Mitigating the economic impact of TB and diabetes in the Philippines

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ABSTRACT

Background

People with tuberculosis (TB) and their households usually incur large costs for care seeking, diagnosis, and treatment. Diabetes increases the risk of developing TB and has adverse effects on TB outcomes, especially if diabetes is not properly managed. Despite increasing awareness of the importance of managing diabetes within TB programmes, the economic burden of TB and diabetes from the household perspective, costs of diabetes services within the TB programme from the provider perspective, and the cost-effectiveness of providing diabetes services for people newly diagnosed with TB are still unclear.

Objectives

The aim of this PhD was to estimate the societal costs of concurrent TB and diabetes in TB-affected households in the Philippines and evaluate the cost-effectiveness of integrated diabetes screening and management for TB, and in so doing identify the limitations and potential implications of the WHO recommended approach for estimating household costs of TB using a cross-sectional data collection design by comparing it to a longitudinal design.

Methods

Costs and coping mechanisms associated with TB and diabetes from the patient perspective were collected retrospectively from 530 people diagnosed with TB in the Philippines at four timepoints during TB diagnosis and treatment: at TB diagnosis, the end of the intensive treatment phase, and midway and end of the continuation treatment phase (longitudinal design). The results of costs incurred for TB services with the longitudinal design were compared with those with the simulated cross-sectional designs to identify methodological issues in the WHO recommended cross-sectional design of national surveys costs incurred by people with TB and their households. The incremental costs of diabetes screening and management of people with TB from the provider perspective were estimated through a micro-costing of equipment, consumables, and staff time. A simple decision tree model, which includes diabetes screening and management during TB diagnosis and treatment, was developed to assess the cost-effectiveness of integrating TB and diabetes services. All primary TB and diabetes provider costs data, as well as secondary TB provider costs data from a separate TB costing study (VALUE-TB), were incorporated in the model.

Results

Using the longitudinal design, the catastrophic cost estimate for TB-affected households was 69%. The catastrophic cost estimates using the simulated cross-sectional design ranged from 40-55%, due to its inherit methodological issues when capturing the reduction and recovery in household income during the episode of TB care. There was no significant difference in the proportion of TB-affected households facing catastrophic costs between those with TB-diabetes (76%) and those with TB-only (69%, p=0.691). From the provider perspective, the cost per a case of people with diabetes detected using different diagnostic algorithms varied from USD 17.43 to USD 80.81. The monthly cost of diabetes treatment per person with diabetes was estimated at USD 8.95 to USD 12.36. Providing diabetes diagnosis and management for people diagnosed with and receiving care for TB would be cost saving: USD 147 per person from a provider perspective and: USD 187 per DALY averted per person from a societal perspective. in the target population of people aged ≥18 years. The probability of the intervention being cost effective was 99% from both the provider and the societal perspectives in people aged ≥18 years, at a threshold of 7.3% of GDP per capita which corresponds to the country-specific willingness to pay threshold. The probability of the intervention being cost effective was highest when the intervention was provided in people with BMI >18.5 kg/m^2 and those aged >45 years. Hence, I concluded that the intervention would be cost saving from both the provider and societal perspectives and providing the intervention to people with BMI >18.5kg/m^2 or those aged >45 years could be an entry point to implement such a policy.

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ABBREVIATIONS AND ACRONYMS

ART: Anti-Retroviral Therapy

BHC: Barangay Health Centre

CEA: Cost-Effectiveness Analysis

DALY: Disability Adjusted Life Year

DM: Diabetes Mellitus

DOH: Department of Health

DOTS: Directly Observed Therapy, Short-course

DR-TB: Drug-Resistance Tuberculosis

DS-TB: Drug-Susceptible Tuberculosis

DSWD: Department of Social Welfare and Development

ECEA: Extended Cost Effectiveness Analysis

FBS: Fasting Blood Sugar

HBC: High Burden Country

HIC: High Income Country

HIV: Human Immunodeficiency Virus

ICER: Incremental Cost Effectiveness Ratio

LIC: Low Income Country

LMIC: Low- and Middle-Income Country

MDR-TB: Multi Drug-Resistance Tuberculosis

MUAC: Middle Upper Arm Circumference

NCD: Non-Communicable Disease

NSP: National Strategic Plan

NTP: National Tuberculosis Programme

ODK: Open Data Kit

OGTT: Oral Glucose Tolerance Test

OOP: Out of Pocket Expenditure

PCS: TB Patient Cost Survey

Philhealth: Philippines Health Insurance Corporation

PLWD: People Living With Diabetes

PMDT: Pragmatic Management of Drug resistant TB

POC: Point of Care

POE: Point of Entry

QALY: Quality Adjusted Life Year

RPG: Random Plasma Glucose

RR-TB: Rifampicin Resistant TB

SRH: Sexual and Reproductive Health

STI: Sexual Transmitting Infection

TB: Tuberculosis

UHC: Universal Health Coverage

WHO: World Health Organization

WTP: Willingness-to-pay

GLOSSARY

Terminology	Definition
Ability to pay	Ability to pay refers an individual's or household's financial capacity to use healthcare services [1]. In the WHO guidance on surveys of costs incurred by people with tuberculosis (TB) and their households, four indicators are suggested to use as a measurement of ability to pay, namely self-reported household consumption, self-reported household expenditure, self-reported income or estimated income based on household asset ownership [2]. In this PhD thesis, self-reported annual household income was used as the main measurement of ability-to-pay to be consistent with the measurement used for the Philippines national surveys of costs incurred by people with TB and their households [3,4].
Catastrophic costs due to TB	The operational definition of "catastrophic costs as a result of TB" refers to medical and non-medical out-of-pocket payments and indirect costs exceeding a given threshold (e.g. 20%) of the annual household income. Both medical and non-medical costs are net of any reimbursements to the individual who made the payments [2,5].
Direct medical costs	Direct medical costs refer to the sum of out-pocket payments for care seeking, TB diagnosis and treatment made by people with TB in a given household [2].
Direct non-medical costs	Direct non-medical out-of-pocket costs are payments made because of the need to access TB health services, such as payments for transportation, accommodation or food and nutritional supplement [2].
Indirect costs	Indirect costs refer to people with TB or their guardian's lost time, lost wages (net of welfare payments) and lost income due to TB health-care seeking and hospitalization during the TB episode [2].
Out-of-pocket (health or medical) payments	Out-of-pocket payments are defined as direct payments made by individuals to health care providers at the time of service use. This excludes any prepayment for health services, for example in the form of taxes or specific

insurance premiums or contributions and, where possible, net of any reimbursements to the individual who made the payment [2].

Tuberculosis

A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or WHO endorsed rapid diagnostic tests (such as Xpert MTB/RIF). All such cases should be notified, regardless of whether TB treatment has started.

A clinically diagnosed TB case is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of x-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed [6].

Extra-pulmonary TB is case with active TB outside of lungs such as lymph nodes, CNS, bones/joints, genitourinary tract, abdomen, and pericardium. The definition includes One specimen from an extrapulmonary site culture-positive for Mycobacterium tuberculosis or smear-positive for AFB or histological or strong clinical evidence consistent with active extrapulmonary tuberculosis.

TB-diabetes status

In this PhD thesis, the status of TB and diabetes was categorized into three: people with TB but without diabetes (TB-non DM or TB-non diabetes), people with TB-diabetes receiving diabetes management (TB-managed DM or TB-managed diabetes), and people with TB-DM not receiving diabetes management (TB-unmanaged DM or TB-unmanaged diabetes).

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PREFACE

This thesis has been developed following the paper-style. Research conducted as part of this thesis has resulted in four publications in international peer-reviewed journals. As the first author, I led in developing the conceptual arguments, methodological approaches, study implementation, conducting the analyses, and writing the manuscripts.

These independent publications were included in this thesis as four results chapters, and they are related to the common theme of assessing the costs incurred by people with TB and diabetes and provider costs of diagnostics and treatment for tuberculosis and diabetes. I have included preambles and linking material where necessary to make the thesis flow as well as possible. Given that this thesis uses the paper-style, there is unavoidable repetition between the chapters, particularly in the content of the background and methods sections.

