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Barriers and facilitators to accessing tuberculosis care in Nepal: a qualitative study to inform the design of a socioeconomic support intervention

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ABSTRACT

Objective Psychosocial and economic (socioeconomic) barriers, including poverty, stigma and catastrophic costs, impede access to tuberculosis (TB) services in low-income countries. We aimed to characterise the socioeconomic barriers and facilitators of accessing TB services in Nepal to inform the design of a locally appropriate socioeconomic support intervention for TB-affected households.

Design From August 2018 to July 2019, we conducted an exploratory qualitative study consisting of semistructured focus group discussions (FGDs) with purposively selected multisectoral stakeholders. The data were managed in NVivo V.12, coded by consensus and analysed thematically.

Setting The study was conducted in four districts, Makwanpur, Chitwan, Dhanusha and Mahottari, which have a high prevalence of poverty and TB.

Participants Seven FGDs were conducted with 54 in-country stakeholders, grouped by stakeholders, including people with TB (n=21), community stakeholders (n=13) and multidisciplinary TB healthcare professionals (n=20) from the National TB Programme.

Results The perceived socioeconomic barriers to accessing TB services were: inadequate TB knowledge and advocacy; high food and transportation costs; income loss and stigma. The perceived facilitators to accessing TB care and services were: enhanced championing and awareness-raising about TB and TB services; social protection including health insurance; cash, vouchers and/ or nutritional allowance to cover food and travel costs; and psychosocial support and counselling integrated with existing adherence counselling from the National TB Programme.

Conclusion These results suggest that support interventions that integrate TB education, psychosocial counselling and expand on existing cash transfer schemes would be locally appropriate and could address the socioeconomic barriers to accessing and engaging with TB services faced by TB-affected households in Nepal. The findings have been used to inform the design of a socioeconomic support intervention for TB-affected households. The acceptability, feasibility and impact of this intervention on TB-related costs, stigma and TB

Strengths and limitations of this study

► The focus group discussions contributed to new knowledge on optimal local strategies to mitigate the socioeconomic impact of tuberculosis (TB).

► The evidence has directly informed the design of a novel socioeconomic support intervention for TB-affected households, which is undergoing pilot evaluation in Nepal.

► The credibility and trustworthiness of the study was maintained through member checking, using multiple coders, conducting a consensus-based coding, recruiting local interviewers for data collection, performing triangulation and including a broad selection of multidisciplinary stakeholders to inform the study conclusion.

► The study was conducted in four districts of Nepal, mostly lowland 'plains' districts, which could affect the transferability of the findings.

► People who were diagnosed with TB in private sectors or those lost to follow-up did not participate in the study despite, in other settings, having been shown to be groups at high risk of severe socioeconomic impact of TB.

treatment outcomes, is now being evaluated in a pilot implementation study in Nepal.

BACKGROUND

Tuberculosis (TB) kills 1.3 million people each year worldwide, more than any other single infectious disease including, up to the time of writing, COVID-19.[1] In 2019, an estimated 10 million became ill with TB, of whom 2.9 million were not notified or remained undiagnosed and untreated.[1] In low-income and middle-income countries (LMICs), stigma, marginalisation and catastrophic costs of accessing TB diagnosis and

care, coupled with limited social protection coverage, can delay diagnosis, decrease TB treatment success rates and push TB-affected households into further impoverishment.[2 3] To address this and move towards TB elimination, the WHO's (WHO) 2015 End TB Strategy set the bold target that 'Zero TB-affected families should face catastrophic costs' and that psychosocial and economic (socioeconomic) support should be provided to TB-affected people.[4]

Nepal is an LMIC in South Asia with significant TB incidence (annual incidence 245/100 000) and mortality.[5] Despite free basic TB diagnostic tests, medicines and financial support for people with drug-resistant (DR-TB), approximately one in two people with TB face catastrophic costs (defined as the total TB-related costs equivalent to greater than 20% of a household's annual income) while accessing TB care in Nepal.[6 7] Such costs include travel for directly observed treatment short-course (DOTS), additional food expenditure and lost income, which can contribute to adverse TB treatment outcomes, especially for the poorest, most vulnerable households.[6 8–10]

The Nepal National TB Programme (NTP) provides NPR3000 (~US$27) in cash incentives monthly for transportation and nutritional support to people with multidrug-resistant TB (MDR-TB)[11] who are enrolled in government treatment centres and receiving ambulatory care. There is currently no cash incentive scheme for people with drug-sensitive TB (DS-TB) in Nepal.[12] In other settings, socioeconomic support for TB-affected households, including mutual support groups and cash transfers, has been shown to help overcome barriers to accessing TB services, defraying catastrophic costs and improving treatment success rates.[3 13–16] However, there is limited context-specific understanding of the barriers and facilitators to TB diagnosis and care in LMICs with which to inform the development of tailored socioeconomic support interventions for people with TB and their households.[1] This study aimed to address this knowledge gap in Nepal.

MATERIALS AND METHODS
Study design
We conducted an exploratory qualitative study, which used semistructured focus group discussions (FGDs) to collate the perceptions of key stakeholders in Nepal regarding socioeconomic barriers and facilitators of accessing and engaging with TB diagnosis and care. The study formed part of a larger programme of mixed-methods research[17] to design a locally appropriate socioeconomic support intervention for TB-affected households. The study adhered to the COnsolidated criteria for REporting Qualitative research (COREQ) Checklist.[18]

Study setting
The study was conducted in four districts of Nepal where Birat Nepal Medical Trust (BNMT), a Nepalese organisation with a focus on TB-related implementation
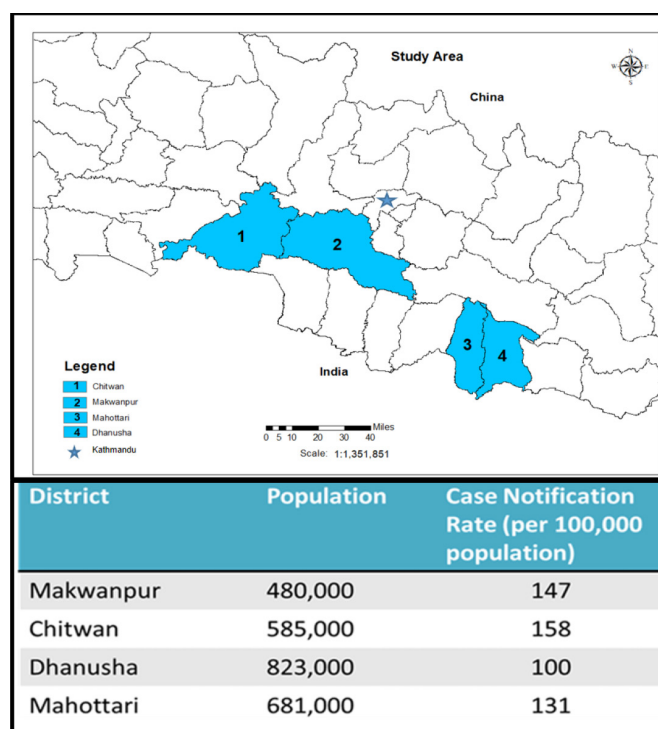

District	Population	Case Notification Rate (per 100,000 population)
Makwanpur	480,000	147
Chitwan	585,000	158
Dhanusha	823,000	100
Mahottari	681,000	131

Figure 1 The highlighted colour represents the study districts in Nepal. Dhanusha, Mahottari and Chitwan are 'plains' or 'Terai' districts. Makwanpur is a hilly district. The district's data for population numbers and TB case notification rate highlight the burden of tuberculosis in each district (National TB Control Center Annual Report, 2018). TB, tuberculosis.

research, implemented IMPACT-TB project. The districts: Makwanpur, Chitwan, Dhanusha and Mahottari have a high prevalence of poverty and TB (figure 1).[11] Makwanpur is a hilly district with limited road networks. Other three districts are lowland plains and challenged by high population density, poor health indicators and high rates of illiteracy.

Sampling
A desk-based scoping exercise was initially performed by team members (KD, RD and TW) to identify participants from relevant stakeholder groups in Nepal. To collate diverse perspectives on barriers and facilitators of TB diagnosis and treatment, the team purposively selected participants who had direct or indirect experiences with TB services. The participants included: people affected by TB who were currently receiving or had recently completed DS-TB or MDR-TB treatment with the NTP (referred to as 'people with TB' in the study); community leaders such as female community health volunteers, teachers and social leaders from civil society organisations (CSOs, referred to as 'community stakeholders'); and TB healthcare professionals, including those working with the NTP, community volunteers and TB-focused non-governmental organizations (NGOs) (referred to as 'NTP stakeholders') (table 1). The list of people with TB, including their demographics, were gathered from the

Table 1 List of FGD stakeholder groups and participants

Stakeholder group	Sex	Age group (years)	District	Total no of participants
People diagnosed with TB, mixed sex group	Female	Under 20	Makwanpur	7
	Male	25–30	Mahottari	
	Male	45–50	Makwanpur	
	Male	20–25	Dhanusha	
	Female	Under 20	Makwanpur	
	Male	30–35	Chitwan	
	Male	55–60	Chitwan	
People diagnosed with MDR-TB	Male	40–45	Chitwan	7
	Male	70–75	Chitwan	
	Male	20–25	Chitwan	
	Male	20–25	Chitwan	
	Male	45–50	Chitwan	
	Male	45–50	Chitwan	
	Female	20–25	Chitwan	
Females diagnosed with TB	Female	60–65	Mahottari	7
	Female	25–30	Makwanpur	
	Female	40–45	Mahottari	
	Female	45–50	Chitwan	
	Female	45–50	Dhanusha	
	Female	25–30	Dhanusha	
	Female	25–30	Makwanpur	
Community leaders	Female	50–55	Chitwan	6
	Male	45–50	Mahottari	
	Male	35–40	Makwanpur	
	Male	45–50	Chitwan	
	Female	50–55	Chitwan	
	Male	40–45	Dhanusha	
Civil society organisation	Male	35–40	Chitwan	7
	Male	40–45	Chitwan	
	Male	65–70	Chitwan	
	Male	25–30	Mahottari	
	Male	45–50	Chitwan	
	Male	45–50	Makwanpur	
	Male	25–30	Dhanusha	
TB healthcare professionals	Male	55–60	Kathmandu	12
	Male	30–35	Kathmandu	
	Male	30–35	Kathmandu	
	Male	30–35	Kathmandu	
	Female	25–30	Kathmandu	
	Male	55–60	Kathmandu	
	Male	45–50	Kathmandu	
	Male	45–50	Kathmandu	
	Male	55–60	Kathmandu	
	Male	55–60	Kathmandu	

Continued

Table 1 Continued

Stakeholder group	Sex	Age group (years)	District	Total no of participants
	Male	55–60	Kathmandu	
	Male	45–50	Kathmandu	
Community mobilisers	Male	45–50	Dhanusha	8
	Female	30–35	Chitwan	
	Female	30–35	Makwanpur	
	Male	25–30	Dhanusha	
	Male	30–35	Chitwan	
	Male	40–45	Mahottari	
	Male	25–30	Mahottari	
	Female	20–25	Makwanpur	
Total	Male: 38 Female: 16			54

Weaver et al[22].
FGD, focus group discussion; TB, tuberculosis.

IMPACT TB database or registers of the health clinics in each district. Community stakeholders were community leaders or those working in civil society and were selected based on their in-depth knowledge on the local context and experiences of working with the communities, preferable in health progammes. TB healthcare professionals, such as those working with the NTP or TB-focused NGOs, have several years' experience in planning, designing and implementing NTP activities. Community volunteers or mobilisers were people working with the IMPACT-TB project, who have first-hand experiences in screening symptoms of TB and supporting people with TB to adhere to and complete their treatment. These participants were selected based on the expertise in delivering community programmes and to bring diverse perception of the stakeholders into the study. Using telephone, email or in-person meetings, we invited 55 individuals to participate in the study. Inclusion criteria were being 18 years of age or older and being able to give informed consent. Seven participants were invited to each of the seven FGDs with the exception of the TB healthcare professional FGD, which consisted of 12 participants. This related to the logistical challenges of organising more than one FGD with this group due to their working hours and time constraints coupled with the aim of representation from the public, private and NGO sectors of TB healthcare.

Data collection
The study team consisted of diverse members from multiple sectors including a physician, senior TB researchers, social scientists, public health professionals and project managers. An interview guide was developed by the coauthors with previous qualitative methods experience: TW (male, principal investigator, TB researcher), KD (female, doctoral student, project manager) and BR (male, public health specialist, research associate); BR and KD are employed by BNMT. The interview guide

consisted of open-ended questions to explore the perceptions of participants concerning protective factors and risk factors for exposure to TB and development of TB disease; barriers and facilitators to accessing and engaging with TB diagnosis and care, including the recommendations for better access and engagement with TB diagnosis and care; and the socioeconomic impact on people with TB of being ill with the disease.

Prior to conducting FGDs, participants were provided with a 'Participant Information Sheet' that explained the purpose of the study, benefit and harm, and confidentiality.[17] Participants were provided time as they would require to read and understand the information in the paper and then decide if they are willing to participate in the study. The FGDs were conducted in a local hotel accessible to participants in the study districts. The topic guide was piloted with a group of seven female and male participants with TB resulting in minor refinements to the FGD structure and delivery techniques. TW moderated the FGD with TB healthcare professional and KD and BR moderated the other six FGDs. Apart from these researchers, district field staff who supported patients attended the discussions and facilitated any dialectic interpretation or contextual explanations related to access to and engagement with TB services.

We conducted seven FGDs with 54 participants, which the project team perceived as giving sufficient information power for the study.[19] Of the participants, three-quarters were male and the average age was 42 years (table 1). To encourage an environment in which participants felt comfortable and able to share their opinions and to balance gender representation, two of these FGDs were specifically for females with DS-TB and female TB community mobilisers. In all the FGDs, there were seven participants, except for the FGD with community leaders (n=6), FGD with TB healthcare professionals (n=12) and

FGD with community mobilisers (n=8). One invitee from the community leader's FGD declined to participate due to lack of time. One additional community mobiliser showed interest to participate in the FGD with community mobilisers' and was also included. We did not conduct any follow-up discussions with participants but some of the participants attended a workshop to discuss the FGD findings, the outputs of which are published elsewhere.[12] We performed real-time member checking in each FGD by noting key points of the discussion, summarising them on a wall chart and clarifying their accuracy with the group. No formal field notes were taken. The FGDs, which lasted 90–120 min, were all conducted in Nepali language apart from the FGD with TB healthcare professionals, which was conducted in English. FGDs were audiorecorded, translated into English from Nepali language and back-translated by an independent translator who was not part of the project team. Each FGD was concluded when the facilitators collectively felt the topics in the FGD interview guide were sufficiently explored.

Analysis

We applied thematic analysis using NVivo V.12 to manage the data.[20] The study used multiple coders, KD and TW, who familiarised themselves with the data through successive reading of transcripts. KD and TW separately generated the initial codes for each transcript before discussing and comparing the perception of understanding of the codes. The codes were updated through regular discussion as further data became available and collated following each successive FGD. To increase trustworthiness of the study, after all the transcripts were coded and analysed, KD and TW independently reviewed coding and themes and refined them through further discussion, triangulation and consensus where necessary.[21] Both open and closed first-order categories were used to label data. Categories were then grouped into second-order and third-order themes (online supplemental file 1). Table 2 shows an example of the analysis process of codes and themes. To better inform the design and delivery of the socioeconomic intervention for TB-affected households within the wider context of health services delivery, the first-order themes were then mapped to four levels of an adapted WHO Treatment Adherence Framework: (1)

TB, health and basic education; (2) social protection and nutrition; (3) psychosocial and (4) healthcare system, TB diagnosis and care delivery.[22] We chose to structure our analysis on the themes mapped to levels 1–4 of the WHO Framework because these levels were the most relevant to the study's aim of informing design and development of a socioeconomic support intervention for TB-affected households. While important, themes identified that mapped to category IV of the Framework, such as governmental policy, political commitment, public–private mix and healthcare infrastructure were perceived by the study team to be largely unmodifiable by a household-level socioeconomic support intervention. These themes are reported under health system categories and are shown in online supplemental file 2.

