costs with patients experiencing catastrophic costs. The optimised TB diagnostic interventions being investigated in the PROSPECT study, did not lead to a reduction in the costs faced by patients. For these interventions to make an impact, further efforts should be made towards ensuring that these interventions significantly reduce the indirect costs faced by patients. However, optimised diagnostic strategies alone are not enough to ensure a significant reduction in the financial burden placed on households. Therefore, community-based interventions and social protection policies should be put in place to ensure the financial protection of individuals that are vulnerable to catastrophic costs.

Data availability

Underlying data

Figshare: Economic costs of accessing TB diagnostic services in Malawi: an analysis of patient costs from a randomised controlled trial of computer-aided chest x-ray interpretation.

https://doi.org/10.6084/m9.figshare.14095569.v2[38].

This project contains the following underlying data and code:

- 01-Economic costs - generating variables: A STATA dofile containing the code needed to generate key variables for analysis.
- 02-Economic costs - stat and cost analysis: A STATA dofile containing the code needed to conduct the analysis and produce the tables and figures presented in this manuscript.
- 03: Economic costs_dataset: A de-identified dataset in CSV format, containing the data needed to conduct the analysis.

Extended data

Figshare: Economic costs of accessing TB diagnostic services in Malawi: questionnaires.

https://doi.org/10.6084/m9.figshare.14207327.v2[25].

This project contains the following extended data:

- Questionnaire

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Contributors

WK conceived and designed the study, conducted cost and statistical analysis, and drafted the manuscript. WK, PM and HM supported the design of the study and data collection tools. All authors interpreted the data, prepared report, and approved final version.

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