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CHAPTER 1. INTRODUCTION

1.1 Background

1.1.1 Global disease burden of TB and diabetes

Tuberculosis

Tuberculosis (TB) is one of the major public health concerns globally. In many low- and middle-income countries (LMICs). TB is a communicable disease caused by the bacillus *Mycobacterium Tuberculosis*, and an airborne disease can be transmitted to other individuals by breath or cough. TB is a chronic disease that requires a minimum of 4-6 months treatment [1]. Since 2011, rapid molecular tests such as Xpert MTB/RIF that are highly specific and sensitive have replaced traditional microscopy and culture methods [2]. The risk of TB infection and disease is associated with poverty, together with poor care-seeking behaviour, delay in diagnosis, and poor treatment adherence and the development of drug-resistant TB (DR-TB) [3-5]. TB has reached epidemic proportions, with a third of the world's population being infected [6]. TB is one of the top 10 causes of death worldwide and ranked as one of the diseases with a heavy burden of disability-adjusted life years (DALYs), calculated as over 66 million in 2019 [7,8]. It is estimated that there were 10.6 million incident TB cases worldwide in 2022, and 1.3 million of them died due to TB [9,10]. More than 95% of TB-related deaths occurred in LMICs [11]. The Western Pacific Region has the third highest number of incident TB cases (1.86 million) after the South-East Asia Region (4.85 million) and the African Region (2.48 million) [9].

Diabetes

Diabetes is a disease with metabolic disorders characterised by chronic hyperglycaemia caused by impaired insulin production [12]. There are three categories of diabetes: Type 1, Type 2 and gestational diabetes. Type 1 diabetes is a chronic autoimmune condition that prevents pancreas from producing insulin and the most common age at diagnosis is the age of 4 to 6 years. Type 2 diabetes usually develops in adulthood and is a lifestyle-related disease caused by persistently high blood sugar levels. Gestational diabetes develops in pregnancy and usually resolves after pregnancy. This PhD thesis focused on Type 2 diabetes, which accounts for more than 90% of the global disease burden of diabetes [13]. Diabetes has a heavy burden of DALYs, calculated as more than 70 million in 2019 [7,8] and was previously thought to be a minor problem in LMIC. Almost 80% of people living with diabetes (PLWD) were in LMIC in 2013 and diabetes incidence is increasing, especially in younger age groups in LMIC [14,15]. Lack of access to diabetes diagnosis and treatment as well as to health facilities can result in the development of earlier, more frequent and more severe complications (e.g. blindness due to retinopathy or cataracts, kidney disease, coronary heart disease, cerebrovascular disease and stroke) and those complications lead to premature disability and death [16]. People with diabetes

have a substantially reduced life expectancy with age-specific mortality rates approximately twice that of the non-diabetic population [17].

1.1.2 Association between TB and diabetes

Diabetes is one of risk factors associated with active TB disease, and WHO estimated that, globally in 2023, 0.38 million incident cases of TB were attributable to diabetes [2]. The mechanisms of the interaction between TB and diabetes involves a compromised immune function, while they are not fully understood [18-20]. The impaired immune function caused by diabetes instigates TB infection and the activation of the disease and also affects the immune response to TB in individuals with diabetes [21]. Conversely, the inflammatory system caused by TB may lead insulin deficiency and persistent hyperglycaemia which can result in an increased risk of progressing to diabetes [21]. The latest Cochrane review of the association between TB and diabetes reported that the people with diabetes are at 1.5-2.4 times higher risk of developing active TB disease is compared to those without diabetes [22], which could be caused by diabetes-related alternation of immune system, metabolism and gene transcription [20,23]. A previous systematic literature review also concluded that diabetes was associated with a 2.3 to 4.3 times increased risk of developing active TB [24,25].

Diabetes not only increases the risk of developing active TB but also associated with increased risk of latent TB infection (LTBI) with a pooled odds ratio of 1.18 [26,27]. Diabetes is also associated with an increased severity of TB disease, and poorly controlled diabetes with impairment of peripheral blood and hyperglycaemia appear to be related to the development of lung cavity and the number of lung lesions [20,28,29]. Furthermore, some evidence suggested that diabetes is related to a prolonged smear and culture positivity, which in turn required a longer TB treatment [19,29,30].

Diabetes is associated with an increased risk of multi-drug-resistant TB (MDR-TB). A meta-analysis showed that odds of having MDR-TB in people with diabetes was 1.97 times higher compared to those without diabetes [31]. Another systematic review also concluded that 2 times higher risk of having MDR-TB among people with diabetes [32]. Finally, diabetes is associated with adverse TB treatment outcomes and death due to TB [33]. A systematic review estimated that people with concurrent TB and diabetes have 2-fold increased risk of death compared to people with TB-only [32]. In addition, diabetes is associated with early mortality during TB treatment with adjusted hazard ratio of 4.4 and also with an increased risk of TB relapse with a relative risk of 3.9 [33-35]. Although it remains unclear whether a good glycaemic control improves TB treatment outcomes [36,37], increased early detection and diagnosis of diabetes and improved glycaemic control may contribute to the rate of decline of TB

incidence and the reduction of adverse TB treatment outcomes, thus contributing to ongoing transmission of TB [38-40].

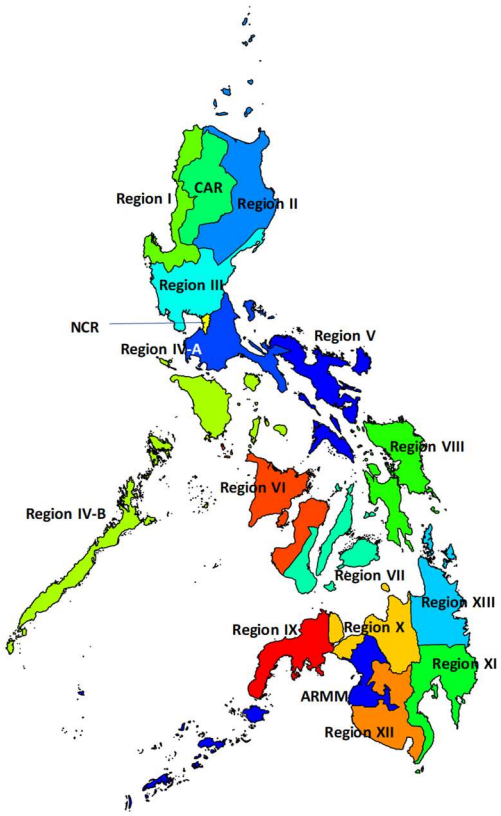
1.1.3 Disease burden of TB and diabetes and study settings in the Philippines

The Philippines is classified as a high TB burden country both for drug susceptible TB (DS-TB) and multidrug- and rifampicin-resistant TB (MDR/RR-TB). WHO estimations of TB prevalence and incidence in the Philippines were 1,159 and 554 per 100,000 in the 2016 TB prevalence survey, and the number of Rifampicin Resistant TB (RR-TB) cases was estimated as 20,000 in the Philippines [9]. From 2013, more than USD 50 million (USD 126 million in 2022) have been invested annually, according to the budgets reported by the NTP, by the national government and from external donors (51%: domestic funding, 49% international funding) [9]. TB incidence, however, has not significantly decreased, rather it has gradually increased to 638 per 100,000 population in 2022 [9,10]. In addition, the case notification rate of people with TB was only 377 per 100,000 in 2016 which means that 41% of incident TB cases were missing from the detection and reporting of TB cases [9].

The Philippines has the seventh highest country incidence of TB associated with diabetes [41]. Diabetes prevalence, based on assessing elevated fasting blood sugar, has been increasing in the Philippines has been increasing over time, at 3.4% in 2003 to 5.8% in 2016 [42]. Based on the estimated number of TB-diabetes concurrent incident cases in 2022, 23,000 adult TB cases were attributable to diabetes [41,43]. It is also expected that incident cases of TB related to diabetes will also increase [44].

The Philippines is a county located in the Western Pacific Ocean and Southeast Asia and characterized as an archipelago with 7,107 islands. The archipelago has three main island groups: Luzon, Visayas, and Mindanao. There are 17 functional regions across the country, and eight are in Luzon, three (Region IV-VIII) are in Visayas, and six are in Mindanao Island group (Region IX-XIII and ARMM) (**Figure 1**).

Figure 1. Location of 17 functional regions in the Philippines



The population of the Philippines was 115 million in 2023, and a large number of the population are concentrated in the National Capital Region (NCR), Region III, and Region IV-A in Luzon Island group. The Philippines has three levels of Local Government Unit (LGU) under 17 functional regions; province, city and municipality, and barangay. LGUs including 81 provinces, 145 cities, and 1,489 municipalities across the country. As a result of decentralization of health services, LGUs are mainly responsible for providing health services under the direction of the Department of Health [45].

TB services including diagnosis and treatment are mainly provided at LGU level at Rural Health Units (RHUs) or City Health Centres (CHCs) besides national or regional hospitals [45]. Recording of TB patient's information such as result of diagnostic test and treatment regimen is initiated at RHUs or CHCs by using patient TB treatment cards. This information is transferred to Municipal or City Health Office (Basic Management Unit of TB programme) where paper-based records are entered into a web-based system namely the Integrated Tuberculosis Information System (ITIS). The case-based data are validated by provincial and regional TB coordinators and reported to NTP on a quarterly basis. Laboratory data on smear and Xpert MTB/RIF tests are also reported to NTP through ITIS. This web-based reporting system started in 2011 and reached nationwide coverage in 2015.