The study protocol is provided in online supplemental file 3. Written consent was obtained from all participants. Confidentiality of the participants was maintained by anonymising FGD responses, keeping any paper data in a locked cabinet at BNMT's office and securing the data in a password-protected database.

Patient and public involvement

Patient and/or the public were not involved in the design or conduct of this research.

RESULTS

Overall, 36 codes related to eight themes were identified (online supplemental file 1). Below, we focus only on the perceived barriers and facilitators that mapped to categories: (1) TB, health and basic education, (2) social protection and nutrition and (3) psychosocial, of the adapted WHO Framework. These barriers and facilitators are shown in figure 2.

TB, health and basic education
Theme: information barrier to access and adhere to TB diagnosis and treatment

Across FGDs, we identified low literacy and education about TB as a barrier to accessing TB diagnosis and engaging with TB treatment (figure 2). Knowledge about TB including transmission, prevention, symptoms how and where to get diagnosed, treatment regimens and

Table 2	An example of coding from the FGDs				
FGD	**Quote**	**First-order category***	**Second-order themes**	**Third-order themes**
People diagnosed with TB	FGD with people diagnosed with TB, 30–35 years age group, male: 'People get criticized for having TB. The community perceives a TB patient isn't the same as a normal person…. due to lack of awareness.'	Psychosocial	► Enacted stigma ► Perceived stigma ► Lack of knowledge	Stigma as social barrier to access

*Adapted from a WHO Medication Adherence Framework.[22]
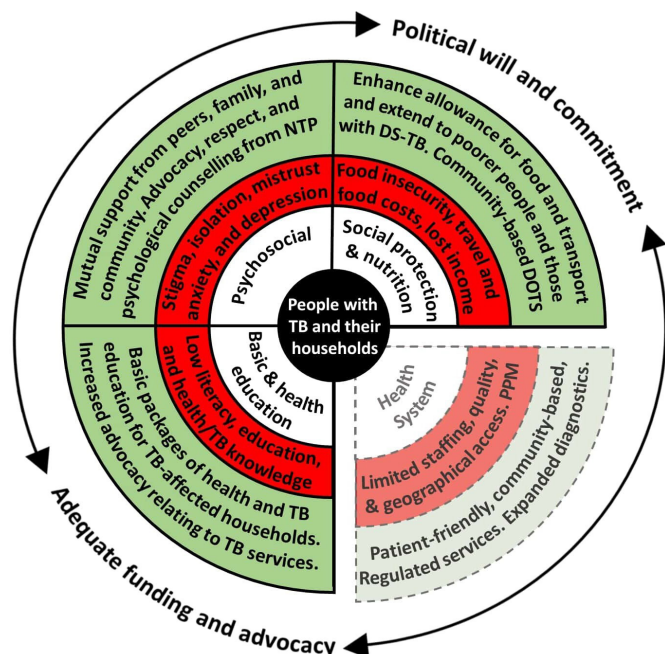FGD, focus group discussion; TB, tuberculosis.

Figure 2 The inner white circle contains the key categories that influence tuberculosis (TB) service access and engagement, which are adapted from a WHO medication adherence framework (see the Methods section).[22] The middle red circle indicates the main barriers identified for each category, which may threaten access to TB services. The outer green circle indicates the main facilitators (current or potential) for each category, which may enhance access to TB services. Barriers relating to 'TB, health and basic education', 'social protection and nutrition', and 'psychosocial' were perceived by the project team to be modifiable by a household level socioeconomic intervention. Barriers relating to the 'health system' were perceived by the project team to be non-modifiable by a household-level socioeconomic intervention and are, therefore, separated from the other categories and represented by dotted lines. 'PPM' as a health system barrier refers to the protracted and convoluted patient journey through public and private healthcare providers, which was reported as being associated with increased economic impact, especially related to out-of-pocket costs. The surrounding bidirectional arrows indicate the cross-FGD finding that adequate funding and advocacy, and political will and commitment were perceived as vital structural factors to enable the facilitators identified to overcome the barriers identified. DOTS, directly observed treatment short-course; DS-TB, drug-sensitive tuberculosis; FGD, focus group discussion; NTP, National Tuberculosis Programme; PPM, public–private mix. Reference: Weaver et al[22].

duration, and the TB services available at health facilities were perceived to be limited, especially among illiterate and underserved groups or rural populations. A female participant with TB said: *'I didn't know that TB medicines were free in hospitals. I knew it only when I visited the health post.'*

The FGD with community stakeholders suggested that this limited knowledge about TB negatively impacted engagement with TB services and treatment adherence. This was noted to potentially increase the likelihood of

a delayed diagnosis, more advanced disease at presentation and acquisition of DR-TB during treatment. The perceived lack of knowledge was predominantly felt to relate to suboptimal TB education, advocacy and political commitment from health system and governmental leaders. Participants also reported that the current health education programmes are scarce and unable to reach poorer, educationally and socially marginalised communities with high TB risk.

Theme: facilitating treatment access through education about TB disease and advocacy about TB services, especially in remote communities

Across all the FGDs, participants described the need to raise community awareness on risk factors for TB, mode of TB transmission, and TB signs and symptoms. Community stakeholders particularly felt that future awareness-raising programmes would benefit by informing communities about available free TB diagnostic and treatment services in their local area and adding a component to reduce TB-related stigma. Further, NTP stakeholders stressed the importance of not only providing education but also, in the face of competing health beliefs, influencing attitudes and promoting behavioural change.

Community stakeholders suggested that the government should take responsibility for the development and implementation of intensive household-level and village-level awareness programmes using technology such as smartphone applications and social media. They also recommended broadcasting educational campaigns on television adapted from similar campaigns in the field of HIV (HIV ka sawal) and maternal care (Aama ko Maya) in Nepal. However, there was concern that information transmitted through media could bypass vulnerable, poor and marginalised populations. To overcome this, the group suggested innovative and interactive community-based approaches such as coordination with local women's group-initiated self-help enterprises, street plays and engaging TB survivors as peer champions and educators to improve TB education. The involvement and ownership of TB education programmes by community leaders, including volunteers, teachers and community mobilisers, was also deemed important to achieve effective, decentralised delivery. Furthermore, the stakeholders acknowledged the essential role of healthcare provider-led education as part of a client–provider contract because people with TB need—and will follow—advice from healthcare providers only when that advice is relayed sensitively and understood thoroughly. Nevertheless, people with TB indicated that both sensitisation and education from a trusted source were key to deliver education successfully and to enable and empower communities.

FGD with community leaders, 50–55 years age group, female: *'We need to create [educational] groups attached to health centres and schools. Community and locally-elected leaders and teachers could give education to their communities and conduct TB awareness training and workshops.'*

Social protection and nutrition

Theme: social and economic barriers to accessing and engaging with TB diagnosis and treatment

Across FGDs, the participants reported food insecurity, high travel and food costs, and lost income as key barriers to accessing and engaging with TB diagnosis and treatment (figure 2). The direct out-of-pocket costs of seeking TB diagnosis and engaging with DOTS at both public and private clinics, including food and transport, were raised repeatedly across FGDs as a significant barrier to timely diagnosis and medication adherence.

FGD with community leaders, 50-55 years age group, female: *'TB medicines are free but people also need money for two-way transportation and food. TB illness [and even] TB treatment can make people weak and nutrition is needed. How can people afford these [nutrition and transportation] costs?'*

Nonetheless, patient journeys were repeatedly reported as long and convoluted, including a public–private mix of traditional medicine, pharmacies, local private healthcare providers and larger private clinics before reaching NTP diagnostic and treatment services (figure 2). As a result, TB-affected households incurred significant expenses.

FGD with people diagnosed with TB, 45-50 years age group, male: *'I visited all the pharmacies in my city, about 15–17 medicals [pharmacies] overall. I used to buy pneumonia medicine and take it every time. TB was not initially identified. After a month without taking any medicines, TB was identified [at the government clinic]… The barrier is more financial. I spent approximately 1.7 lakhs [~1530 USD] for my treatment.'*

Undernutrition and food insecurity were recognised as risk factors for TB and to contribute to suboptimal adherence. Across FGDs, it was noted that many TB-affected households have insufficient resources to buy nutritious food. In addition, it was perceived that lack of education negatively impacted decision making related to nutrition to recover during TB treatment. In particular, community leaders and people with DR-TB raised concerns that the current monthly governmental nutrition allowance was insufficient to obtain nutritional food, such as meat and fruits, which is often recommended by healthcare providers. Female participants with TB mentioned a trade-off between out-of-pocket expenses to purchase the recommended nutritional food vs transportation expenses associated with DOTS at TB clinics.

Lost income was identified in the majority of FGDs as a notable barrier to accessing diagnosis and engaging with TB care, which compounded the economic impact of out-of-pocket travel and food costs. People with TB expressed guilt and stress related to having to stop work following their TB diagnosis and the fear of not getting employment again. Female participants described the impact as hardest on poorer populations, women working in the fields, and labourers, who lack the free time required to go to the health facility for daily DOTS, especially when opening hours and prime labouring hours coincide.

Community stakeholders and people with TB frequently cited that TB-affected households use coping strategies to mitigate the economic impact of TB, most commonly to obtain funds to buy food. Selling assets, such as livestock, milk, land and jewellery, was reported as a predominant coping strategy. However, it was noted that some vulnerable patients were so poor that they have nothing to sell. Other coping strategies mentioned included borrowing money, formally and informally, which led to further economic hardship and difficulties maintaining adherence.

FGD with people diagnosed with TB, 25-30 years age group, male: *'I had difficulties [to pay money to access TB services] and wasn't able to go [to the clinic] for a month. I had to borrow money from my friends.'*

Theme: facilitating treatment adherence by people with TB through nutritional and/or economic support

Participants discussed the need for social protection including insurance, transportation allowance and nutritional support for TB-affected people (figure 2).

The potential for economic support to improve nutrition, defray travel and other out-of-pocket costs, and increase TB treatment success, was raised in all FGDs. It was acknowledged, particularly in FGDs with NTP stakeholders and people with TB, that the government of Nepal provides Rs 3000/month (~US$ 27 for ambulatory MDR-TB cases and Rs 1000/month (~US$8) for those staying at DR-TB hostels. While the NTP stipulates that this is intended as nutritional and/or transport allowance, participants noted that how the cash is spent is not monitored. In addition, issues were raised with this existing transfer scheme, including delays in delivery of the allowance.

FGD with CSO, 45-50 years age group, male: *'The most important question is when to give the allowance. It would be better in the first phase [of treatment] because it is [most] valuable at this time when one needs it most.'*

There was further debate concerning whether cash or nutritional support was most appropriate. Some community stakeholders raised concerns regarding misuse of cash payments (eg, to buy alcohol) and suggested that it would be preferable to provide nutritious food such as milk, ghee (local butter), meat and eggs. However, females with TB perceived that any cash received would nevertheless be spent on food, primarily staple foods such as rice, to feed their household.

Finally, it was perceived across FGDs that any nutritional or economic support should either be provided to all or stratified by need rather than TB drug resistance profile.

FGD with people diagnosed with TB, 30-35 years age group, male: *'The government should provide nutritious food based on the economic status of patients. Drug-sensitive patients should also be provided with an allowance based on their level of poverty.'*

Psychosocial

Theme: psychosocial barriers to treatment adherence

Across all FGDs, stigma was perceived to be a significant barrier to seeking, accessing, and engaging with TB diagnostic and treatment services. People with TB

described feeling discriminated against, mistreated, isolated or hated. They reported perceptions or instances of people talking behind their back or remaining physically distanced. Participants of the FGD with community stakeholders shared that sometimes people with TB experienced extreme negative behaviour such as physical or psychological mistreatment from their own family members. The situation was discussed as being even more pronounced for young married females because of a lack of personal agency within their husband's family. While this stigmatising behaviour towards people with TB was reported to occur across socioeconomic groups, participants described that a 'blame and shame culture' was prevalent among family members belonging to groups perceived as 'higher' in the caste related, social hierarchy. In alignment with this assertion, community mobilisers mentioned that lack of social and family support can cause people to conceal their TB status and not adhere to or complete TB treatment.

Reports of stigmatising behaviour were not limited to the community and family members. Perceived negative behaviour of healthcare providers towards people with TB was noted across FGDs as an issue that compounded self-stigma and led to a breakdown of trust within the client–provider relationship. Although participants felt that, generally, enacted stigma had decreased in Nepalese communities, FGDs with people with TB and community stakeholders shared that people still fear TB disease, especially in rural villages.

FGD with people diagnosed with TB, 30-35 years age group, male: *'People may know they have symptoms of TB but are too ashamed to go to the health facilities. People can't say out loud that they have TB. TB is regarded as a big disease and people get criticized for having it. The community perceives a TB patient differently than a normal person due to lack of awareness. That's why it's difficult to end TB.'*

People with MDR-TB reported profound psychosocial impact including anxiety and isolation, especially during the first months of treatment. Depression, suicidal ideation and shame related to stigma and also well-recognised side effects of MDR-TB medications were mentioned.[23]

FGD with people diagnosed with MDR-TB, 45-50 years age group, male: *'I wanted to die. One of my friends [with MDR-TB] committed suicide after 16 months [of treatment].'*

Theme: Mutual or social support as a facilitator to treatment adherence

Social support from family and friends was perceived as a facilitator to adhering to TB treatment and becoming cured (figure 2). This included visiting, spending time with and showing affection towards people with TB to demonstrate solidarity and reduce feelings of isolation.

People with TB also shared the importance of mutual support beyond family and friends, including the wider community, leaders, elders and other important local figures. The participants believed that this kind of support would help people with TB to cope and reflected the

close communities and rich socio-cultural values inherent to Nepalese culture.

FGD with people diagnosed with MDR-TB, 40-45 years age group, male: *'My friends and the people in my village told me 'TB is a normal disease and encouraged me that, if I took my medicine, I'd be alright.'*

Interactions and consultations with healthcare providers were also seen as opportune occasions to provide education and counselling to address the psychological impact of TB. FGD with community stakeholders raised the perceived importance of healthcare providers simply recognising, acknowledging and being understanding of patients' fears, concerns and expectations. While healthcare provider-led counselling on medication adherence was noted to be commonplace at treatment initiation, counselling patients with TB about TB-related fear, stigma, depression and anxiety was broadly overlooked. It was noted that integration of medication and psychological counselling by healthcare providers could be a suitable method to deliver clear and open information about stigma and discrimination, which could improve TB treatment adherence and completion rates and potentially support mental wellness and empowerment.

DISCUSSION

This qualitative study generated new evidence regarding barriers and facilitators to accessing and engaging with TB services in Nepal. Multisectoral stakeholder participants highlighted that the barriers were predominantly related to the poor socioeconomic conditions of people with TB, including lack of education and endemic poverty. The findings showed that the costs of care-seeking and clinic-based DOTS can further compound poverty and, when combined with psychological impacts including stigma and anxiety, were perceived to negatively influence access to TB services. Participants cited multiple potential socioeconomic interventions, both integrated and discrete, including TB education, economic, nutritional and social support, to mitigate catastrophic costs of TB-affected households and support people with TB to get cured.