1.1.4 Global and country policy contexts addressing TB comorbid with diabetes

Given the dual disease burden of TB and diabetes, in 2012, WHO published a guideline to develop and implement collaborative actions aimed at reducing this burden. The guideline consists of three pillars including bi-directional screening of TB in people living with diabetes and of diabetes in people with TB; plus monitoring and evaluation of collaborative diabetes and TB activities [46]. The recommendation of the 2011 WHO framework included the implementation of surveillance of diabetes prevalence in people with TB in all countries and providing diabetes screening for people with TB. However, a slow uptake of WHO recommended policies for TB and diabetes was reported in the WHO global tuberculosis report 2021; out of 30 high TB burden countries, only nine recommended diabetes screening for people with TB in the national strategic plan for TB and only six recommended the management of diabetes for those with TB [47].

In order to accelerate the implementation of policies addressing dual burden of TB and diabetes, WHO is developing new guidance on diabetes management for people with TB, and it will be added to the operational handbook on tuberculosis: TB and comorbidities [48]. The current WHO guidance for managing comorbidities in people with TB recommends three different models of integrated care: stand-alone screening provided separately for TB and comorbidities, followed by referral for diagnosis and treatment (separate service delivery model); screening and diagnosis provided by service providers for TB and for comorbidities located in the same premises, followed by referral for treatment (co-located services model); screening, diagnosis and treatment fully integrated and provided by a single service provider (one-stop-shop model) [48-50].

Policy contexts addressing TB comorbid with diabetes in the Philippines

For TB control, Philippines Health Insurance Corporation (PhilHealth) covers costs for TB diagnosis, treatment, reporting, drugs, consultation and health education [51,52]. For diabetes management, PhilHealth covers diabetes diagnosis, but not routine monitoring costs. To address the increasing burden of NCDs, PhilHealth started providing limited coverage of diabetes drug (metformin) costs in 2014 for specific population groups [53]. For example, in the indigent population, only one person per household with 10-year cardiovascular risk is covered [54]. The current service integration for TB and diabetes services differs by area and level of facility (further details are available in **Section 1.6.2**). Social support is provided by the NTP for people with drug-resistant TB (DR-TB) with the purpose of improving treatment adherence and includes food packages and transportation fees for visiting health facilities [55-57]. Furthermore, The Department of Social Welfare and Development (DSWD) of the Philippines has a nationwide conditional cash transfer (CCT) programme for households living in

poverty, and as of 2016, the CCT programme covered 4.4 million households, equivalent to 20% of the total population [58].

This situation may result in increased and potentially catastrophic costs in people with TB and co-morbid diabetes due to the necessity for life-long diabetes drugs payments (direct medical cost) and separate facility visits (transportation costs, cost of time lost). It also may contribute to reduced effectiveness of investments in TB control, which might be mitigated by providing integrated diagnosis and treatment.

Given the need to address the issue of dual disease burden between TB and diabetes in the Philippines, the Department of Health in the Philippines introduced a policy for bi-directional screening of TB and diabetes in 2017, as proposed by the End TB strategy and technical recommendation from International Union Against Tuberculosis and Lung Disease [46,59-61]. Also, managing diabetes in parallel with TB control is listed in the TB-NSP for 2017-2022 as a key priority to prevent and treat the multiple burden of diseases in the Philippines [62,63]. Furthermore, the current national strategic plan (NSP) for TB in the Philippines has a target to provide diabetes screening for 90% of people newly diagnosed with TB [62]. Therefore, to accelerate the implication of the policy in the Philippines, a study assessing costs and cost-effectiveness of diabetes diagnosis and treatment in people with TB was necessary in the country context.

1.2 Literature review for economic evaluation of TB and diabetes

1.2.1. Methods and data required for economic evaluations

Cost-effectiveness analysis (CEA) assesses economic efficiency of a range of healthcare interventions that maximize health benefits at population level, and therefore the analysis is usually based on aggregated costs and health consequences regardless of who suffers costs and gains health [64,65]. The purpose of CEA is to help decision making by maximising health outcomes where there are limited available resources [66,67]. The main results of economic evaluation and cost-effectiveness analysis is presented as the incremental cost-effectiveness ratio (ICER), which is calculated as the incremental costs of an intervention divided by the incremental health outcomes of the intervention and used for choosing the best among various interventions with limited resources [68].

The denominator of ICER which corresponds to the incremental health outcomes by an intervention is usually expressed using a quality adjusted life year (QALY) or disability adjusted life year (DALY) [69]. While both QALY and DALY measures quality of life and can be used for different disease areas, DALY is the metric which is most frequently used in economic evaluations in the settings of LMICs [70]. DALY was developed by the Global Burden of Diseases, Injuries, and Risk Factors, and it counts the total years of life lost due to premature death and years lived with disability [71,72]. In the disability weights used for DALY, "0" refers to no disability and "1" means to the dead state. Therefore, a new intervention should aim at reducing DALY, and the unit of ICER is incremental costs per DALY averted.

The definition of the numerator of ICER which corresponds to the incremental costs by an intervention can vary depending on its perspective, which includes a patient, healthcare provider, entire health sector or entire society [73]. While the healthcare provider perspective only considers costs incurred by healthcare service providers such as treatment costs and other health and non-health resource use related to disease management, the societal perspective includes costs beyond the provider perspective such as transportation and associated costs to visit health facilities, informal care costs and productivity loss dues to health conditions [73,74].

1.2.2 Economic evaluations addressing the dual burden of TB and diabetes

In the course of developing new WHO guidance on managing TB and diabetes, many evidence gaps were identified including optimal algorithms and timing for diabetes testing and association of early diabetes screening and case detection with improvement of TB treatment outcomes. Costs and cost-effectiveness of providing diabetes screening and detection for people with TB were also listed as areas with evidence gaps. The cost-effectiveness of providing diabetes screening in populations with

a high prevalence of diabetes such as older age groups, people with high body mass index (BMI) or people with cardiovascular diseases has been suggested as well as the cost-effectiveness of early screening and diagnosis of diabetes. All of the 19 studies included in a systematic review that assessed the cost-effectiveness of providing diabetes screening and management to high-risk populations such as people aged 45 years or above or individuals with a high BMI from the health system or societal perspective, reported the interventions to be cost-effective, with five of the studies reporting cost saving results [75]. A recent study reported the prevalence of diabetes among people with TB in the Philippines to be 20.6% for DS-TB and 34.1% for drug-resistant TB (DR-TB) [76]. This result suggests that the prevalence of diabetes in people with TB is much higher than in the general population, which was estimated at 6.1% for 2021 [77], and raises a question as to whether providing integrated diabetes screening and diagnosis for people with TB where there is a high population prevalence of diabetes is as cost-effective as is the case for other high-risk populations. However, since little is known about the cost-effectiveness of early detection and management of diabetes in people with TB, it was first necessary to understand and contribute to the data available for provider costs of TB and diabetes services as well costs incurred by people with concurrent TB and diabetes in the Philippines. Subsequently, a cost-effectiveness analysis of providing diabetes screening and diagnosis for people with TB from the societal perspective in the Philippines needed to be conducted.

Integration of healthcare services: examples and lessons from other diseases

Integrated health care services may reduce the economic impact for people with multiple long-term diseases such as TB and HIV and their households [78]. HIV is a key risk factor for developing active TB, and since HIV infection weakens immune functions, people living with HIV are at high risk of developing active TB; the relative risk is 26.7 times higher than for people without HIV [79,80]. The integration of TB and HIV services is supported by evidence of cost savings and improved treatment outcomes for both infections [81,82]. A systematic review suggested that integrated services may facilitate less frequent facility visits, which results in reduced transportation costs and lost time for people with TB-HIV and their households [83]. A study that assessed costs incurred by people with TB-only, HIV-only, and TB-HIV and their households showed that people with TB-HIV visited health facilities (on average 18.4 times per month) more frequently than those with TB-only (on average 16.0 times) or with HIV-only (on average 2.2 times) due to fragmented services [78]. In another recent literature review, 32 included publications assessed TB-HIV service integration, and showed that initiation of Anti-Retroviral Therapy (ART) in parallel with TB treatment lead to improved mortality rates and ART adherence [82,84-86]. However, operational challenges due to complex clinical management of people with co-infected TB and HIV often resulted in poor implementation of service

integration. Also, although the reduction of resource utilization in integrated care for TB and HIV by efficient use of existing equipment, infrastructure, and personnel has been suggested, the detailed costs and its drawback of the integrated care especially from the patient perspective has not been described well [87].

In other diseases, a study, which assessed technical efficiency of integration of HIV and sexual/reproductive health (SRH) services in Kenya and Swaziland, showed that on one hand, the number of additional services for HIV within maternal and child health unit was positively associated with improved technical efficiency, and on the other hand, the number of additional HIV and Sexually transmitted infections (STI) services provided in the same room at the facility was negatively associated with technical efficiency [88]. The study suggested that service providers may require multiple rooms to manage their patient flow without sacrificing technical efficiency of integrated HIV and STI care [88]. In the same study settings in Kenya and Swaziland, costs for three different models of integrated care for HIV and SRH were assessed (Model 1: Integrating HIV service into family planning, Model 2: integrating HIV services into postnatal care and family planning, Model 3: integrated care for HIV and SRH) [89]. The study concluded that the wide variation in costs between the models might be driven by maturity of the integrated services at facility level [89].

1.2.3. Global progress on measuring TB and diabetes provider costs

TB provider costs

In the context of moving toward Universal Health Coverage (UHC), the robust estimation of TB provider costs is necessary for countries to capture the financial needs, to utilize the limited financial resources cost efficiently, and to improve the allocation of the resources for TB control. A systematic review included 67 studies that assessed TB provider costs [90] and reported that mean total provider costs widely varied from USD 258 in low-income countries (LIC) to USD 14,659 in high-income countries (HIC) per person treated for DS-TB, and the costs were much higher for people with DR-TB ranging from USD 1,218 in LIC up to USD 83,365 in HIC [90]. In the Western Pacific Region, only China, Cambodia, and the Philippines have previous studies of TB provider costs [91-95]. In the Philippines, two studies were conducted to assess TB provider costs as a part of cost-effectiveness analysis, and showed that costs per person with TB ranged from USD 34 to USD 118 for all types of TB [91,93]. However, both studies were conducted in early 2000s and the data are outdated. WHO also estimates the estimated cost per person treated for TB, and in 2022, the cost per person treated for DS-TB was USD 236 in the Philippines [10].

Diabetes provider costs

Diabetes also causes a substantial financial burden for people with the disease, their households and health systems that treat them, and the disability and mortality burden is also high [96-98]. Costs for diabetes management are usually covered by out-of-pocket payments by people with diabetes and their households that causes financial difficulties, particularly in LMICs [98-100]. As with TB, accurate estimates of diabetes screening and management costs aid in the design of measures to mitigate the financial hardships in TB-affected households by achieving UHC [101]. A recent systematic review for diabetes provider costs included 52 publications, and investigated costs per outpatient visit and annual inpatient, laboratory, and drug costs [99]. The review showed that costs for outpatient services ranged from USD 5 (in Brazil 2011, N=121) to USD 42 (in Mexico 2012, N=766) per visit, and annual inpatient costs ranged from USD 25 (in Thailand 2011, N=475) to USD 1,790 (in China 2016, N=41,875), annual laboratory costs were USD 5 (in Iran 2012, N=60) to USD 152 (in Argentina 2013, N=300), and annual drug costs were USD 26 (in Thailand 2011, N=475) to USD 668 (in Turkey 2015, N=116 which was mainly for insulin) [99,102-107].

1.2.4. Global progress on measuring costs incurred by people with TB and those with diabetes

Financial protection in disease control

Financial protection is the one of key elements of UHC along with equity, quality and service availability. It can be achieved when direct expenditures to obtain quality health services do not expose people to financial hardship and devastating consequences such as losing their savings, taking loans and selling household assets [108]. There are previous studies assessing disease-specific financial protection and the societal impact both for communicable and non-communicable diseases (e.g. malaria, HIV, cancer) for reasons of protecting specific vulnerable groups and to perform economic evaluations from a societal perspective [109-112]. TB is a chronic disease that still requires a minimum of 4-6 months of treatment [1]. The risk of TB infection and disease is associated with poverty, together with poor care-seeking behaviour, delay in diagnosis, and poor treatment adherence leading to the development of drug-resistant TB [3-5]. Despite free TB services available in public health facilities, people with TB usually incur large costs for care seeking, diagnosis, and treatment. The costs include not only out-of-pocket (OOP) payments for direct medical costs, but also direct non-medical costs such as transportation, food or nutritional supplements and indirect costs such as income loss [90,113,114]. TB also impacts poverty as it can reduce the physical ability to work, and as a result leads to income loss [5,90,113]. In addition, households affected by long-term diseases such as TB usually mobilize their money for treatments by dissaving, selling assets, or taking loans,

making them poorer and trapped in the cycle of poverty [115], which can in the long-term have an economic impact on people with TB and their households [78].

Global progress on assessing costs incurred by people with TB and their households

TB is both a cause and consequence of poverty and potentially traps people with TB and their households in a cycle of poverty [116]. Poverty is linked to a higher risk of TB infection and disease, poor care-seeking behaviour, delay in diagnosis, and poor treatment adherence which could result in adverse treatment outcomes and developing MDR/RR-TB, which may lead TB-affected households to further impoverishment [3-5,116]. To inform policies to improve accessibility of services, WHO recommends a national survey to understand the magnitude of the financial burden, its main cost drivers, and the incidence of catastrophic costs in line with achieving End TB strategy and UHC [3,59,117].

Previous systematic reviews revealed that TB-affected households often face heavy financial burdens not only from medical expenses during a TB treatment course, but also from costs for care seeking before TB diagnosis and income loss before and during TB treatment [90,113,114]. The systematic review in 2014, which included results from 49 studies on TB patient costs in LMICs, showed that the mean total TB patient costs ranged from USD 55 to 8,198 (unweighted average: USD 847, median: USD 379) [113]. Income loss accounted for the largest proportion of total TB patient costs at 60% (ranged from 16-94%) [113]. This systematic review concluded from eight studies that 50% of the total costs was incurred before starting TB treatment, and income loss was the main cost driver both before and during TB treatment [113]. Total TB-related costs as a proportion of both individual and household incomes of people with TB was high at 58% and 39% respectively [113]. The proportions were higher in lower socioeconomic status groups and people with MDR-TB [113]. The latest systematic review in 2015 assessed mean direct costs and income loss by country income group (high, upper-middle, lower-middle, or low income country) [90]. The results were consistent with the previous systematic review that people with TB have a heavier burden from income loss (USD 248) compared with direct costs (USD 155) in low income countries [90]. The financial burden for people with MDR-TB in low income countries was considerably higher compared to people with DS-TB (direct costs: USD 406, income loss: USD 1,256) [90]. Nine studies were conducted in the countries in the Western Pacific Region such as Cambodia, China, Malaysia, and Philippines, and of those only 5 studies assessed both direct and indirect costs [90]. In Cambodia, the mean total costs were USD 477 (HIV negative) to USD 555 (HIV positive) for DS-TB and USD 1,525 for DR-TB, and in Malaysia the mean total costs were USD 727 for

all forms of TB [94,118]. China had three studies, and the total costs ranged from USD 902 to USD 1,712 for all forms of TB [92,119,120].

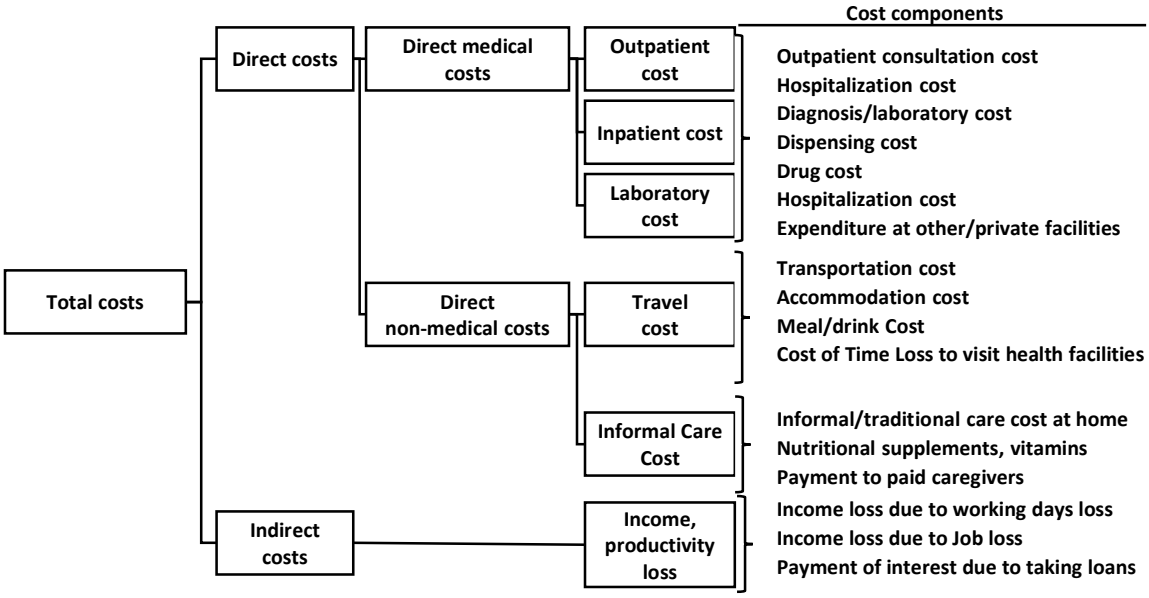
In 2014, WHO developed the End TB Strategy that outlined the ambitious goal of ending the TB epidemic worldwide by 2035 [59]. Recognizing the need to address the financial burden due to TB, the Strategy promotes assessment of costs incurred by people with TB and their households and sets a new target of zero "catastrophic costs" for TB-affected families in the context of Universal Health Coverage, in addition to two traditional epidemiological targets (reduced incidence and deaths) [59].