Knowledge and awareness about TB

Low education levels and limited awareness of TB are associated with delays in healthcare seeking.[24–26] A study in Nepal showed inadequate knowledge of TB was associated with increased likelihood of consulting traditional healers, resulting in TB diagnostic delay.[27] Our findings are also similar to other studies that suggested knowledge about TB was limited in poor, marginalised and/or rural communities in Nepal.[8 28] This implies that any existing TB education and advocacy programmes may not be reaching crucial, high-risk target groups and new approaches are required if Nepal is to end TB.

Educational support interventions that enhance knowledge about TB transmission, symptoms, treatment and prevention, are important contributory factors in both care-seeking behaviour and treatment outcomes

in diverse settings.[27 29 30] In India, the Global Fund-supported advocacy, communication and social mobilisation project, 'Axshya', has made progress towards reaching underserved groups through intense community outreach and education.[31] FGD participants in our study cited a dearth of awareness-raising interventions and campaigns in recent years in Nepal. Previously, similar campaigns focused on TB awareness through door-to-door visits, health promotion at health facilities or educational outreach into communities. Such campaigns were perceived to increase knowledge on TB, advocate for free TB services and empower communities to make informed choices. As highlighted by participants, in addition to commonly used platforms such as leaflets, radio and television, future educational campaigns in Nepal would benefit from using technology such as mobile phones—which are used by over 90% households in both urban and rural areas[32]—or, where appropriate, social media.

Psychosocial impact

Of the perceived psychosocial barriers to accessing TB diagnosis and care in Nepal, stigma predominated. Participants mentioned feelings of guilt among people with TB, fear of disclosure and experience of discrimination. This mirrors findings from diverse settings, which show that experiences of stigma are highly prevalent among people with TB and can impede access to TB services.[33] For example, in Zambia, a cohort study showed that anticipated and enacted stigma of people with TB resulted in delayed diagnosis, poor treatment adherence, reduced quality of life and represented a distinct challenge to successful screening of their household contacts.[34]

It was notable that people with MDR-TB reported severe negative psychosocial impacts of their illness. These included profound feelings of anxiety, isolation related not only to their diagnosis but also to physical distance from their families, and recognised side effects of certain MDR-TB medications (eg, cycloserine) such as depression and despair.[35–37] Participants perceived an association between the psychosocial impact of MDR-TB and the potential for non-adherence to long, arduous treatment regimens including injectable agents. Discussion across FGDs suggested that existing medication adherence counselling delivered by NTP staff at treatment initiation would be a suitable platform on which to integrate complementary psychosocial counselling about overcoming TB-related stigma and addressing ill mental health.

Economic burden of TB

The economic impact of accessing TB diagnosis and care was perceived to be severe. This was mainly due to high costs associated with transportation to clinics, maintaining adequate nutrition and time and income loss. Participants with MDR-TB indicated that there was delay or unavailability of the NTP's financial assistance scheme during their treatment. The financial impact of belonging to a household affected by TB was cited in

FGDs as forcing households to resort to coping strategies such as taking out loans, using savings and selling assets. These findings are in line with the rapidly growing global body of evidence relating to the economic burden of TB. Such findings suggest that coping strategies remain common and only limited progress has been made towards the WHO target of 'zero TB-affected families face catastrophic costs by 2020'.[1 38] TB Patient Costs Surveys conducted in various LMICs have demonstrated that a substantial proportion of TB-affected households incur catastrophic costs, which can push them into further impoverishment and contribute to adverse TB treatment outcomes.[6 39–44] Studies demonstrated that more than 60% of TB-affected households in Nepal incurred catastrophic costs[6 7] and stark economic impact.[27 45–47]

Although this study focused on barriers amenable to interventions at the household level rather than health system level, our findings showed that when TB diagnosis and care were sought from both the public and private sector, patient pathways to TB diagnosis and care were protracted and their costs, especially out-of-pocket costs, escalated (described in detail in online supplemental file 2). This finding is consistent with the findings of systematic reviews from Nepal, India and Uganda,[48–54] which also highlighted that interventions to strengthen public–private partnerships can streamline diagnostic and referral pathways and potentially increase TB notifications to the NTP. Studies in India and Vietnam have demonstrated enhanced engagement with private pharmacies and medical practitioners by providing them subsidies directly or through intermediary agencies for every notified case.[55 56] This could be a potential strategy to improve access to TB care in Nepal, where approximately 20% people with TB receive paid treatment from the private sector.[57]

Social and economic support

To address the psychosocial and economic impact of TB and improve TB cure and prevention rates, our findings imply a need for both social and economic support. This is supported by the results of studies in Nepal and other LMICs, which showed that providing both counselling and economic assistance to people with MDR-TB improved cure rates.[9 58–60] However, it must be noted that a significant proportion of people with DS-TB in Nepal experience enduring psychological, social and economic impacts of TB but receive no additional support.[6 7 12] In line with a study from Ethiopia,[61] our findings also suggest that the timing of provision of financial support is important. Participants advocated for early cash support delivery in the initiation phase of treatment when they perceived it to be needed most. Involvement of family members and peers in such interventions was also noted by participants as a vital aspect of support to complete TB treatment. This has also been reported in a systematic review of factors affecting medication adherence in LMICs.[62]

A well-designed socioeconomic support intervention would ideally be tailored or stratified to the individual or household needs of a person with TB and include overlapping elements such as increasing knowledge, awareness-raising, cost mitigation (eg, through cash transfers or transport vouchers) and stigma-reduction activities (eg, mutual support, peer groups, enhanced medication counselling sessions), integrated into existing TB services.[63][64] However, it must be acknowledged that such an intervention would need to balance stratification with feasibility and pragmatism.

Strengths and limitations

Our study fills an important gap in knowledge about household-level socioeconomic barriers to accessing TB services in Nepal and expanded on perceived facilitators and enablers to overcome these barriers. A major strength of the study methods was the trustworthiness and validity harnessed by garnering perspectives of the diverse study participants.[65]

The study has several limitations. As the participants were predominantly from Terai plains districts the findings, therefore, should be cautiously applied in other settings or countries. Nevertheless, we described the study setting to improve transferability. Second, participants from NGOs and healthcare professionals working with the NTP were over-represented within the participant cohort. However, we tried to strike a suitable balance by including the views of people with TB and community groups, which historically have been overlooked in similar research. FGDs consisted of limited women participants. We minimised the issue by specifically describing the female participants' viewpoint in the analysis. Similarly, there was no participation of people diagnosed with TB in private sectors or those who had been lost to follow-up who are the vulnerable to restricted access to TB services and poor outcomes. Their engagement would enable us to fully understand the most important barriers to care.[39][64]

CONCLUSION

There are multiple socioeconomic barriers to accessing and engaging with TB services in Nepal. TB education and advocacy, economic support and psychosocial counselling integrated with medication adherence counselling could address these barriers and potentially reduce stigma, mitigate TB-related costs and improve TB treatment outcomes. These elements are now being incorporated into the design of a locally appropriate socioeconomic support intervention for TB-affected households for pilot implementation in Nepal.

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Supplementary File I: Focus group discussion coding framework

Category 1: TB, health, and basic education

TB, health, and basic education barriers

FGD	First order category	Second order themes	Third order themes	Example Quote
People diagnosed with TB	TB, health, and basic education	Inadequate knowledge on TB services	Information barrier to access	**FGD with people diagnosed with TB, 20-25 years age group, female:** *"I didn't know that medicines were free in hospitals. I knew it only when I visited health post."*
People diagnosed with MDR-TB	TB, health, and basic education	Limited knowledge on TB disease	Information barrier to access	**FGD with people diagnosed with MDR-TB, 70-75 years age group, male:** *"No one told me anything [about TB] but I knew that it was a communicable disease."*
Community leaders	TB, health, and basic education	Inadequate advocacy on TB services	Information barrier to access	**FGD with community leaders, 45-50 years age group, male:** *"There is no person to advocate about [available health and TB] services."*
People diagnosed with MDR-TB	TB, health, and basic education	Limited knowledge on TB disease and TB medicines dosages	Information barrier to adhere to TB services	**FGD with people diagnosed with MDR-TB, 45-50 years age group, male***: "I took medicine for 2 months and then left for 15 days because I thought I was feeling better."*
Civil society organization	TB, health, and basic education	Lack of awareness raising activities particularly in poorer and	Information barrier to access	**FGD with civil society organization, 45-50 years age group, male:** "*In addition, programmatic TB awareness-raising activities were seen as scarce, especially among poorer, "educationally and socially marginalized."*

		socially marginalized		
Civil society organization	TB, health, and basic education	Inadequate awareness raising educational materials	Information barrier to access	**FGD with civil society organization, 45-50 years age group, male: "***There has been few educational materials development for TB awareness at present in comparison to the past. Therefore, people do not go to the health facility."*

TB, health, and basic education facilitators

FGD	TB, health, and basic education	**Second order theme**	**Third order theme**	**Quotes**
Civil society organization	TB, health, and basic education	Improvements in basic education on TB	Education on TB disease and advocacy about its services	**FGD with civil society organization, 45-50 years age group, male***: "TB education should be spread intensively to village households."*
People diagnosed with TB	TB, health, and basic education	Awareness about TB disease, treatment and prevention	Education on TB disease and advocacy about its services	**FGD with people diagnosed with TB, 30-35 years age group, male:** *The government should develop TB awareness raising programs….[including] in the media, to tell people about TB symptoms, check-ups….. and that it's a curable disease."*

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People diagnosed with TB	TB, health, and basic education	Community engagement Mobilization of TB champions and peers	Education on TB disease and advocacy about its services	**FGD with people diagnosed with TB, 30-35 years age group, male:** *"People previously affected by TB could tell their story to community and mother's groups. I am 100% sure this will work."*
People diagnosed with TB	TB, health, and basic education	Awareness about TB Information on TB medications	Education on TB disease and advocacy about its services	**FGD with people diagnosed with TB, 45-50 years age group, male:** *"People in the villages will take medicines regularly if they are educated….the government should strengthen education on TB medication."*
Civil society organization	TB, health, and basic education	Community engagement Mobilization of community leaders for TB awareness	Education on TB disease and advocacy about its services	**FGD with civil society organization, 50-55 years age group, female:** *"We need to create [educational] groups attached to health centres and schools….Community and locally-elected leaders and teachers could give education to their communities and conduct TB awareness training and workshops."*
TB healthcare professional	TB, health, and basic education	Awareness about TB Communication to influence health beliefs and change behaviour	Education on TB disease and advocacy about TB services	**FGD with TB healthcare professional, 55-60 years age group, male:** *"Changing [people's] attitude [about TB] is one of the things we can start doing to….. make a change in [people's] behaviour."*

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Community Mobilizers	TB, health, and basic education	Awareness about TB Improved communication to influence health beliefs and change behaviour	Education on TB disease and advocacy about TB services	**FGD with Community Mobilizers, 30-35 years age group, male:** *"[Some] patients don't believe us when we tell them that they have been diagnosed with TB. They say they'll go to India for check-up. In our region, people who believe in a certain religion think that TB will cure itself."*
People diagnosed with TB	TB, health, and basic education	Advocacy on TB services	Expansion of TB services in community	**FGD with people diagnosed with TB, 30-35 years age group, male:** *"Health facilities should conduct door to door campaign. [Health facility] should collect sputum in a timely manner. That's it, actually there is a lack of advocacy."*
Community leaders	TB, health, and basic education	Prioritize underserved people	Education on TB disease and advocacy about TB services in remote communities	**FGD with community leaders, 65-70 years age group, male:** *"One of the reasons is that many people do not have adequate information because in this era radio, television, mic, seminars, workshops are organized where people/ community are literate. But those people who do not have access to any of these media are disadvantaged from these programs. So, we should focus more to those people as well."*

Category 2: Social protection and nutrition

Social protection, nutrition, and economic barriers

FGD	First order categories	Second order themes	Third order themes	Quote
People diagnosed with TB	Social protection, nutrition, and economic	Out-of-pocket expenses for transportation to engage with treatment	Economic barrier to treatment adherence	**FGD with people diagnosed with TB, 55-60 years age group, male**: *"When I don't have money, I cannot ride auto [local vehicle] because it costs Rs 300 [$2.5 USD] to reach home or clinic. I can't earn three pennies! How can I pay Rs 300 to go to home?"*
People diagnosed with TB	Social Protection, nutrition and economic	Out-of-pocket expenses for diagnostic tests	Economic barrier to access	**FGD with people diagnosed with TB, 45-50 years age group, male:** *"I visited all the pharmacies in my city, about 15-17 medicals [pharmacies] overall. I used to buy pneumonia medicine and take it every time. TB was not initially identified. After a month without taking any medicines, TB was identified [at the government clinic]….. The barrier is more financial. I spent approximately 1.7 lakhs [~1530 USD] for my treatment."*
Civil society organization	Social Protection, nutrition and economic	Out-of-pocket expenses for transportation and nutrition	Economic barrier to treatment adherence	**FGD with civil society organization, 50-55 years age group, female:** *"TB medicines are free but people also need costs for two-way transportation, food. TB illness [and even] TB treatment can make people weak and nutrition is needed. How can people afford [nutrition and transport costs]?"*
People diagnosed with MDR-TB	Social Protection, nutrition and economic	Lost income Reduced productivity related to TB illness Psychological stress	Economic barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 20-25 years age group, male:** *I used to be a conductor on a bus but I can't do any work now. I suffer headaches just going to the kitchen to cook rice. How can such a person work?"*

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People diagnosed with MDR-TB	Social Protection, nutrition and economic	Lost income Reduced productivity related to TB illness	Economic barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 40-45 years age group, male:** *"I used to work outside but after being affected by MDR-TB, I stopped going to work. I didn't earn money"*
People diagnosed with TB	Social Protection, nutrition and economic	Out-of-pocket expenses for accessing TB services Borrowing money as coping strategies	Economic barrier to access and adhere to TB treatment	**FGD with people diagnosed with TB, 25-30 years age group, male:** *"I had difficulties [to pay money to access TB services] and wasn't able to go [to the clinic] for a month….I had to borrow money from my friends."*
People diagnosed with TB	Social Protection, nutrition and economic	Out-of-pocket expenses for accessing TB services Selling assets as coping strategies	Economic barrier to treatment adherence	**FGD with people diagnosed with TB, 20-25 years age group, male:** *"I can't pay back the loan [I took out during treatment], which causes problems…..we might have to sell assets to pay back the loan."*
People diagnosed with MDR-TB	Social Protection, nutrition and economic	Inadequate financial support	Economic barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 20-25 years age group, male:** *"The TB hostel where I am staying assured us that they would give money but they still haven't [up to 20 months into treatment]."*
Social protection and nutrition				
FGD	**First order categories**	**Second order themes**	**Third order themes**	**Quote**
Civil society organization	Social Protection,	Provision of nutrition or cash incentives	Nutrition and or economic support	**FGD with civil society organization, 50-55 years age group, female:** "*When patients take medicine, they will feel weak but they will not have the facility of proper*

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	nutrition and economic		to treatment adherence	*nutritious food. Thus, if certain amount of money is made available to them, then it will help them."*
Community leaders	Social Protection, nutrition and economic	Delivery mechanism and timing of incentives	Economic support to treatment adherence	**FGD with community leaders, 45-50 years age group, male:** *"The question is when to give the allowance. It would be better in the first phase [of treatment] because it is [most] valuable at the time one most needs it."*
People diagnosed with TB	Social Protection, nutrition and economic	Provision of economic and nutrition support Prioritization of nutrition and economic support	Nutrition and or economic support to treatment adherence	**FGD with people diagnosed with TB, 30-35 years age group, male:** *"Government should provide nutritious food based on the economic status of patients……drug-sensitive patients should also be provided with an allowance based on their socio-economic condition."*

Category 3: Psychosocial barriers

FGD	First order categories	Second order themes	Third order themes	Quote
Female: diagnosed with TB	Psychosocial category	Stigma Enacted stigma in the community Perceived stigma Lack of knowledge	Social barrier to adhere during treatment	**FGD with female: diagnosed with TB, 25-30 years age group, female:** *"I have not told anyone in my family about my disease because they will hate me. I fear that if my family or friends know about my disease, they'll start talking behind my back and not come near me."*

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Civil society organization	Psychosocial category	Stigma Enacted stigma in the community Perceived stigma Lack of knowledge	Social barrier to access and adhere during treatment	**FGD with civil society organization, 45-50 years age group, male:** *"People don't want to sit close to or make contact with someone with TB. They can act scared when they're near a patient with TB. Ironically, the same society promotes TB treatment and encourages people with TB to get themselves tested and treated."*
People diagnosed with TB	Psychosocial category	Stigma Enacted stigma in the community Perceived stigma Lack of knowledge	Social barrier to access	**FGD with people diagnosed with TB, 30-35 years age group, male:** *"People may know they have symptoms of TB but are too ashamed to go to the healthposts. People can't say out loud that they have TB. TB is regarded as a big disease and people get criticized for having it. The community perceives a TB patient differently than a normal person due to lack of awareness. That's why it's difficult to end TB."*
Healthcare professional	Psychosocial category	Stigma Enacted stigma in the community Perceived stigma Lack of knowledge Limited social support	Social barrier to adhere to treatment	**FGD with TB healthcare professional, 30-35 years age group, male:** *"Some people have very low social support, including from their family. Those people are at risk of not taking a full course of TB treatment."*

People diagnosed with MDR-TB	Psychosocial category	Psychological impact Stress, anxiety, and depression	Psychological barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 45-50 years age group, male:** *"After seeing the healthcare workers, I felt angry and depressed. I didn't want to stay with others, not even with my family. I just sat alone."*
People diagnosed with MDR-TB	Psychosocial category	Psychological impact Stress, anxiety, and depression	Psychological barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 20-25 years age group, male:** *I felt depressed at first. No one in my clan had suffered from this disease. I wondered how I'd got affected."*
People diagnosed with MDR-TB	Psychosocial category	Psychological impact Stress, anxiety, and depression	Psychological barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 45-50 years age group, male:** *"I wanted to die. One of my friends [with MDR-TB] committed suicide after 16 months [of treatment]."*
Category 3b: Psychosocial facilitators				
FGD	**First order categories**	**Second order themes**	**Third order themes**	**Quote**
emale: diagnosed with TB	Psychosocial category	Family care and support	Mutual support as facilitator to treatment	**FGD with female: diagnosed with TB, 40-45 years age group, female:** *"When I restarted taking medicines, it was very difficult for me. My husband helped me at that time and, slowly, I started getting better."*

People diagnosed with MDR-TB	Psychosocial category	Peer support and motivation	Mutual or social support as facilitator to treatment	**FGD with people diagnosed with MDR-TB, 40-45 years age group, male:** *"My friends and the people in my village told me TB is normal disease and encouraged me that if I took my medicine, I'd be alright."*

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Category 4: Healthcare system, TB diagnosis and care delivery

Category 4a: Healthcare system, TB diagnosis and care delivery barriers				
FGD	**First order categories**	**Second order categories**	**Third order categories**	**Quote**
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Delay in diagnosis Self-perception of disease and choice of treatment Repeated visits for diagnosis Inadequate referral mechanisms	Convoluted pathway to diagnosis as barrier to access	**FGD with TB healthcare professional, 45-50 years age group, male:** *"When people feel sick [with TB symptoms], they start by using herbal medication at home. When they do not get relief from that medication, they go to Dhami/Jhakri [traditional healers], then the pharmacy, then to a government clinic. So, from the start of their illness to getting the right treatment, is around 1-2 months."*
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Inadequate treatment regulation Under-recognition of TB symptoms Inadequate referral mechanisms	Unregulated policy for medicines distribution	**FGD with TB healthcare professional, 55-60 years age group, male:** *"If I have a cough, the local pharmacy will give me amoxicillin. [If I continue to cough] I might get a more expensive antibiotic like cefixime. If I tell the pharmacist that I am coughing up blood - a clear sign in a place like Nepal that this could be TB - I might get some bigger, more expensive antibiotics but the thought would not be about tuberculosis. The pharmacist should tell me to get checked for TB but instead I will get sold antibiotics. There are thousands of pharmacies [like this] in South Asia."*

Community Mobilizers	Healthcare system, TB diagnosis and care delivery	Geographical inaccessibility to reach TB centers Natural disasters Centralised location of health facilities	Geographical barriers to access TB diagnosis and care	**FGD with Community Mobilizers, 30-35 years age group, female:** *"In rainy season, flooding makes it difficult for patients to go and get medicine and [health posts] are inaccessible"*
Community Mobilizers	Healthcare system, TB diagnosis and care delivery	Geographical inaccessibility to reach TB centers Poor quality of road and transportation network	Geographical barriers to access TB diagnosis and care	**FGD with Community Mobilizers, 20-25 years age group, male:** *"One of the main reasons for not taking medicine is because the health posts are far away….and difficult to reach….especially when the rivers get bigger and wider; they can sweep people away. If the health post was nearer, it would be easier."*
Civil society organization	Healthcare system, TB diagnosis and care delivery	Poor healthcare services Limited or inconvenient opening times of health facilities	Inadequate services from health centers as barrier to adhere to treatment	**FGD with civil society organization, 50-55 years age group, female:** *"If we don't go on time, we don't meet the doctor. The patients must reach the hospital clinic before 11 and take a ticket.*
Community leaders	Healthcare system, TB diagnosis and care delivery	Geographical inaccessibility to reach TB centers Poor quality of road and transportation network	Geographical barriers to access TB diagnosis and care	**FGD with community leaders, 35-40 years age group, male:** *"The health facilities are far and also may be the difficult road."*

Community leaders	Healthcare system, TB diagnosis and care delivery	Geographical inaccessibility to reach TB centers	Geographical barriers to access TB diagnosis and care	**FGD with community leaders, 45-50 years age group, male:** *"They are far from the access of Health facilities. Due to this reason they do not get medicine regularly."*
People diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Poor healthcare services Limited human resources	Inadequate services from health centers as barrier to adhere to treatment	**FGD with people diagnosed with TB, 25-30 years age group, male:** "*There are no health workers. It's such a small hospital [where I attend for TB medicine], there are five employees but four of them don't work. When I go to find and take my medicines, they say they don't know and ask me to look for it myself. The main doctor is in a meeting all the time, he doesn't know."*
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Poor healthcare services	Inadequate patient centric care as barrier to treatment adherence	**FGD with TB healthcare professional, 55-60 years age group, male:** *"If we try to put ourselves in the patient's shoes, be a TB patient, do you think it would be possible for us to visit the health centre for six months? Ruin our careers and everything to attend the health centre? We need to implement innovative ideas to support treatment adherence that are patient-centred rather than program-centred."*
People diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Poor TB service delivery	Care not being patient-centred acting as barrier	**FGD with people diagnosed with TB, 20-25 years age group, male:** *"I stayed for one hour in queue and then waited a long time for*

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			to treatment adherence	*treatment, spent money, and got a delayed report."*
Female: diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Poor TB service delivery	Care not being patient-centred acting as barrier to treatment adherence	**FGD with female: diagnosed with TB, under 20 years age group, female:** *"Getting a delayed test report was a barrier for me, we had to come and go [to health facilities] for 4 days."*
People diagnosed with MDR-TB	Healthcare system, TB diagnosis and care delivery	Poor TB service delivery	Care not being patient-centred acting as barrier to treatment adherence	**FGD with people diagnosed with MDR-TB, 45-50 years age group, male:** *"Our community mobiliser told us to go health post and they will administer the injection [injectable medication for TB]. I went but they told me that they couldn't give me an injection at that time."*
Community leaders	Healthcare system, TB diagnosis and care delivery	Poor TB service delivery	Care not being patient-centred acting as barrier to treatment adherence	**FGD with community leaders, 45-50 years age group, male:** *"The behaviour of NTP healthcare workers needs to change. There's a difference between saying 'your father' and 'your respected father' isn't it? Imagine how bad an ill person will feel….when spoken to in an ill-mannered way; the speech will feel like an arrow."*
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Poor TB service delivery	Care not being patient-centred acting as barrier to treatment adherence	**FGD with TB healthcare professional, 55-60 years age group, male:** *"The perception of lack of patient friendly services was also acknowledged as a problem in the NTP and patient FGDs and that although there are 4200 DOTS centres and many microscopic and GeneXpert centres, many are not patient*

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				friendly and this can contribute to delayed initiation of treatment."
People Diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Poor TB service delivery	Care not being patient-centred acting as barrier to treatment adherence	**FGD with people diagnosed with TB, 25-30 years age group, male:** *"They don't ask anything. They just give medicines and give a tick mark in the card. It is just this at our place. They make a register. But if the main doctor [health worker] is not there, they don't even do it. They ask to take medicines by ourselves. In our village, we are asked to take medicines from the box."*

Category 4b: TB diagnosis and care delivery facilitators				
FGD	**First order categories**	**Second order themes**	**Third order themes**	**Quotes**
Civil society organization	Healthcare system, TB diagnosis and care delivery	Standardization of TB treatment	Proper regulation and management of TB services delivery	**FGD with civil society organization, 45-50 years age group, male:** *"If TB medicines are only available from registered governmental health facilities, people will take them from there."*

People diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Standardization of TB treatment	Proper regulation and management of TB services delivery	**FGD with people diagnosed with TB, 30-35 years age group, male:** *"The main point is TB medicine is available in pharmacies and those who can pay will get it because pharmacies want money. Pharmacies don't care much about treatment and cure….or if patients take medicines at the right time or at all. That is why….TB medicines should only be provided under the supervision of government health facilities only. This will help to control TB."*
People diagnosed with MDR-TB	Healthcare system, TB diagnosis and care delivery	Improved access to TB diagnostic and treatment services	Provision of community based healthcare services and patient-centred care	**FGD with people diagnosed with MDR-TB, 40-45 years age group, male:** *"What I like the most is they come to our houses to collect sputum."*
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Availability of diagnostic services	Early diagnosis of TB	**FGD with TB healthcare professional, 30-35 years age group, male:** *"GeneXpert, X-ray and symptoms are three things that the program is focusing on."*

Community leaders	Healthcare system, TB diagnosis and care delivery	Improved access to TB diagnostic and treatment services	Provision of community based healthcare services and patient-centred care	**FGD with community leaders, 45-50 years age group, male:** "We conduct screening camps for other diseases so why can't we do screening camp for tuberculosis? In the past, NGOs collected sputum from households where there was a patient on the basis of exposure history in family members. If we could collect and screen by understanding the patient's location that easier for them or visiting their workplace, it might increase the number of cases identified."
Female: diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Improved access to TB diagnostic and treatment services	Provision of community based healthcare services and patient-centred care	**FGD with female: diagnosed with TB, 45-50 years age group, female:** *"It's good to bring medicine at home. Sometimes, we have work at the time when we have to go to take medicines."*
Female: diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Good behavior of healthcare providers	Patient-centred care	**FGD with female: diagnosed with TB, 60-65 years age group, female:** *"The doctor treated me like a normal patient, cared for me, asked how I was feeling and gave me medicine."*

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Community Mobilizers	Healthcare system, TB diagnosis and care delivery	Good behavior and communication between patient and healthcare providers	Patient-centred care	**FGD with Community Mobilizers, 40-45 years age group, male:** *"We provide time to patients….meet them on their way to work or when coming back from work…..they are in constant contact with us…..we consult them properly…they trust us more [than doctors]."*
Female: diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Proper communication between patient and healthcare providers	Patient-centred care	**FGD with female: diagnosed with TB, 45-50 years age group, female: "***Doctor told that medicines should be taken for six months completely."*
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Standardization of TB treatment and referral services	Proper regulation and management of TB services delivery	**FGD with TB healthcare professional, 30-35 years age group, male:** *"Government hospitals should mandate pharmacies and private providers to refer people with TB to government services but it was noted that legislation was insufficient."*
People diagnosed with TB	Healthcare system, TB diagnosis and care delivery	Standardization of TB treatment and referral services	Proper regulation and management of TB services delivery	**FGD with people diagnosed with TB, 30-35 years age group, male: "***TB medicines should only be provided under the supervision of government health facilities only. This will help to control TB."*

TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Decentralization of advanced diagnostic services in	Expansion of advanced diagnostic services	**FGD with TB healthcare professional, 55-60 years age group, male:** *"Decentralization of GeneXpert had revolutionized the TB diagnosis in the hills of Nepal to do better diagnosis and find MDR TB roll out GeneXpert."*
TB healthcare professional	Healthcare system, TB diagnosis and care delivery	Prioritization of vulnerable groups for increased diagnosis	Strategies and policies for TB diagnosis	**FGD with TB healthcare professional, 55-60 years age group, male:** *"I think we have to change our strategy of active case finding, based on the level of vulnerability and the level of risk that a person can be exposed to. If we are following the same strategy for prisoners that we are following in the community, we might not find many cases."*

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Supplementary File II: Healthcare system, TB diagnosis and care delivery barriers and facilitators

During thematic analysis, it was noted that the FGD participants identified "higher level" barriers and facilitators to accessing and engaging with TB services including governmental policy, political commitment, public-private mix, and healthcare infrastructure that would not be directly modifiable through a socioeconomic support intervention for TB-affected households. While important and informative, the research team felt that such themes could not practically be addressed by – and hence would not directly inform the design of - a discrete socioeconomic support package for TB-affected households for future trial evaluation. Here, the perceived higher level barriers and facilitators are mapped to Category IV "Healthcare system, TB diagnosis and care delivery" of the adapted WHO treatment adherence framework.[1] These barriers and facilitators are summarized in Figure 2 of the main article and expanded on in more detail below.

Theme: Healthcare system, TB diagnosis and care delivery barriers

Across FGDs, participants reported limited staffing at health centers, poor geographical access, unsatisfactory quality of the TB services and multiple visits in public and private health centers for diagnosis and treatment as the major barriers to accessing and engaging with TB treatment. Participants mentioned that the incorrect diagnosis of TB caused long and convoluted journey during the diagnosis and treatment, including a public-private (PPM) mix of hospitals and clinics and pharmacies before reaching NTP diagnostic and treatment services:

> **FGD with female diagnosed with TB, 25-30 years age group, female:** *"For many times, I went to hospitals and bought medicines. My health was worsening. A doctor prescribed medicines for increased blood pressure, I had those medicines. Also, later another doctor prescribed me medicines for gastritis. I had those medicines as well. None of the medicines made me feel better. It took a long time until I was diagnosed [of TB] in a government hospital."*

The NTP stakeholders mentioned that the pharmacy services were perceived to be compromised because of the practice of prescribing antibiotics without suitable clinical or microbiological confirmation of infection. Moreover, the practice of changing to new and more expensive antibiotics was noted if the disease wasn't cured. However, such services were noted to be thriving and supported a culture of, as one NTP stakeholder noted, *"medicine dependence in South Asia"*.