Methodology for assessing costs incurred by people with TB and their households

To establish the baseline against which to monitor the progress towards elimination of catastrophic costs, WHO recommends a national survey to be carried out in each country [59]. In 2015, WHO further developed a generic survey protocol and data collection tool (field testing version) to support countries in planning and implementing the national surveys of costs incurred by people with TB and their households, which was later refined and published as a WHO handbook in 2017 [117].

The WHO-recommended survey instrument was designed to collect a range of cost data including direct medical costs (i.e. costs for medical consultations, examinations, drugs, hospitalization), direct non-medical costs (i.e. transportation, foods and accommodation), and indirect costs (i.e. loss of income) (**Figure 2**).

Figure 2. Summary of costs incurred by people with TB and their households



Developed based on WHO handbook on national TB patient cost surveys and Drummund et al 2005 [117,121]

Using the WHO's generic protocol and handbook, national surveys of costs incurred by people with TB and their households have already been implemented in 31 countries as of January 2024 including Myanmar (2015), Viet Nam (2016), Timor-Leste (2017), Ghana (2016), Mongolia (2017), Philippines (2017), Uganda (2017), China (2017), Kenya (2017), Fiji (2018), Lao PDR (2019), and Solomon Islands (2019) [117,122-126]. The global pooled average of the percentage of TB-affected households facing catastrophic costs due to TB was 49% (95% confidence interval: 37-61%) in 2023 [10]. Preliminary results of the surveys in the Western Pacific Region showed that the proportion of TB-affected households facing catastrophic costs greatly varied; 42% in the Philippines, 40% in Fiji, 56% in China, 63% in Viet Nam and Lao PDR, and 68% in Mongolia [56,117]. Main cost drivers also differed by country; while direct non-medical costs were high in the Philippines, Lao PDR and Fiji, direct medical costs and income loss were equally high in Mongolia and China [117,122-126]. Direct non-medical costs and income loss were the main cost drivers in Viet Nam [117,122-126].

Recommendations from national surveys of costs incurred by people with TB and their households

The results of surveys of costs incurred by people with TB and their households informed a wide range of recommendations as listed below [122,124,125,127,128]:

Direct medical costs:

1. Improve access to quality TB diagnostic services through the decentralization and streamlining of pathways for people with TB to access care at all levels, which may result in minimizing diagnostic delay and reduction of costs incurred by people with TB, in collaboration with local government authorities.

2. Actively engage in the discussion on the integration of TB services into the national health insurance scheme including TB benefit package design and its costing

Direct non-medical costs:

3. Improve nutritional support for people with TB including systematic nutrition assessment, counselling, and therapeutic and supplementary feeding for those in need, in coordination with the national nutrition programme

For income loss:

4. Establish a streamlined claim mechanism for people with TB to access sickness and unemployment benefits

5. Explore a possible collaboration with labour and corporate sectors to improve workplace policies and services for people with TB including a way to protect employment of people with TB.

Costs incurred by people with diabetes and their households

Not only TB, but diabetes also usually causes a substantial financial burden for people with diabetes and their households due to the necessity of lifetime disease management and the consequences of diabetes-related complications [129]. Delay in diabetes detection and also in the initiation of diabetes management can result in earlier and more frequent development of severe complications such as blindness, kidney disease, coronary heart disease, cerebrovascular disease and stroke, and those complications lead to premature disability and death which incur a higher financial burden in affected households [16,17]. In Kenya, a study assessed direct and indirect costs of diabetes, for which this study applied WHO recommended methods of national surveys of costs incurred by TB-affected households to diabetes [130]. In 163 people with diabetes, the mean total annual costs for diabetes services was USD 673, and 10% and 12% of study participants reported costs for hospitalizations and irregular facility visits, respectively [130]. In that study, more than 50% of diabetes-affected households faced catastrophic costs using a threshold of 20% of annual household income, which is the definition of catastrophic costs due to TB used by WHO [117]. A study with a larger sample size in China (N=6,359 people with diabetes), reported that hospitalizations accounted for 73% of total diabetes costs, and the incidence of catastrophic costs was 24%, even with a higher threshold (40%) of annual household income [131].

Given this dual burden of TB and diabetes, there is a concern that people with concurrent TB and diabetes may be more likely to suffer damaging levels of associated costs than those with TB alone, yet there is limited data available on how co-morbidity impacts household costs associated with TB.

1.2.5 Status of measuring costs of TB and diabetes from the provider and patient perspectives in the Philippines

TB provider costs in the Philippines

A multi-country study (VALUE-TB project) that sought to assess a comprehensive set of unit costs for providing TB services was conducted in five high-TB burden countries (HBCs) including the Philippines [132]. The study assessed costs for vaccination, case finding, diagnosis, and treatment including overhead costs from the provider perspective in 25 public and private facilities across 3 regions in the Philippines in 2018 in collaboration with NTP Philippines, WHO and London School of Hygiene and Tropical Medicine. The data produced by this study can be used for priority setting and to assess the cost-effectiveness of a range of TB interventions in the Philippines.

Diabetes provider costs in the Philippines

In the Philippines, only one study was identified that assessed provider costs and availability of diabetes services. However the study was conducted in 2009, and only assessed unit cost for diabetes medications (e.g. price for oral hypoglycaemic agent or Insulin) [133]. Other cost categories for diabetes management such as costs for screening, human resources, equipment and total annual management costs per person have not yet been investigated in the Philippines. Furthermore, additional costs when diabetes services are within the TB programme were not identified in the Philippines context.

Therefore, it was necessary to assess the costs of screening and diagnostic equipment, medications, human resources as well as costs for additional building space and necessary training for integrated diabetes services within the TB programme. These data are required to investigate the cost-effectiveness of averting TB-related catastrophic costs in the current settings in the Philippines.

Costs incurred by people with TB and their households in the Philippines

Following the WHO recommendation, NTP in the Philippines conducted the first national TB patient cost survey in 2016-2017, which assessed direct costs (e.g. costs for TB drugs, consultations, hospitalization, transportation, or nutritional supplement and additional foods) and indirect costs (e.g. opportunity costs due to time lost due to travelling to health facilities, and waiting for and accessing healthcare services, loss of job or being too unwell to work) [117,134]. In the survey, 1,912 people with TB (1,592 DS-TB and 320 DR-TB) were enrolled as nationally representative samples. Overall, 42.4% of TB-affected households faced catastrophic costs, and the incidence was much higher among households with people with DR-TB (89.7%). The total costs were driven by direct non-medical costs (43%) followed by income loss (40%) and direct medical costs (17%) [135]. The survey recommended a wide range of policy interventions to minimize costs incurred by TB-affected households such as "*Coordinate with other health programmes to maximize the resources (e.g. collaborative activities for TB-HIV and TB-diabetes)*" and "*Integrate the NTP with the Social Welfare Program.*" [135]. Since the survey was designed as a cross-sectional study following the WHO guideline, this survey (and all PCSs) could not provide information on "to whom" and "when" the interventions or social protections are more likely to be needed, and the extended impact on each individual was not captured [117,124,125,127].

While there is evidence on costs incurred by people with TB and their households in the Philippines from the national survey, there are no studies that assessed costs incurred by people with diabetes nor costs of comorbidity associated with TB and diabetes.

1.2.6. Methodological issues in assessing "catastrophic costs due to TB" with WHO recommended methods

The WHO's handbook for national surveys of costs incurred by people with TB and households provides the standardized methods of the cross-sectional survey design for countries to assess the baseline and progress toward the target of "no TB-affected households facing catastrophic costs due to TB", with feasibility, practicality and affordability [117]. However, since the publication of the handbook, several suggestions have been made to improve the survey methodology, such as implementation of multiple methods for indirect cost estimation, improving data collection methods for pre-diagnosis costs, adapting multidimensional wealth index to estimate ability to pay of TB-affected households [136-139]. In this PhD project, I addressed two additional areas that may need to be considered in the WHO guidance on national surveys of costs incurred by people with TB and their households.

1. Sampling and cost extrapolation

In the WHO recommended national surveys of costs incurred by people with TB and their households, the surveys collect the cost data of TB episode from those who were in TB treatment at the time of the interview, and since the surveys are designed cross-sectionally, the data collection is conducted only once per participant [48]. For those who are in the TB intensive phase, the data before TB diagnosis and during the TB intensive phase are collected, and for those who are in the TB continuation phase, only data during the TB continuation phase are collected [135,140]. Therefore, in order to estimate the costs for the total duration of a TB episode, the costs of the other treatment phase were extrapolated based on the median costs incurred by other people in that treatment phase at the time of the interview. For example, to estimate costs before TB diagnosis and during TB intensive phase for those in continuation phase at the time of interview, the median costs pre-treatment and during the intensive phase were taken from those interviewed during the intensive phase [128,141]. In this cost extrapolation method, cost differences between DS-TB and DR-TB, and those with and without hospitalizations were considered separately.

When there are changes in health service utilization between the TB intensive and continuation phases and there are also changes in household income over the course of the TB episode due to

health status of the people with TB (e.g. become too unwell to work, start working again during TB treatment), the proportion of sampling from the intensive or continuation phase can affect the value of the total costs and the catastrophic costs when the WHO recommended cross-sectional data collection and cost extrapolation methods are used. However, in the current WHO handbook for national surveys of costs incurred by people with TB and their households, there is no concrete guidance on how the balance of sampling from intensive and continuation phases should be taken into consideration in the survey planning phase. As a result, in 14 journal publications so far based on the national surveys of costs incurred by people with TB and their households, the proportion of sampling from the TB intensive and continuation phases varied widely, from 19%:81% (Philippines [56]) to 53%:47% (Solomon Islands [142]). This variation in the sampling method and the lack of global guidance might have resulted in potential over- or under-estimation of the total costs incurred by TB-affected households and the proportion of TB-affected households facing catastrophic costs due to TB.

2. Measuring indirect costs using the output approach

"Catastrophic expenditure", which is being used as a part of UHC measurement, only assesses direct medical costs incurred by the general population in the cost assessment [143]. The WHO recommended national surveys of costs incurred by people with TB and their households includes direct non-medical costs and indirect costs (i.e. income loss or productivity loss) incurred by TB-affected households, in addition to direct medical costs [140]. Prior to the development of the survey methods, WHO conducted a systematic review of studies that assessed costs incurred by TB-affected households, and the review revealed that indirect costs before TB diagnosis accounted for 26% of total costs [113]. This finding became the basis of the methodology development to include indirect costs in the surveys of costs incurred by people with TB and their households, and the WHO handbook clearly states that the surveys measure "*indirect costs for the entire TB episode before and during TB treatment*" [140].

Indirect (household) costs are estimated through two different methods: the output approach and human capital approach [117]. The output approach relies on self-reported household income before and during the TB episode, while the human capital approach uses reported time spent for care seeking and treatment during the TB episode multiplied by an individual's hourly income estimated from reported income and working hours. The scope of indirect costs varies for these two approaches since the human capital approach includes the cost associated with care seeking before TB diagnosis while the output approach does not [56,124,142,144-151]. Therefore, the currently presented survey

results with the output approach might have underestimated the total costs borne by TB-affected households due to the exclusion of the indirect costs before TB diagnosis, and this means that an inconsistency exists between the global guidance and the actual implementation of surveys of costs incurred by people with TB and their households.

1.3 Rationale for PhD

1.3.1 Evidence gaps for integrated care for TB and diabetes

Despite increased political and public health awareness of diabetes management within TB services, there is a lack of evidence to inform policy for people with concurrent TB and diabetes. In the Philippines, integrated service delivery for PLWD within TB diagnostic and care network was identified as a goal to be achieved in the last WHO joint programme review in March 2016. The current TB-NSP includes integrating TB with other health programs including NCDs as a key activity targeting 90% of TB cases to be screened for diabetes by 2022 [62,63].

Towards ending TB in the sustainable development era and specifically for goal three, to achieve zero catastrophic costs faced by TB-affected households by 2030, assessment of economic impact of TB in TB-affected households is globally on-going especially in TB high burden countries. However, no studies or national surveys assessed whether people with concurrent TB and diabetes face a greater economic burden than those without diabetes. Although the policy for bi-directional screening of TB and diabetes is recommended in the Philippines, the incremental health system costs for providing the integrated care, how the integration impacts the economic burden on people with concurrent TB and diabetes and their households and the cost effectiveness of providing diabetes screening and diagnosis for people with TB are also not yet assessed.

1.3.2 Methodological gaps for catastrophic costs due to TB

In this PhD project, two methodological gaps assessing TB-related catastrophic costs will be addressed:

In the WHO recommended approach to assess “catastrophic costs due to TB”, surveys are implemented with a cross-sectional design as it is the most feasible, practical and affordable approach, and therefore a number of simplified assumptions are used to estimate total costs throughout TB treatment. No publications document the degree of effect of these assumptions on estimated total costs by comparing results from longitudinal and cross-sectional approaches.

Also, in the surveys of costs incurred by people with TB and their households that relied on the output approach, the indirect costs were excluded from the estimation of the total costs while the WHO handbook for the surveys clearly recommended including it as a part of the total cost estimation. This PhD project assessed the impact of indirect costs before TB diagnosis to highlight the inconsistency between the survey recommendation and the actual implementation.

1.4 Aim and objectives of the thesis

The key research question of this project was: could integrated care for TB and diabetes cost-effectively reduce catastrophic costs faced by TB-affected households in the Philippines. The aim of this study was to assess whether economic impacts faced by people with concurrent TB and diabetes and their households are greater than those with TB-only, and to assess the cost-effectiveness of integrated care for TB and diabetes which mitigates the economic impacts in TB-affected households in the Philippines.

There were four PhD objectives:

Objective 1: To estimate the direct medical, direct nonmedical and indirect costs incurred by people with concurrent TB and diabetes and their households using longitudinal data collection.

Objective 2: To identify the potential biases of the WHO recommended cross-sectional study design for TB catastrophic cost estimates and to explore optimal approaches for sampling and analysing cross-sectional cost data for the catastrophic cost estimates.

Objective 3: To assess the provider costs of diagnosing and managing diabetes for people with TB across 2 different levels of integration of diabetes services within TB services.

Objective 4: To assess the cost-effectiveness of integrating diabetes services within TB programme in the Philippines.

1.5 Conceptual framework of this PhD

1.5.1 Framework of PhD studies

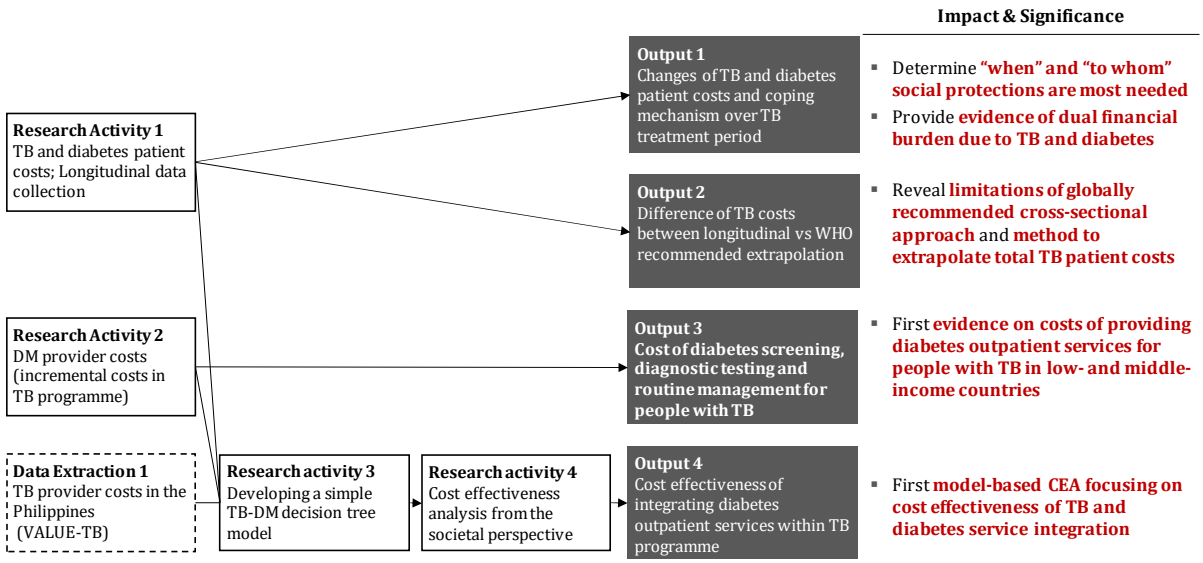
This PhD project consists of four research activities and one data extraction for four main objectives (**Figure 3**). Data collection for costs incurred by people with TB-only and with concurrent TB and diabetes and their households (activity 1) provided the evidence for changes of TB- and diabetes-related costs and coping mechanism over TB treatment period (output 1) which determine "when" and "to whom" social protection and supports are most required, and the evidence on difference of TB patient costs between longitudinal and cross-sectional study designs (output 2) which informed

the validity of the globally recommended cross-sectional method to extrapolate costs used in national surveys of costs incurred by people with TB and their households.