> **FGD with NTP stakeholders, 55-60 years age group, male:** *"If I have a cough, the local pharmacy will give me amoxicillin. [If I continue to cough] I might get a more expensive antibiotic like cefixime. If I tell the pharmacist that I am coughing up blood - a clear sign in a place like Nepal that this could be TB - I might get some bigger, more expensive antibiotics but the thought would not be about tuberculosis. The pharmacist should tell me to get checked for TB but instead I will get sold antibiotics. There are thousands of pharmacies [like this] in South Asia."*

Participants from the FGD with NTP stakeholders raised concerns about the risk of such antibiotic practices driving increasing rates of drug-resistant TB (DR-TB) and multidrug-resistant TB (MDR-

TB) in Nepal. The practice of seeking private care initially was felt to be commonplace among those of higher socioeconomic position because of sufficient household resources coupled with a perception of private services being quicker and/or higher quality than public services and more likely to help them to become cured. Nevertheless, poorer households were reported to visit cheaper, independent private healthcare providers, some of whom were reported to have no or limited formal training, in their local village. Ultimately, it was reported across FGDs that the decision to seek private care and the level of quality of private care provided was dictated by money.

> **FGD with civil society organization, 45-50 years age group, male:** *"The majority of the patients go to medical [pharmacy]. If they have to go to district [larger referral hospital], then the expenses will be higher. If they attend health centres, the expense depends on the distance."*

Geographical barriers such as long distances to reach health facilities, weather conditions such as rain, natural disasters (landslides and flooding), difficult roads and limited transportation options were discussed in depth across FGDs. These barriers were perceived as hampering access to TB diagnosis, impeding engagement with TB treatment and DOTS, and had a knock-on impact on access to broader health services.

The participants in FGDs with community stakeholders and people with TB perceived restricted opening hours, delayed opening, limited time available for clinical investigation [in hospitals], and prolonged waiting times for consultation and receiving reports as barriers to both TB diagnosis and treatment. Community stakeholders reported that this was especially important for labourers given the competing demands to earn money during peak labour hours or seek healthcare during clinic opening hours. These barriers were compounded by issues relating to staff lateness and staff shortages or absence at healthcare centers that provided TB services:

> **FGD with people diagnosed with TB, 25-30 years age group, male:** *"There are no health workers. It's such a small hospital [where I attend for TB medicine], there are five employees but four of them don't work. When I go to find and take my medicines, they say they don't know and ask me to look for it myself. The main doctor is in a meeting all the time, he doesn't know."*

Moreover, participants perceived that there was negative behaviour of healthcare workers towards people seeking TB diagnosis or who were taking TB treatment as a notable barrier and disincentive to attend. There was a perception that some NTP staff at health centers took little interest in people with TB. A participant with TB disease mentioned that the healthcare workers at the DOTS center only provide medicines and put a tick mark in the treatment card or sometimes even proper recording is missed in the card. Another participant with TB also shared his experience during his treatment where he was often told to take medicines from the shelf at the DOTS center. There were also reports of discourteous consultations

During FGDs with people with MDR-TB, room conditions, atmosphere, and quality of TB services at MDR-TB centers were reported as not being patient-friendly and a significant barrier to engagement. Apart from waiting times, issues raised included crowded waiting rooms and

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inadequacies in cleanliness and hygiene of clinics and hospitals. Although people with MDR-TB reported supportive care and staff at the DR-TB hostels in which some were managed during their treatment, others reported that the facilities were not as expected. One participant describing their room to have been *"colder than snow"* and another shared that the substandard conditions of the hostel rooms made him feel even worse and so he did not remain there. The perception of lack of patient friendly services was also acknowledged as a problem in the FGDs with NTP stakeholders and people with TB:

Theme: Healthcare system, TB diagnosis and care delivery facilitators

During the FGD with NTP stakeholders, PPM was discussed in detail and, specifically, integration of the public and private sector TB services as a potential facilitator. Both NTP stakeholders and people with TB cited that government hospitals should mandate pharmacies and private providers to refer people with TB to government services. However, it was noted that current legislative powers were insufficient to realise this:

> **FGD with NTP stakeholders, 30-35 years age group, male:** *"We can regulate the health professionals but we cannot regulate the pharmacies….where the majority of TB cases are going and taking pills."*

It was noted across FGDs that outreach and decentralized community-based services that incorporate use of advanced diagnostic tools would be beneficial to reach healthcare facilities. NTP stakeholders reported that decentralization of GeneXpert had revolutionized TB diagnosis in the hills of Nepal, increasing TB case detection while promptly identifying people with DR-TB and MDR-TB. The NTP stakeholders mandated roll out of GeneXpert across Nepal and suggested integration of GeneXpert with targeted active-case finding strategies such as TB camps and door-to-door campaigns. The participants also suggested community screening, which focused on reaching underserved, vulnerable people at high risk of TB, was appropriate. People with MDR-TB reported that such active case finding strategies had been well received:

> **FGD with people with MDR-TB, 40-45 years age group, male:** *"What I like the most is they come to our houses to collect sputum."*

In addition to reports of negative behaviour from NTP staff during treatment, participants with TB also reported experiences of positive behaviour towards them as a motivating factor, which had encouraged them to take their medicines regularly. Supportive behaviour coupled with education about medication – including side effects, importance of adherence, and duration - during initial consultations was seen as an enabler for treatment engagement and adherence. During the FGD with NTP stakeholders, it was mentioned that providing adequate time to patients, proper counseling, and consultation enable people with TB disease to complete their treatment and get cured. This was perceived to be enhanced by community outreach activities by community mobilisers and female community health volunteers to ensure patients had the best opportunity to achieve treatment success:

> **FGD with female with TB, 60-65 years age group, female:** *"The doctor treated me like a normal patient, cared for me, asked how I was feeling and gave me medicine."*

Furthermore, during the FGD with people with TB, participants mentioned the necessity of patient-centric treatment services such as taking TB-medications at home instead of daily visits to the DOTS centers, which is often time consuming.

FGD with female diagnosed with TB, 45-50 years age group, female: *"It's good to bring medicine at home. Sometimes, we have work at the time when we have to go to take medicines."*

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STUDY PROTOCOL

REVISED Research protocol for a mixed-methods study to characterise and address the socioeconomic impact of accessing TB diagnosis and care in Nepal [version 2; peer review: 2 approved]

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Abstract

Background: WHO's 2015 End TB Strategy advocates social and economic (socioeconomic) support for TB-affected households to improve TB control. However, evidence concerning socioeconomic support for TB-affected households remains limited, especially in low-income countries.

Protocol: This mixed-methods study in Nepal will: evaluate the socioeconomic impact of accessing TB diagnosis and care (Project 1); and create a shortlist of feasible, locally-appropriate interventions to mitigate this impact (Project 2). The study will be conducted in the Chitwan, Mahottari, Makawanpur, and Dhanusha districts of Nepal, which have frequent TB and poverty.

The study population will include: approximately 200 people with TB (Cases) starting TB treatment with Nepal's National TB Program and 100 randomly-selected people without TB (Controls) in the same sites (Project 1); and approximately 40 key in-country stakeholders from Nepal including people with TB, community leaders, and TB healthcare professionals (Project 2).

Open Peer Review

Reviewer Status ✔ ✔

	Invited Reviewers	
	1	**2**
version 2 (revision) 16 Jun 2020	✔ report	✔ report
version 1 05 Feb 2020	? report	? report

1. **Delia Boccia** [ID], London School of Hygiene and Tropical Medicine, London, UK

2. **Priya B. Shete**, University of California San Francisco, San Francisco, USA

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During Project 1, visits will be made to people with TB's households during months 3 and 6 of TB treatment, and a single visit made to Control households. During visits, participants will be asked about: TB-related costs (if receiving treatment), food insecurity, stigma; TB-related knowledge; household poverty level; social capital; and quality of life.

During Project 2, stakeholders will be invited to participate in: a survey and focus group discussion (FGD) to characterise socioeconomic impact, barriers and facilitators to accessing and engaging with TB care in Nepal; and a one-day workshop to review FGD findings and suggest interventions to mitigate the barriers identified.

Ethics and dissemination: The study has received ethical approval. Results will be disseminated through scientific meetings, open access publications, and a national workshop in Nepal.

Conclusions: This research will strengthen understanding of the socioeconomic impact of TB in Nepal and generate a shortlist of feasible and locally-appropriate socioeconomic interventions for TB-affected households for trial evaluation.

Keywords
Tuberculosis, poverty, catastrophic costs, socioeconomic support, social protection, healthcare access, Nepal

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REVISED **Amendments from Version 1**

In response to the reviewers' constructive comments, we have updated the following:

1. Provided more detail concerning coding methods for Project 2
2. Provided clarification concerning the selection and recruitment of controls, including limitations and weaknesses in this method
3. Included a conceptual framework that informed the study design and analysis (new Figure 3)
4. Included a logic model on the development of the socioeconomic intervention, in line with MRC methods (new Figure 4)
5. Clarified on data collection relating to social protection

These comments have been helpful in improving the protocol and we are grateful to the reviewers for their time and expertise.

Any further responses from the reviewers can be found at the end of the article

Introduction

Tuberculosis (TB) disease, which kills 1.5 million people annually, is driven by poverty[1]. Having TB disease can also worsen impoverishment through loss of income and costs of accessing care[2–5]. Such costs can become "catastrophic", leading patients to abandon treatment, develop drug-resistance, and die[6]. WHO's 2015 End TB Strategy advocates elimination of catastrophic costs and provision of socioeconomic support for TB-affected households[5]. Nevertheless, there is minimal evidence concerning the ideal interventions to realise this policy change[6–10]. This research will generate preliminary evidence to fill this knowledge gap in a low-income country: Nepal. The findings will inform a randomised controlled trial of socioeconomic support for TB-affected households in Nepal.

Research from Peru has demonstrated that the severe socioeconomic impact of TB can lead to catastrophic costs (defined by WHO as >20% of a household's annual income)[6]. The same team also demonstrated that socioeconomic interventions for TB-affected households can mitigate catastrophic costs (Figure 1a), improve TB preventive therapy uptake (Figure 1b), and increase TB treatment success (Figure 1c)[11–15].

However, despite these encouraging findings, Peru is a middle-income country with a strong TB program and existing national cash-transfer schemes. To make this research replicable and applicable in diverse settings, interventions similar to those in Peru need to be adapted to other country contexts, especially low-income countries (LICs) with less developed social protection schemes and high TB burden. One such country is Nepal.

The estimated incidence of TB in Nepal is 154/100,000 people with 45,000 cases of TB being notified. Amongst these cases, there were 6,800 TB-related deaths. Multi-drug resistance (MDR) rates were 2.2% in new cases and 15% among retreatment

cases. Importantly, despite good treatment success rates overall of more than 90% reported in Nepal, there remain shortcomings in TB care: treatment success rates were 70% for patients with MDR-TB and only 9% for those with HIV-TB co-infection; and accessibility of TB care remains low with treatment coverage of 70%[16].

The poor treatment coverage in Nepal may, in part, be due to the financial impact on TB-affected households, which is estimated to be high[17]. Responding to this estimated burden, the Nepal National TB Programme (NTP) national strategic plan for 2016–2021 identifies provision of a support package to TB-affected households (specifically targeting MDR-TB-affected households) as a priority aim for the country with the goal of reducing catastrophic costs. There is currently limited evidence concerning the potential acceptability, impact, or cost-effectiveness of such a package, with which to inform and guide this policy decision. A cohort study has suggested that, during their illness, TB patients in Nepal experience decreased income and the total costs of accessing free TB treatment equate to nearly one quarter of annual household income[17]. Further studies in Nepal have shown that clinic fees make up the largest proportion of direct costs and that TB patients who are poorer, are migrants, or are from rural areas, experience a disproportionate burden of total costs[18–20]. It is vital that vulnerable TB patient households most at risk of incurring TB-related costs are identified in order to prevent and cure TB and mitigate further impoverishment and its consequences. In non-randomized studies, incurring higher TB-related costs and not receiving education about TB have both been found to be associated with worse TB treatment adherence and adverse TB treatment outcomes[18,21]. Therefore, the financial impact of having TB disease in Nepal constitutes a challenge to achieving TB control and elimination.

To date, no study of TB-affected households' costs in Nepal has been performed using the standardised global methodology for measuring costs related to accessing and engaging with TB care: the WHO TB Patient Costs Survey[22,23]. The studies above collected data at only one time point rather than repeated time points (e.g. cross-sectional rather than longitudinal) and did not robustly analyse the socioeconomic position, nutritional status, coping strategies, or linkage to social protection of TB-affected households. There have been no trials of socioeconomic support for TB-affected households in Nepal but formative qualitative analysis and a non-randomized pilot interventional study (offering education and financial support to patients with MDR-TB) suggested improved treatment outcomes[24].

However, studies reporting quantitative data alone will be insufficient to influence and change policy. Interaction with and among stakeholders has been described as the key facilitator for knowledge translation and evidence-informed health policymaking[25]. These interactions can include policy dialogues between stakeholders to deliberate on a priority topic. Therefore, complementary to quantitative data, the focus group
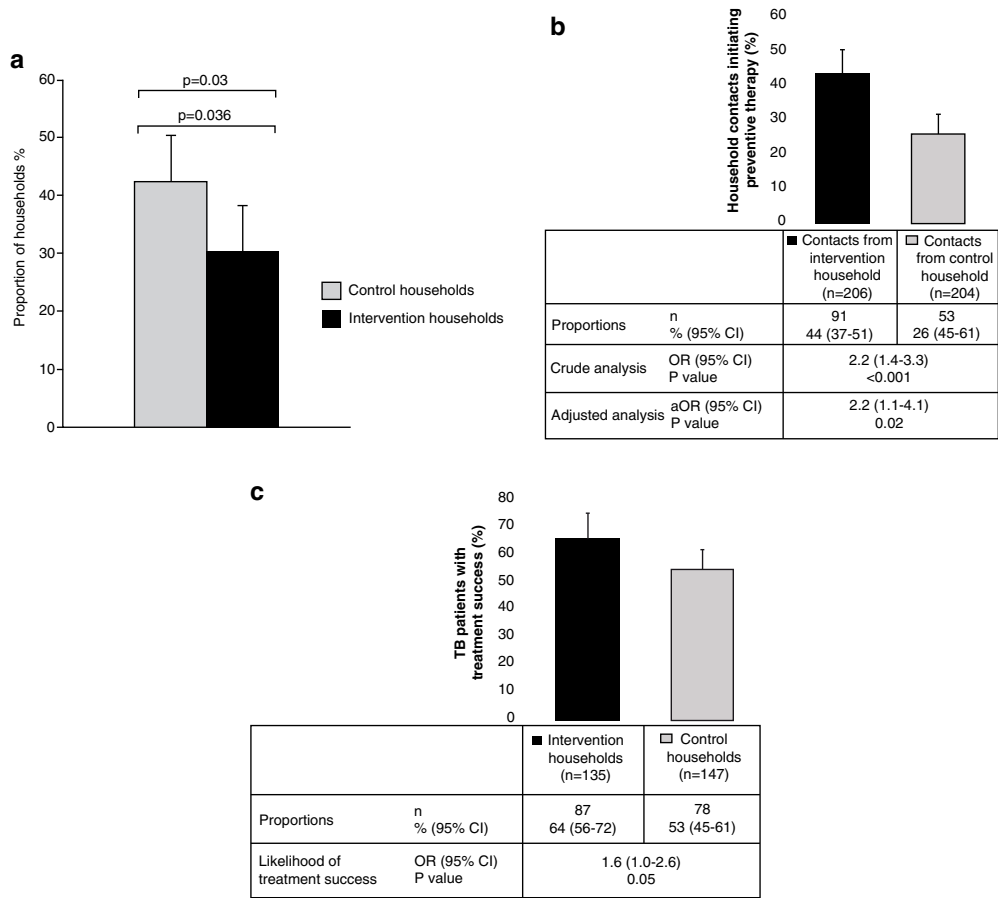
Figure 1. **a**) Catastrophic costs incurred by intervention (n=135) and control (n=147) TB-affected households of Callao, Peru. **b**) Preventive therapy initiation in household contacts of intervention (n=206) and control (n=204) TB-affected households of Callao, Peru. **c**) TB treatment success in patients from intervention (n=135) and control (n=147) TB-affected households of Callao, Peru. Part **a**) has been reproduced with permission from Wingfield *et al.*[13] Parts **b**) and **c**) have been reproduced with permission from Wingfield *et al.*[15].

discussions (FGDs) and workshop detailed within this protocol will aim to expand a policy dialogue on socioeconomic support for TB-affected households among key stakeholders in Nepal, from people with TB to community leaders to TB healthcare professionals. Policy dialogues represent knowledge translation to support the integration of research evidence with tacit knowledge of local health policy-makers to: inform future policy decisions in often complex and dynamic contexts; and foster proactive collaboration[26,27]. These elements will be critical for successful implementation of any future interventions[28].