Data collection for the provider costs of diabetes was conducted as activity 2 of this PhD project to inform the policy making process about the health system costs of implementing TB and diabetes service integration (output 3).

The ultimate goal of this PhD project, cost-effectiveness of TB and diabetes service integration (activity 4) to mitigate catastrophic costs (output 4), was achieved by using the TB and diabetes patient cost data (activity 1), diabetes provider costs within TB programme (activity 2), TB provider costs (data extraction 1 from VALUE-TB), and a simple TB-diabetes decision tree model (activity 3).

Figure 3. PhD Conceptual Framework



1.5.2 Overall structure and methodological approach of the thesis

The research gaps identified in background and literature review of this thesis, the objectives and methods of this PhD addressing identified research gaps are summarised in **Table 1**.

Chapter 2 provides the estimates of direct costs and income loss associated with TB and diabetes care seeking, diagnosis and treatment. The study was conducted as a longitudinal study, which adapted the WHO recommended cross-sectional design of national surveys of costs incurred by people with TB and their households [117], with four data collection time points over an episode of TB (**Objective 1; Research paper 1**). The research paper included the comparison of costs, household income,

received social protection support, coping mechanisms and social consequences between people with concurrent TB and diabetes and those with TB-only.

Objective 2 was addressed using the data collected for Objective 1; Research paper 1. The analysis was to identify the potential biases of the WHO recommended cross-sectional study design for TB catastrophic cost estimates and to explore optimal approaches for sampling and analysing cross-sectional cost data for the catastrophic cost estimates. This was conducted by comparing the results of total TB patient costs and the catastrophic cost estimates between the longitudinal study design and the simulated cross-sectional study designs with different sampling proportions from TB intensive and continuation phases, i.e. 20%:80%, 35%:65% and 50%:50% (**Research paper 2**). The analysis also assessed the impact of income loss before TB diagnosis on the catastrophic cost estimates, which were identified in this thesis as an existing inconsistency between the WHO guidance and the actual implementation of national surveys of costs incurred by people with TB and their households.

For **Objective 3**, this PhD project assessed the health system costs of providing diabetes outpatient services for people with TB. The data collection was conducted as a cross-sectional micro-costing study and assessed costs of drugs, staff time, consumables and equipment required for various diabetes outpatient services (**Research paper 3**). The WHO ''Costing Guidelines for Tuberculosis Interventions'' was adapted for the data collection, analysis, and reporting to assess the cost of diabetes outpatient services [152-155]. This research paper provided the unit cost of diabetes outpatient services, cost per diabetes case detected as well as estimated monthly costs of routine diabetes management per patient.

Objective 4 was addressed by conducting a cost effectiveness analysis of providing diabetes outpatient services, using data collected and used for **Objective 1** (TB and diabetes patient costs) and **Objective 3** (diabetes provider costs) as well as the extracted data from VALUE-TB project (TB provider costs). A decision tree model was developed to assess the cost-effectiveness of providing diabetes testing for 90% of people with an unknown diabetes status at their TB diagnosis (based on the national strategic plan of TB in the Philippines) and subsequent routine diabetes care (**Research paper 4**). Incremental costs and DALYs averted of the intervention scenario were compared to a scenario of providing TB treatment only. Cost-effectiveness of the intervention was assessed from the provider and societal perspectives.

In addition to the contents from the published research papers and submitted manuscripts, additional analyses and methodological considerations and clarifications that could not be featured in detail in the publications were included in chapter 2-5.

Table 1. Synopsis of research gaps, objectives, methods and corresponding chapters and research papers

#	Research gaps	PhD Objectives	Methods	Chapter and research paper
1	Lack of evidence on financial burden incurred by TB and diabetes.	To estimate direct costs and income loss associated with TB and diabetes care seeking, diagnosis, and treatment using longitudinal data collection.	Longitudinal study assessing TB and diabetes patient costs, with four data collection timepoints over the TB episode (at TB diagnosis, the end of TB intensive phase, the mid- and end-points of TB continuation phase) in the Philippines	Chapter 2 Research paper 1
2	Lack of evidence on the degree of effect of assumptions used in the WHO recommended methods on estimating TB patient costs and the catastrophic cost estimates.	To identify the potential biases of the WHO recommended cross-sectional study design for TB catastrophic cost estimates and to explore optimal approaches for sampling and analysing cross-sectional cost data for the catastrophic cost estimates.	Using data from the longitudinal study assessing TB and diabetes patient costs: 1) compare the results of total TB patient costs and the catastrophic costs between the longitudinal study design and the simulated cross-sectional study designs with different sampling proportions from TB intensive and continuation phases 2) reassessing the impact of indirect costs before TB diagnosis on the total TB patient costs and the catastrophic cost estimates	Chapter 3 Research paper 2
3	Limited evidence on costs of providing diabetes services for people with TB.	To assess the provider costs of diagnosing and managing diabetes for people with TB within TB services.	Cross-sectional micro-costing study assessing diabetes outpatient services provided for people with TB at their TB diagnosis	Chapter 4 Research paper 3
4	Lack of evidence on the cost-effectiveness of providing diabetes screening and diagnosis for people newly diagnosed with TB.	To assess the cost-effectiveness of integrating diabetes services within the TB programme in the Philippines.	Using data on patient costs for TB and diabetes, provider costs for diabetes outpatient services within the TB programme, assessing the cost-effectiveness of providing diabetes screening and diagnosis from the provider and societal perspectives.	Chapter 5 Research paper 4

1.5.3 Study setting

Objectives and study settings of main cohort study (St-ATT study)

All of the longitudinal data collection for costs incurred by people with TB and diabetes and their households and provider costs for diabetes outpatient services for people with TB were conducted within a cohort study conducted by Dr Sharon Cox (a former Professor of Nutrition at Nagasaki University): “main study”. The aim of the main study was to measure the effects of malnutrition and diabetes in people with TB and investigate associations with treatment outcome through potential