In summary, this mixed-methods research will complement and extend the existing knowledge base on social determinants and consequences of TB. More specifically, the culmination of the research will be the creation of a shortlist of feasible and locally-appropriate socioeconomic interventions for TB-affected households for future randomized controlled trial evaluation in Nepal.

Protocol
Ethical statement
Ethical approval was granted from the University of Liverpool, UK, research ethics committee in April 2018 (approval number 2436) and then the National Health Research Council of Nepal (NHRC) research ethics committee in May 2018 (approval number 320/2018).

Participant information leaflets will be provided and written informed consents will be obtained from all study participants for Project 1 Interviews (separate consent forms and information leaflets for patients and healthy controls), Project 2 Surveys, FGDs, and the workshop. These documents are available in the Extended Data section attachments[29].

All medical records obtained from the Nepal NTP will be kept confidential. Practically, through liaison with NTP Project Staff (as already organised for IMPACT-TB), the PM, PI, and

RA will photocopy patient records from the Nepal NTP TB register obscuring the patient's identifiable details. Photocopies will be marked with that patient's unique study number identifier. No individual patients will be identifiable from publications resulting from this study.

Study design

This mixed-methods study was funded by a Wellcome Trust Seed Award in Science (awards provided to early-career researchers to develop a novel idea that will go on to form part of a larger grant application) and will be divided into two complementary projects. Project 1 consists of a cohort study characterising the socioeconomic impact of TB on TB-affected households and a nested case-control study examining the social determinants of TB. Project 2 consists of a mixed quantitative-qualitative cross-sectional study using surveys, FGDs and a workshop to identify the barriers and facilitators to accessing and engaging with TB diagnosis and care in Nepal and suggesting potential interventions to mitigate the socioeconomic impact and improve access and engagement. The study will take place within the infrastructure of the larger EU-Horizon 2020 funded "IMPACT-TB" project, which is a study evaluating proven TB active case-finding (ACF) interventions in Nepal and Vietnam (grant 733174, http://www. impacttbproject.org/).

Primary aims

The primary aim of Project 1 is to evaluate the socioeconomic impact on TB-affected households of accessing and engaging with TB diagnosis and care in Nepal and compare that impact in people with TB identified through standard passive case finding (PCF) versus ACF. The primary aim of Project 2 is to collaborate with key stakeholders in Nepal to create a shortlist of potentially feasible and locally-appropriate socioeconomic interventions to mitigate this impact.

Secondary aims

The secondary aim of Project 1 is to compare the social determinants of TB (including socioeconomic position, housing situation, knowledge about TB, comorbidities, quality of life, food security, and social capital) in people with TB versus people without TB from the same districts. The secondary aim of Project 2 is to collate the opinions of key stakeholders from diverse sectors about barriers and facilitators to accessing and engaging with TB care in Nepal.

An additional aim across the study is to generate a policy dialogue and form a collaborative research network to support development and implementation of a future randomised control trial of socioeconomic support for TB-affected households in Nepal.

Study setting

The study will take place within the infrastructure of the larger IMPACT-TB study, which works with a well-established international non-governmental organisation, Birat Nepal Medical Trust (BNMT), to implement ACF activities including sputum-microscopy camps and roll-out of GeneXpert

OMNI in four intervention and two control districts (with PCF only). The four districts are located in the central development region of Nepal and were selected for the IMPACT-TB project based on comparable populations and TB case detection rates (Figure 2).

The primary outcome of IMPACT-TB is the effect of ACF on early TB case detection and the study does not involve support packages for TB-affected households during treatment. This presents a unique opportunity for the complementary research described in this protocol to add value to IMPACT-TB, explore the socioeconomic impact of accessing TB care, and shortlist locally-driven strategies to reduce this impact.

Study population

Participant identification, recruitment and follow-up. During Project 1, approximately 200 people with TB (cases) consecutively recruited to Work Package 3 (WP3) of IMPACT-TB (Health Economic Analysis) in the four study sites will be further recruited to this study. 100 of these cases will have been diagnosed through ACF and 100 diagnosed through PCF. Whilst attending the NTP TB clinic, these people with TB will be invited to participate in this mixed-methods research with a separate written, informed consent (see Project 1 Interview Patient Consent Form, *Extended data*)[29]. During months three and six of their TB treatment, household visits will be conducted by BNMT project staff including community mobilisers.

Concurrently, 100 people without TB from the study sites (controls) will be invited to participate with written, informed consent (see Project 1 Interview Healthy Control Consent Form, *Extended data*)[29]. Due to constraints in study budget, duration, and field logistics, it will not be possible to age and sex match cases and controls nor to randomly select controls using geospatial or other household randomisation techniques. Therefore, a convenience sampling strategy was used. In order to be as widely representative of and generalisable to the background population as possible, following project team and community mobiliser discussions in the study sites, we opted to recruit control participants from diverse locations within the districts, which were attended by a broad demographic cross-section of the local population in terms of age, gender, and socioeconomic position. These diverse study site locations include: tea houses, primary healthcare centres, antenatal and immunization clinics, door-to-door visits following sputum camps (e.g. people who tested negative for TB), and public gathering places. Interviewers will visit the control recruitment locations at similar times of the morning and aim to consecutively recruit all individuals in attendance at that location. Similar numbers of participants from each recruitment location will be recruited until the sample size of 100 people without TB is reached. We acknowledge that convenience sampling may be associated with a higher likelihood of a non-generalisable control cohort than other techniques. To try to address this, the survey used to collect data from the controls has incorporated multiple questions concerning sociodemographic variables, including education level, occupation, amenities, and assets, from the most recent version of the Nepal Household Survey, which is publicly available. Descriptive

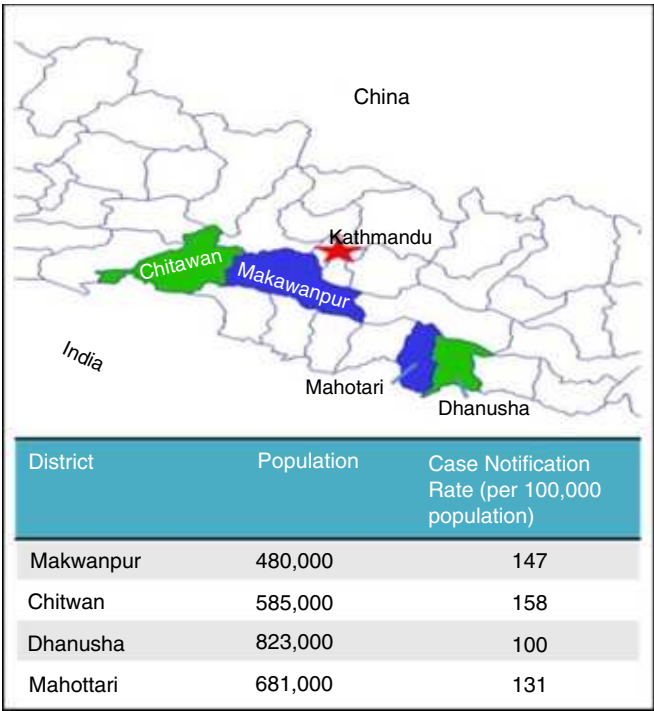| District	Population	Case Notification Rate (per 100,000 population)
Makwanpur	480,000	147
Chitwan	585,000	158
Dhanusha	823,000	100
Mahottari	681,000	131

Figure 2. Map, population, and TB case notification rate of the four study site districts. Data for population and TB cases notification rate shown is taken from the Nepal TB Centre 2018 report. The four study site districts are labelled and highlighted in blue and green.

analysis will evaluate whether the controls recruited are representative of the wider population in those districts through comparison of their sociodemographic data with respondents to the national survey in the same districts. Any differences between the control population and background population will then be highlighted transparently in corresponding research outputs and publications.

Project 1 inclusion criteria for Cases included: being a person with TB notified to the NTP and recruited to WP3 of the IMPACT-TB study; being aged 18 years or above; and giving verbal and written informed consent to participate. Project 1 exclusion criteria for Cases included: being under 18 years of age; being a person with TB not notified to the NTP and/or not recruited to WP3 of the IMPACT-TB study; being a person with TB notified to the NTP but with a recorded domiciliary address outside of the study site districts; and being unable or unwilling to give written and/or verbal informed consent to participate.

Project 1 inclusion criteria for Controls included: being 18 years or above with primary residence in the study site communities; not currently known to be a person with TB or have a member of the household currently known to be a person with TB (e.g. not diagnosed or notified or receiving TB treatment); and giving verbal and written informed consent to participate. Project 1 exclusion criteria for Controls included: being under

18 years of age; not having primary residence in the study site communities; known to be a person with TB or have a household member with TB currently (e.g. diagnosed and/or notified and/or receiving TB treatment); and being unable or unwilling to give verbal and written informed consent to participate.

To generate the population for Project 2, a literature review and desk-based scoping review will identify a list of key in-country stakeholders from Nepal from diverse groups including: civil-society representatives; community leaders; and TB healthcare professionals including NTP managers and multi-disciplinary staff. Approximately 50 stakeholders will be selected through purposive sampling and invited to participate in: a pre-FGD survey, FGD, and a one-day workshop. A subset of purposively sampled TB patients recruited to Project 1 (including those with multi-drug resistant TB) will be among the stakeholders invited to participate.

Project 2 inclusion criteria include: being aged 18 years or above; belonging to a stakeholder group as defined above and/or identified during scoping exercise; and being able and willing to provide verbal and written, informed consent. Exclusion criteria for Project 2 are not meeting the inclusion criteria and/or being a person with TB who has not yet taken two weeks of TB treatment or is otherwise considered to still be infectious (e.g. MDR-TB with positive sputum smear or culture).

Sample size and statistical power. The sample size for Project 1 is approximately 200 Cases recruited to WP3 of the IMPACT-TB project and 100 Controls from the four study site districts. This sample size is opportunistic and pragmatic: related research suggests that data from 100 people with TB gives a representative spread of costs for a given context[30,31].

For Project 2, each FGD will consist of approximately eight stakeholders. The estimated number of FGDs at which information power (or saturation level) will be reached is six[12]. Thus, the sample size for Project 2 is approximately 40 stakeholder participants. We will invite 55 stakeholders as a contingency because we anticipate an attrition rate of 20–30% during the course of Project 2.

Given that this Seed Award research will be exploratory, preparatory (e.g. for the future trial), and does not include an intervention, no calculations of statistical power are required.

Study interventions
The study will not include any interventions or require any patient samples (e.g. blood / sputum / tissue).

Study activities
Broadly, the activities involved in the research will include interviews with Cases and Controls during household visits, and a pre-FGD survey, FGD, and workshop with key stakeholders.

During Project 1, the project team will support BNMT district coordinators, community mobilisers, and community volunteers to do household visits to approximately 200 Cases with TB (100 diagnosed through ACF and 100 through PCF) recruited to WP3 of the IMPACT-TB project. People with TB will receive two household visits, the first during month three of TB treatment and the second visit during month six of TB treatment (to correspond with treatment completion). For controls, a single household visit and interview will be done. The interviews will be structured (see Project 1 Interview, *Extended data*)[29] and gather data on: i) socioeconomic position, evaluated by a multi-dimensional poverty score[6,9,13,15] assessing dwelling characteristics, assets, and access to amenities; ii) household structure, including distribution of age, sex, and employment of household members; iii) food expenditure and security; iv) costs of engaging with TB care including direct costs (e.g. medicines, clinic visits, food, and travel) and indirect costs (e.g. lost income), which will be evaluated using an adapted version of WHO's TB Patient Costs Survey integrated into the interview[22,23]; v) coping strategies including dissaving (e.g. selling assets), schooldays lost, and temporary income-generating activities; vi) TB-related knowledge including understanding of transmission, prevention, and treatment of TB; vii) psychosocial situation evaluated through questions relating to social capital, quality of life, and stigma (Controls without TB will not be asked any questions about the impact that having TB disease has on their psychosocial situation); and viii) access and uptake of existing social protection schemes (whether TB-specific or TB-inclusive) and support for TB-affected households, evaluated through use of both closed ranking and open free-text questions to establish what socioeconomic and other support people with TB and their households receive or would like to receive.

Prior to implementation of household visits, the questionnaire will be translated from English into Nepali and then back-translated into English. It will be assessed by members of the study team and BNMT implementation staff before being piloted in approximately 10 patients. The questionnaire may subsequently be refined and questions deleted or added, depending on the pilot outcomes.

In addition to the above, Cases' TB treatment outcomes will be collated from NTP and IMPACT-TB data and their association with interview responses analysed. This will provide an exploratory analysis of the association of socioeconomic position, socioeconomic impact of having TB, and TB treatment outcomes. A comparison of the socioeconomic position of households of Cases and Controls will also be made.

Project 2 will use and develop mixed methods research techniques[10–15] to conduct a pre-FGD survey, FGDs, and workshop with approximately 40 key stakeholders in Nepal to identify the socioeconomic impact, barriers and facilitators to accessing and engaging with TB diagnosis and care. To inform the design of the FGDs and workshop, we created a conceptual framework for the barriers and facilitators to TB diagnosis and care, which was adapted from a World Health Organisation framework for medication adherence (Figure 3)[32].

A short individual pre-FGD survey (see Project 2 Survey, *Extended data*)[29] will be provided to participants prior to the initiation of an FGD. The survey will detail: participants' demographics; the stakeholder group to which the participant belongs; and their opinions on community, patient, health system, existing social protection schemes, and wider obstacles to achieving successful TB treatment outcomes.

The FGDs will be semi-structured and incorporate open-ended questions concerning barriers and facilitators to accessing and engaging with TB care in Nepal, and existing platforms and potential opportunities to mitigate these barriers including social protection schemes (see Project 2 Focus Groups, *Extended data*)[29]. The FGDs will be conducted with separate groups of approximately eight key stakeholders. Stakeholders will be invited to participate according to their background (e.g. people with TB will be asked to participate in one FGD, and TB healthcare professionals will be asked to participate in another separate FGD). Towards the end of each FGD, participants will be asked to privately rank the top three most important barriers or facilitators to accessing TB diagnosis and care identified by the group during the FGD, and these responses will be collated for each FGD and across FGDs. The FGDs will be moderated by members of the project team trained in qualitative methods including conducting FGDs. The discussions will be audio recorded in Nepali language, translated into English, and back-translated by a translator who is not part of the project team. Each FGD group will be asked to elect a representative to feed their group's outputs back at the subsequent workshop.

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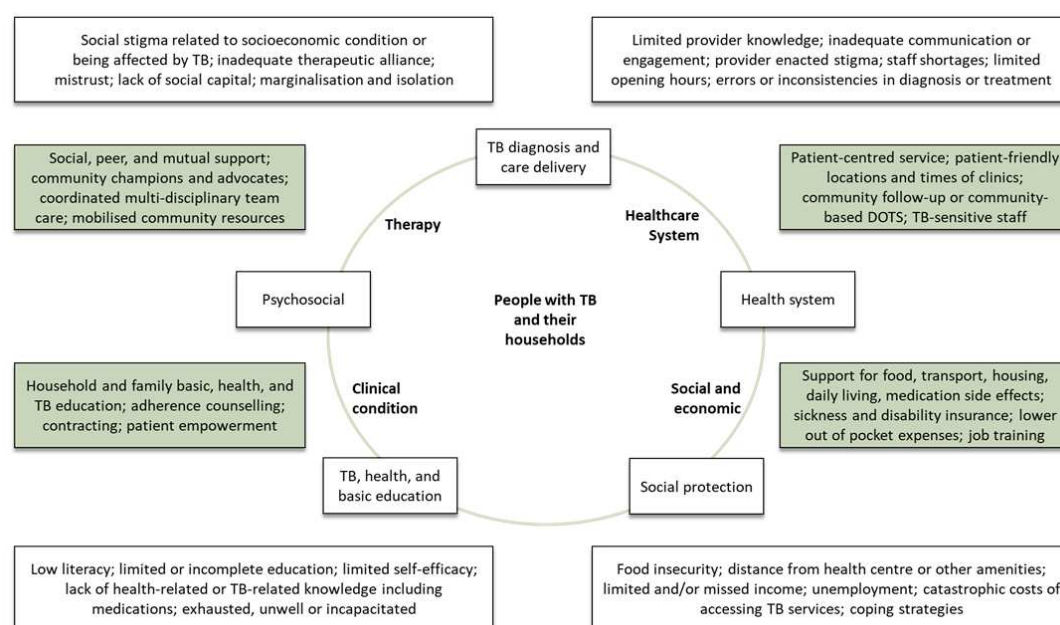
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Figure 3. Conceptual framework: the barriers and facilitators to TB diagnosis and care. The central circle, which contains dimensions of medication adherence adapted from the World Health Organization[33], is surrounded by the five main categories of relevant potential interventions. The factors that may promote access to and engagement with TB services (facilitators) are shown in green boxes and factors that may threaten access and engagement (barriers) are shown in white boxes. Therapeutic alliance refers to strong provider-patient relationships. Although Project 2 would gather data on all five dimensions, the psychosocial and social protection dimensions were perceived by the project team to be most pertinent to development of the socioeconomic intervention and were selected for further focus and discussion during Project 2's workshop.

The final activity in Project 2 will be a one-day workshop bringing together the 40 key stakeholders (see Project 2 Workshop, *Extended data*)[29]. The morning section of the workshop will consist of interactive presentations from the project team and stakeholder group representatives (including leaders of national social protection schemes in Nepal), and discussions exploring and validating the barriers and opportunities identified during the pre-FGD survey and interviews during FGDs. The afternoon section of the workshop will consist of multi-sectoral working groups (≤10 diverse stakeholders) developing a shortlist of potential socioeconomic interventions for TB-affected households in Nepal. The shortlist is not intended to consist of defined, unalterable packages, which are immediately ready for trial implementation. Rather, the potential interventions selected are intended to consist of what stakeholders perceive to be key elements or ingredients of psychosocial and economic support for TB-affected households, which are feasible and locally-appropriate to the Nepalese context. The interventions will be presented to the group including strengths, weaknesses, and potential sources of funding for implementation.

The activities involved in this research form part of a process to develop and evaluate a complex, socioeconomic support intervention. In line with the Medical Research Council's guidance on process evaluation of complex interventions, we developed a logic model to illustrate the developmental stages of the intervention (Figure 4)[32].

This Wellcome research will aim to achieve the short-term outcomes described in the logic model. If follow-on funding is successfully obtained, the process to develop and implement the intervention and achieve the long-term outcomes will continue beyond this Wellcome research. This will include adaptation, piloting, and then large-scale randomised trial evaluation of the refined intervention.

Outcomes to be measured
This exploratory Wellcome Trust funded Seed Award in Science research in four districts of Nepal will:

i. characterise social determinants of TB by comparing poverty level, education level, food security, and other socioeconomic factors of people with TB (Cases) versus people without TB (Controls);

ii. provide new insight into the barriers, facilitators, and socioeconomic impact of being ill with TB and accessing TB diagnosis and care, and compare this in Cases diagnosed by ACF versus PCF; and
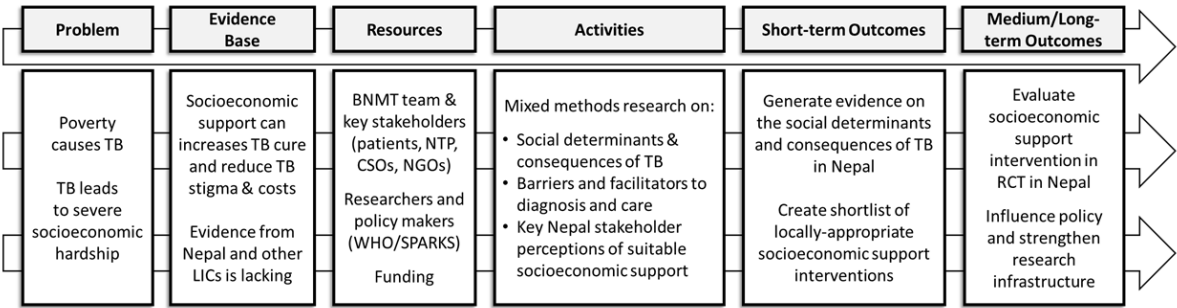
Problem	Evidence Base	Resources	Activities	Short-term Outcomes	Medium/Long-term Outcomes
Poverty causes TB TB leads to severe socioeconomic hardship	Socioeconomic support can increases TB cure and reduce TB stigma & costs Evidence from Nepal and other LICs is lacking	BNMT team & key stakeholders (patients, NTP, CSOs, NGOs) Researchers and policy makers (WHO/SPARKS) Funding	Mixed methods research on: • Social determinants & consequences of TB • Barriers and facilitators to diagnosis and care • Key Nepal stakeholder perceptions of suitable socioeconomic support	Generate evidence on the social determinants and consequences of TB in Nepal Create shortlist of locally-appropriate socioeconomic support interventions	Evaluate socioeconomic support intervention in RCT in Nepal Influence policy and strengthen research infrastructure

Figure 4. Logic model for research in Nepal to develop a locally-appropriate socioeconomic support intervention for TB-affected households. Abbreviations: CSOs = Civil Society Organisations; NGOs = Non-governmental organisations; NTP = National Tuberculosis Programme; WHO = World Health Organisation; SPARKS = Social Protection Action Research and Knowledge Sharing network (www.sparks.ki.se)

iii. generate a community-led shortlist of the most feasible, equitable, and locally-appropriate socioeconomic interventions for TB-affected households to mitigate the socioeconomic impact of TB.

Data collection and management

During the implementation of Project 1, information will be collected by BNMT district coordinators, community volunteers, and community mobilisers with support from the project team during visits to recruited patient households. This information includes but is not limited to socioeconomic, health, psychosocial, and behavioural data. This data will be collected on paper due to digital collection (e.g. on tablets or mobile phones) having issues with security and feasibility. The data of consenting TB patients will subsequently be linked with data from NTP's TB patient register as part of its routine surveillance data collection at the intervention and control areas, with pre-existing permission from the NTP.

During Project 2, key stakeholders identified by the scoping exercise will complete a short pre-FGD survey in person, participate in an FGD, and participate in a one-day workshop.

All paper-based copies, including medical records, informed consent forms and participant information leaflets, will contain only a unique study identifier for each participant. These documents will be stored in a locked room in the BNMT office. Data will be checked for consistency and completeness by the project manager and double-checked by the PI prior to entering into an encrypted access database. The database will be managed by the data management team at KNCV TB Foundation in The Netherlands in line with data collected during the IMPACT-TB project. The data will be protected by KNCV on a password-secured server with availability limited to only key members of the study team when required for analysis.

Data analysis and statistical plan

The quantitative data collected during the household visits of Project 1 will be analysed using simple descriptive statistics.

Continuous costs data will be summarised by their arithmetic means and their 95% confidence intervals whether the data is Gaussian or non-Gaussian, because this approach is considered to be robust for health economics data analysis[6,34–36]. Furthermore, because of the skewed nature of some expenditure data, median values may be zero or close to zero limiting the descriptive usefulness of presenting median values. As described in the PI's previous research[6], any direct expenses, lost income, or annual income recorded as "zero" or missing will be replaced with the mean cost of each costs category, i.e. mean direct costs or lost income. The local currency, Nepalese rupee, will be converted into United States Dollars (conversion rate and date estimated through Oanda at time of data collection). Categorical data will be summarised as proportions with 95% confidence intervals.

With regards to analysis of household income and expenditure, the WHO TB Patients Costs Survey methods will be followed. In order to evaluate the optimal analytical strategy for costs data in Nepal, the analysis will compare and contrast the different approaches used in the WHO Survey to estimate household income (self-reported household consumption; self-reported household expenditure; self-reported household income; and estimated income based on household asset ownership and dwelling characteristics) and lost income (output approach of reported income pre- and during TB versus human capital approach of multiplying hours of work lost by hourly rate or daily in rate in cases of hospitalised patients).

Social determinants of TB including sociodemographic characteristics, socioeconomic position, stigma and social capital levels, and TB-related knowledge will be compared between ACF patients, PCF patients, and controls using Chi-squared test, Pearson's test, one-way ANOVA, and multiple logistic regression models where appropriate. No comparison will be made between patients and controls concerning healthcare expenditure as this data was not collected from controls. Statistical analysis will be performed using the statistical software package STATA v13.1 (Statacorp, TX, USA).

The Framework method of thematic analysis will be used to manage and analyse data from Project 2 via the NVivo qualitative software package (Version 12) as per published social policy and tuberculosis research[21–24]. Specifically, two researchers (KD and TW) will familiarize themselves with the data through successive reading of transcripts; use both open and closed first order data coding to label data within NVivo; group codes together into a second order codebook of themes and sub-themes. Themes and subthemes will then be further stratified by third order coding to the level at which they predominantly occurred (e.g. individual or household level, health systems level, community level, or governmental level). The primary approach to codes, themes, and sub-themes will be deductive (top down), being informed by our conceptual framework and preliminary analysis of data from Project 1 relating to the social determinants and consequences identified. As coding continues, a secondary approach will integrate inductive (bottom up) coding in order to be iterative, responsive, and flexible as further data becomes available and is collated following each successive FGD.

Plans for dissemination of study findings

The intended research outputs of this work are to: i) present the interim and final findings at the International Union Against TB and Lung Disease in October 2019 and October 2020, respectively; ii) publish, by June 2020, at least two papers in high-impact, peer-reviewed journals concerning the socioeconomic impact of accessing TB care in Nepal and the collaborative development of a shortlist of locally-appropriate socioeconomic interventions in Nepal; iii) feedback findings to the IMPACT-TB team, key stakeholders (including NTP and TB civil-society), the SPARKS (Social Protection Action Research and Knowledge Sharing) network, and WHO; iv) consolidate a close collaboration, good working relationship, and strong research infrastructure between BNMT and the NTP; and iv) to develop the protocol for a robust, large-scale randomised controlled trial to evaluate socioeconomic support for TB-affected households using the evidence generated by this mixed-methods study.

Study status

Data collection for Project 1 during household visits began in May 2018 and is nearly complete at the time of writing with only TB treatment outcome data still being collected. Data collection for Project 2 during pre-FGD surveys and FGDs began in August 2018 and was completed in July 2019. The national workshop with key stakeholders was conducted on 11 and 12 September 2019 in Kathmandu, Nepal.

Data analysis, write-up, and dissemination of findings will begin in February 2020.

Discussion

The overarching pledge of the Sustainable Development Goals (SDGs) is to "leave no one behind". In 2018, over 3 million people with tuberculosis (TB) were not diagnosed, not notified, or their quality of care was unknown. In the same year, 1.5 million people with TB died and nearly a fifth of people diagnosed with TB did not have a successful treatment outcome[16]. While millions of people with TB continue to be left behind, the SDG pledge is far from being realised.

Despite renewed interest in addressing social determinants of tuberculosis, there remain stark global inequalities in disease burden and access to TB care[8]. At a population level, LICs bear the highest TB prevalence[16]. At an individual level, people with TB are often vulnerable, impoverished, and their households suffer disproportionate financial shock due to their illness[6,13]. To eliminate such gross disparity, SDG slogans must be turned into actions.

WHO's 2015 End TB Strategy acknowledges the need to reduce inequalities in TB prevention and care. A key component of Pillar 2 (Bold policies and supportive systems) of the strategy is social protection and poverty alleviation to reduce catastrophic costs of TB-affected households and improve TB outcomes[2]. However, there is minimal evidence to guide this policy change.

This mixed-methods will generate evidence concerning the socioeconomic position of TB-affected households, the impact that having TB disease has on that position and explore the coping strategies that households use to mitigate the impact of the disease. Moreover, this research will: use methods to measure costs of TB-affected households to which members of the study team contributed as part of the WHO Task Force on Catastrophic Costs of Tuberculosis; and provide the first known comparison of the socioeconomic impact of TB on people with TB diagnosed through PCF versus ACF. The case-control element of Project 1 will allow comparison of the sociodemographic characteristics, socioeconomic position, stigma and social capital levels, and TB-related knowledge between people with TB (Cases) and people without TB (Controls).

The further significance of the study lies in its development of a shortlist of a locally-generated intervention to provide socioeconomic support to TB-affected households. Through collaboration with diverse stakeholders in Nepal from patients to NTP managers to civil-society representatives, it is hoped that the shortlist created will feature interventions that are both locally-appropriate and feasible. Furthermore, this tight collaboration should aid design and implementation of a larger, randomised-controlled trial, and also future translation of research findings into national policy in Nepal. Beyond the national impact, these findings and those of the future trial will also offer evidence for scale-up of socioeconomic support in other resource-limited countries with a high TB burden. Complementary to pills and tests, this socioeconomic support will be an essential part of eliminating TB by 2050.

Conclusions

This mixed-methods study will fill this existing evidence gap by examining the costs of accessing TB care at a household level through longitudinal application of an adapted WHO TB Patient Costs Survey throughout TB treatment. This data will be enriched by collecting complementary data on household socioeconomic position, coping strategies, food insecurity,

TB knowledge, social capital, and quality of life. The findings will then feed into a short survey and semi-structured FGDs with key stakeholders in Nepal to consider, at a local, regional, and national level, what are the leading barriers and facilitators to accessing and engaging in TB care, and what might be the most locally-appropriate interventions to address the socioeconomic impact of having TB disease.

Data availability
Underlying data
No data are associated with this article

Extended data
Open Science Framework: Research protocol for a mixed-methods study to characterise and address the socioeconomic impact of accessing TB diagnosis and care in Nepal. https://doi.org/10.17605/OSF.IO/6TC4F[29]

This project contains the following extended data:

- Final_Wellcome Seed Award Project 1 Patient Interview v8.pdf

- Final Patient _Wellcome Seed Award Project 1 Consent Form NEPALI.pdf

- Final Patient _Wellcome Seed Award Project 1 Interview v8 NEPALI.pdf

- Final Patient _Wellcome Seed Award Project 1 Patient Info Leaflet NEPALI.pdf

- Wellcome Seed Award Project 1 Patient Consent Form.pdf

- Wellcome Seed Award Project 1 Patient Information Leaflet ENGLISH.pdf

- Wellcome Seed Award Project 2 Survey and Focus Group Consent Form.pdf

- Wellcome Seed Award Project 2 Survey and Focus Group Participant Information Leaflet.pdf

- Wellcome Seed Award Project 2 Survey v4 20180525.pdf

- Wellcome Seed Award Project 2 Workshop Consent Form.pdf

- Wellcome Seed Award Project 2 Workshop Participant Information Leaflet.pdf

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

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Wellcome Open Research

Wellcome Open Research 2020, 5:19 Last updated: 11 SEP 2020

Open Peer Review

Current Peer Review Status: ✓ ✓

Version 2

Reviewer Report 11 September 2020

https://doi.org/10.21956/wellcomeopenres.17629.r39129

✓ **Delia Boccia** (iD)

Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, UK

I confirm that the authors have appropriately and convincingly addressed all my comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Social determinants of TB, social protection.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 07 August 2020

https://doi.org/10.21956/wellcomeopenres.17629.r39128

✓ **Priya B. Shete**

University of California San Francisco, San Francisco, CA, USA

No further comments. I appreciate the authors attention to my previous suggestions and feel that they have taken care to improve the paper with these details.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Implementations science, tuberculosis, social protection.

Wellcome Open Research

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 26 February 2020

https://doi.org/10.21956/wellcomeopenres.17181.r37807

Priya B. Shete
University of California San Francisco, San Francisco, CA, USA

The major area for improvement with this protocol would be more discussion in the methods about how the qualitative data will be coded and subsequently used to then generate a menu of feasible options for pilot implementation and evaluation to overcome targeted barriers. I would appreciate further discussion of the conceptual framework that informs the data collection tools/interview guides in Project 2. As Project 2 is particularly important for identifying targeted barriers and facilitators of care for future interventions, I would also like to see what deterministic framework or model is being used to develop those interventions. Any reference to frameworks from implementation science or social epidemiology would perhaps be helpful.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Implementations science, tuberculosis, social protection.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Wellcome Open Research

Author Response 11 Jun 2020

Tom Wingfield, Liverpool School of Tropical Medicine, UK

We are indebted to Reviewer 2 for these excellent comments, which we have addressed and which we now believe serve to strengthen the protocol. It is important to note that this Wellcome Trust funded study began in 2018 and data collection had already been completed prior to submission of the protocol to Wellcome Open Research. When the research team became aware of Wellcome Open Research, we approached the editorial team who advised that it was still appropriate to submit a study protocol despite data collection being complete. While this is important for critical peer review of the protocol it does, unfortunately, mean that we are unable to adjust parts of the protocol that have been completed and written-up including, for example, the coding strategy.

However, we were able to address Reviewer 2's comments by providing further detail about the coding techniques used and necessary clarification about how the quantitative and qualitative data fed informed outline of the design of the socioeconomic support interventions. In addition, we omitted to include the conceptual framework and logic model that we employed for this research, which we have now rectified and, again, this has helped to improve the protocol and will also be included in subsequent, related publications. Thank you to the Reviewer for their constructive review.

Study activities section: "Project 2 will use and develop mixed methods research techniques [10–15] to conduct a pre-FGD survey, FGDs, and workshop with approximately 40 key stakeholders in Nepal to identify the socioeconomic impact, barriers and facilitators to accessing and engaging with TB diagnosis and care. To inform the design of the FGDs and workshop, we created a conceptual framework for the barriers and facilitators to TB diagnosis and care, which was adapted from a World Health Organisation framework for medication adherence (Figure 3).[30]

(PLEASE SEE FIGURE IN UPDATED PROTOCOL)

Figure 3. Conceptual framework: the barriers and facilitators to TB diagnosis and care.

The central circle, which contains dimensions of medication adherence adapted from the World Health Organization[30], is surrounded by the five main categories of relevant potential interventions. The factors that may promote access to and engagement with TB services (facilitators) are shown in green boxes and factors that may threaten access and engagement (barriers) are shown in white boxes. Therapeutic alliance refers to strong provider-patient relationships. Although Project 2 would gather data on all five dimensions, the psychosocial and social protection dimensions were perceived by the project team to be most pertinent to development of the socioeconomic intervention and were selected for further focus and discussion during Project 2's workshop."

Study activities section: "The final activity in Project 2 will be a one-day workshop bringing together the 40 key stakeholders (see Project 2 Workshop, Extended data) [29] . The morning section of the workshop will consist of interactive presentations from the project team and stakeholder group representatives (including leaders of national social protection schemes

in Nepal), and discussions exploring and validating the barriers and opportunities identified during the pre-FGD survey and interviews during FGDs. The afternoon section of the workshop will consist of multi-sectoral working groups (≤10 diverse stakeholders) developing a shortlist of potential socioeconomic interventions for TB-affected households in Nepal. The shortlist is not intended to consist of defined, unalterable packages, which are immediately ready for trial implementation. Rather, the potential interventions selected are intended to consist of what stakeholders perceive to be key elements or ingredients of psychosocial and economic support for TB-affected households, which are feasible and locally-appropriate to the Nepalese context. The interventions will be presented to the group including strengths, weaknesses, and potential sources of funding for implementation.

The activities involved in this research form part of a process to develop and evaluate a complex, socioeconomic support intervention. In line with the Medical Research Council's guidance on process evaluation of complex interventions, we developed a logic model to illustrate the developmental stages of the intervention (Figure 4).[31]

(PLEASE SEE FIGURE IN UPDATED PROTOCOL)

Figure 4. Logic model for research in Nepal to develop a locally-appropriate socioeconomic support intervention for TB-affected households.

This Wellcome research will aim to achieve the short-term outcomes described in the logic model. If follow-on funding is successfully obtained, the process to develop and implement the intervention and achieve the long-term outcomes will continue beyond this Wellcome research. This will include adaptation, piloting, and then large-scale randomised trial evaluation of the refined intervention."

Data analysis and statistical plan section: "The Framework method of thematic analysis will be used to manage and analyse data from Project 2 via the NVivo qualitative software package (Version 12) as per published social policy and tuberculosis research [21–24] *. Specifically, two researchers (KD and TW) will familiarize themselves with the data through successive reading of transcripts; use both open and closed first order data coding to label data within NVivo; group codes together into a second order codebook of themes and sub-themes. Themes and subthemes will then be further stratified by third order coding to the level at which they predominantly occurred (e.g. individual or household level, health systems level, community level, or governmental level). The primary approach to codes, themes, and sub-themes will be deductive (top down), being informed by our conceptual framework and preliminary analysis of data from Project 1 relating to the social determinants and consequences identified. As coding continues, a secondary approach will integrate inductive (bottom up) coding in order to be iterative, responsive, and flexible as further data becomes available and is collated following each successive FGD."*

Competing Interests: None.

Supplemental material

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Wellcome Open Research

Reviewer Report 21 February 2020

https://doi.org/10.21956/wellcomeopenres.17181.r37826

Delia Boccia

Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, UK

This paper describes in detail the protocol of a study aiming at understanding better the social determinants of TB as well as the financial consequences of TB. The study is very relevant: it is epidemiologically sound and the rational for it is clear and strongly supported by the existing literature.

There are two gaps that – in my opinion – should be better filled to make the protocol stronger:

1. The selection of controls for the case-control study. This requires a further dissertation about how practically controls will be selected and how the authors are planning to minimise selection biases. Authors explain why an age-sex matching approach could not be adopted; however, the description of the selection of controls remain elusive which triggers questions like: what sampling strategy will be adopted? How randomness as well as representativeness will be respected? General population controls may be a good option for answering questions around the social determinants of TB; however, I am not convinced they are also the best choice when looking at catastrophic health expenditures. Obviously healthy controls will be better off and wonder whether this second research question could be not better addressed by selecting hospital controls or among people who are ill-affected (albeit not from TB). I suggest the authors to better justify their choices and discuss why alternative options have been dismissed.

2. The qualitative work should include a stronger effort to address not just barriers to access to TB care, but also barriers to existing social protection schemes experienced by TB-patients. It feels like a gigantic missed opportunity if not embedded into the existing plans. If indeed the authors are planning to ascertain existing social protection options for TB patients and access can be maximised, then this should be explicitly stated in the paper.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Partly

Are sufficient details of the methods provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?

Wellcome Open Research

Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Social determinants of TB, social protection.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 11 Jun 2020

Tom Wingfield, Liverpool School of Tropical Medicine, UK

1. The selection of controls for the case-control study. This requires a further dissertation about how practically controls will be selected and how the authors are planning to minimise selection biases. Authors explain why an age-sex matching approach could not be adopted; however, the description of the selection of controls remain elusive which triggers questions like: what sampling strategy will be adopted? How randomness as well as representativeness will be respected? General population controls may be a good option for answering questions around the social determinants of TB; however, I am not convinced they are also the best choice when looking at catastrophic health expenditures. Obviously healthy controls will be better off and wonder whether this second research question could be not better addressed by selecting hospital controls or among people who are ill-affected (albeit not from TB). I suggest the authors to better justify their choices and discuss why alternative options have been dismissed.

Author response: Thank you for raising this important issue with which we wholeheartedly agree. It is important to note that this Wellcome Trust funded study began in 2018 and data collection had already been completed prior to submission of the protocol to Wellcome Open Research. When the research team became aware of Wellcome Open Research, we approached the editorial team who advised that it was still appropriate to submit a study protocol despite data collection being complete. While this is important for critical peer review of the protocol it does, unfortunately, mean that we are unable to adjust the protocol including, for example, sampling strategies at this stage. However, we have attempted to respond to the reviewer's comments about sampling strategy and control population randomness and representativeness. We have also made it clearer that the data from controls will only be used to characterise social determinants of TB and there will be no analysis comparing health expenditure in controls vs people with TB, which we agree would be inappropriate with general population controls.

Study population section: "Concurrently, 100 people without TB from the study sites (controls) will be invited to participate with written, informed consent (see Project 1 Interview Healthy Control Consent Form, Extended data) [29] *. Due to constraints in study budget, duration, and field logistics, it will not be possible to age and sex match cases and controls nor to randomly select controls using geospatial or other household randomisation techniques. Therefore, a convenience sampling strategy was used. In order to be as widely representative of and generalisable to the background population as*

possible, following project team and community mobiliser discussions in the study sites, we opted to recruit control participants from diverse locations within the districts, which were attended by a broad demographic cross-section of the local population in terms of age, gender, and socioeconomic position. These diverse study site locations include: tea houses, primary healthcare centres, antenatal and immunization clinics, door-to-door visits following sputum camps (e.g. people who tested negative for TB), and public gathering places. Interviewers will visit the control recruitment locations at similar times of the morning and aim to consecutively recruit all individuals in attendance at that location. Similar numbers of participants from each recruitment location will be recruited until the sample size of 100 people without TB is reached. We acknowledge that convenience sampling may be associated with a higher likelihood of a non-generalisable control cohort than other techniques. To try to address this, the survey used to collect data from the controls has incorporated multiple questions concerning sociodemographic variables, including education level, occupation, amenities, and assets, from the most recent version of the Nepal Household Survey, which is publicly available. Descriptive analysis will evaluate whether the controls recruited are representative of the wider population in those districts through comparison of their sociodemographic data with respondents to the national survey in the same districts. Any differences between the control population and background population will then be highlighted transparently in corresponding research outputs and publications."

"Data analysis and statistical plan section: "Social determinants of TB including sociodemographic characteristics, socioeconomic position, stigma and social capital levels, and TB-related knowledge will be compared between ACF patients, PCF patients, and controls using Chi-squared test, Pearson's test, one-way ANOVA, and multiple logistic regression models where appropriate. No comparison will be made between patients and controls concerning healthcare expenditure as this data was not collected from controls."

2. The qualitative work should include a stronger effort to address not just barriers to access to TB care, but also barriers to existing social protection schemes experienced by TB-patients. It feels like a gigantic missed opportunity if not embedded into the existing plans. If indeed the authors are planning to ascertain existing social protection options for TB patients and access can be maximised, then this should be explicitly stated in the paper.

Author Response: We agree entirely with the reviewer and are grateful for this apposite point. Within the confines of not being able to alter the protocol given that data collection is now completed, we have clarified this important issue in the protocol to explain that, across Projects 1 and 2, quantitative and qualitative data concerning social protection in Nepal was gathered, including the coverage, target recipients, barriers to access, and limitations of existing packages.

Study activities section: "The interviews will be structured (see Project 1 Interview, Extended data) [29] and gather data on: i) socioeconomic position, evaluated by a multi-dimensional poverty score [6, 9, 13, 15] assessing dwelling characteristics, assets, and access to amenities; ii) household structure, including distribution of age, sex, and employment of household members; iii) food expenditure and security; iv) costs of engaging with TB care including direct costs (e.g. medicines, clinic visits, food, and travel) and indirect costs (e.g.

lost income), which will be evaluated using an adapted version of WHO's TB Patient Costs Survey integrated into the interview [22, 23] ; v) coping strategies including dissaving (e.g. selling assets), schooldays lost, and temporary income-generating activities; vi) TB-related knowledge including understanding of transmission, prevention, and treatment of TB; vii) psychosocial situation evaluated through questions relating to social capital, quality of life, and stigma (Controls without TB will not be asked any questions about the impact that having TB disease has on their psychosocial situation); and viii) access and uptake of existing social protection schemes (whether TB-specific or TB-inclusive) and support for TB-affected households, evaluated through use of both closed ranking and open free-text questions to establish what socioeconomic and other support people with TB and their households receive or would like to receive."

Study activities section: "A short individual pre-FGD survey (see Project 2 Survey, Extended data) [29] will be provided to participants prior to the initiation of an FGD. The survey will detail: participants' demographics; the stakeholder group to which the participant belongs; and their opinions on community, patient, health system, existing social protection schemes, and wider obstacles to achieving successful TB treatment outcomes.

The FGDs will be semi-structured and incorporate open-ended questions concerning barriers and facilitators to accessing and engaging with TB care in Nepal, and existing platforms and potential opportunities to mitigate these barriers including social protection schemes (see Project 2 Focus Groups, Extended data) [29] .

Study activities section: "The final activity in Project 2 will be a one-day workshop bringing together the 40 key stakeholders (see Project 2 Workshop, Extended data) [29] . The morning section of the workshop will consist of interactive presentations from the project team and stakeholder group representatives (including leaders of national social protection schemes in Nepal), and discussions exploring and validating the barriers and opportunities identified during the pre-FGD survey and interviews during FGDs."

Competing Interests: None.