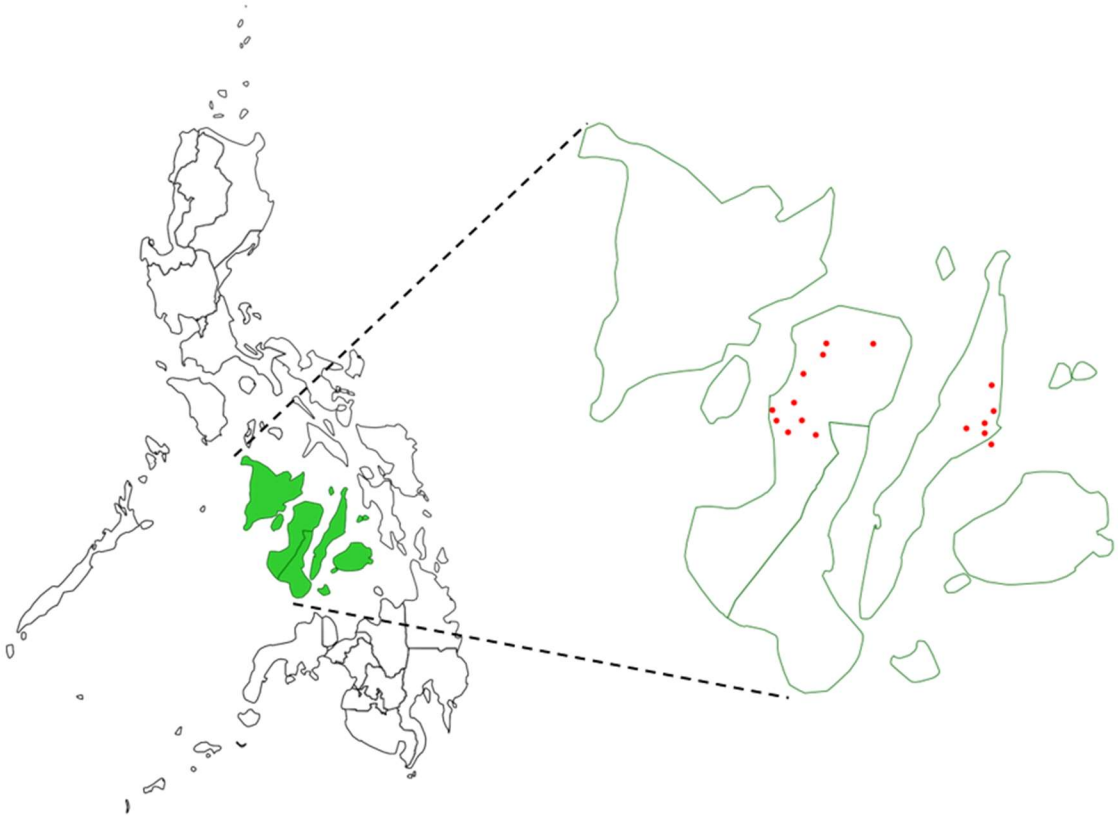
effects on treatment compliance, drug side effects, glycaemic control, weight gain and nutrition during treatment and cell-mediated immune responses [76,156]. The primary objective was to estimate the effect of malnutrition (BMI <17.0 kg/m2) and diabetes on risk of adverse treatment outcome (death, loss to follow-up, incomplete treatment or treatment failure) in people with DS-TB and people with DR-TB enrolled on the WHO shorter regimen. Study participants aged 18 years or more who initiated a new TB treatment regimen were recruited from participating NTP DOTs and iDOTS centres (i.e. those implementing the WHO 9-month all-oral regimens to eligible people with DR-TB) within the National Capital Region (NCR), Negros Occidental (Region IV) and Cebu (Region VII). Therefore, the selected sites of the main study included:

- **Manila, NCR (not used for our study sites):** San Lazaro Hospital**,** San Nicholas Health Centre
- **Negros Occidental, Western Visayas (used for our study sites):** Valladolid Health Centre**,** Bago City Health Centre**,** Bacolod Health Centre**,** La Carlota Health Centre**,** Pablo O. Torres Memorial Hospital
- **Cebu, Central Visayas (used for our study sites):** Compostela Health Centre**,** Carmen Health Centre**,** Consolacion Health Centre**,** Eversley Childs Sanitarium and General Hospital**,** Lapu-Lapu Health Centre**,** Vicente Sotto Hospital.

Study sites of this PhD

For this PhD project, the study sites of Negros Occidental (Region IV) and Cebu (Region VII) were used for assessing costs incurred by people with TB and diabetes and their households (**Objective 1; Research paper 1 & Objective 2; Research paper 2**), and those of Negros Occidental (Region IV) were used for assessing costs of providing diabetes outpatient services for people with TB (**Objective 3; Research paper 3**) (**Figure 4**). To perform the cost-effectiveness analysis of providing diabetes screening and diagnosis for people with TB, the required parameters including the proportion of known diabetes, proportion of people with suspected diabetes by screening test and proportion of people diagnosed with diabetes by confirmatory test, were extracted from the main study (**Objective 4; Research paper 4**).

Figure 4. Study sites of the PhD research



*Red dots represent the location of the PhD study sites

1.6 Methodological approach: details

1.6.1 Objective 1. To estimate the direct medical, direct nonmedical and indirect costs incurred by people with concurrent TB and diabetes and their households using longitudinal data collection.

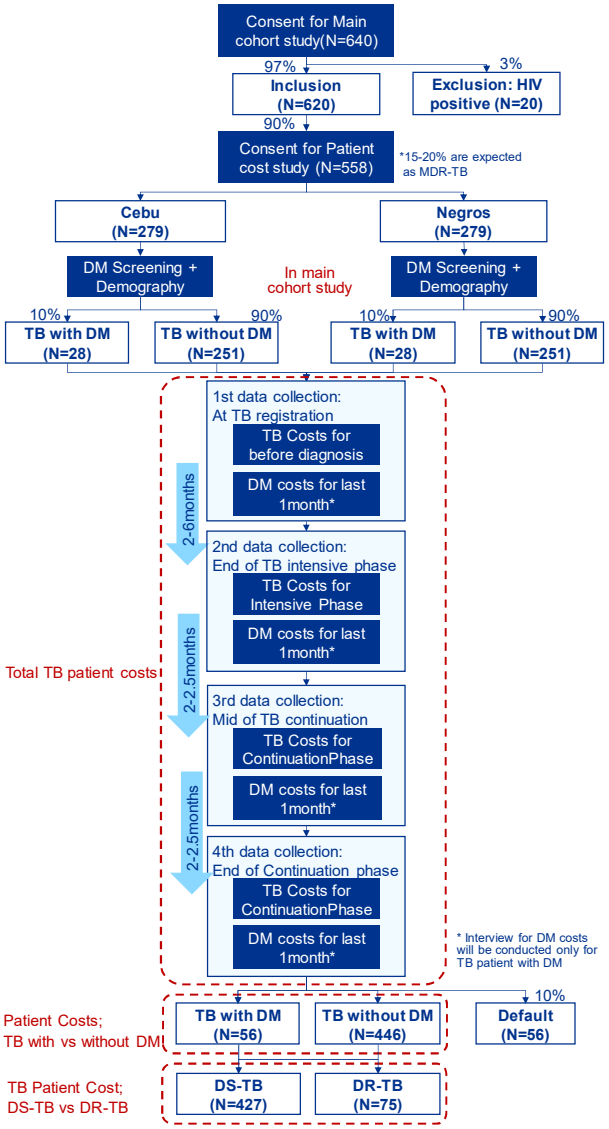
Cost data were collected from people with concurrent TB and diabetes and also from those with TB only who were enrolled in the main study between November 2018 and October 2020. The aim was to assess the costs incurred, income earned and coping mechanisms before TB diagnosis until completion of TB treatment and also to assess the difference in costs incurred by people with TB-diabetes and TB-only. People with pulmonary TB including DR-TB who were 18 years and over were eligible to participate in this study following the eligibility criteria of the main study. Although people with TB-HIV were included in the main study, they were excluded in this costing study to exclude the financial impact from TB-HIV coinfection.

Data Collection of TB and diabetes costs

Research nurses hired through a local research collaborator, the Nutrition Centre of Philippines (NCP), and trained for research ethics and data collection tools were based in each study site to recruit study participants from the main study into this economic sub-study. After the research nurses explained the purpose of this research with written information sheet while people diagnosed with TB were waiting at each study site, people who agreed to participant in the research and signed the informed consent form were enrolled. Data collection for costs incurred by people with TB and their households, household income and coping strategy was conducted by interview at each participant's home and/or by telephone during the COVID-19 outbreak since they were unable to conduct face to face interviews during that period. To capture the total costs incurred by people with TB and affected households, the in-person interview was held four times for each participant; 1. To determine the costs incurred prior to TB diagnosis the first interview was conducted at the time of starting TB treatment; 2. To determine the costs incurred during the TB intensive phase (2 months for DS-TB, 4-6 months for 9-month all-oral DR-TB regimens) the second interview was conducted at the end of TB intensive phase; 3. To determine the costs incurred during TB continuation phase (4 months for DS-TB and 5 months for 9-month all-oral DR-TB regimens) third and fourth interview were conducted at the middle and end of the TB continuation phase. In the last half of the continuation phase, participants can usually return to their normal working schedule since they are likely to have recovered physically and TB symptoms have resolved, therefore, the costs or income loss and the impacts on the TB-affected household during the first half and last half of the continuation phase might be different. Hence, to capture accurate cost data, in-person interviews were conducted twice in the TB continuation phase.

Costs collected in this study consisted of direct medical costs (e.g. medical consultation fees, drugs, diagnostic tests before starting treatment, monitoring tests, hospitalization), direct non-medical costs (e.g. transportation costs, food and supplements, and accommodation), and indirect costs (e.g. income and asset losses due to illness, including time to seek medical care and get tests done, collect drugs, being too unwell to work and paying for a care giver e.g. for a child or other dependents). Costs during TB screening and follow-up until the end of TB treatment, was assessed using the WHO tool for national surveys of costs incurred by people with TB. The tool was adapted for concurrent TB and diabetes in Open Data Kit (ODK). The tool for costs incurred for diabetes management was developed using the same structure and framework as the WHO tool for national surveys of costs incurred by people with TB, and included questions about costs, lost time, and income loss for diabetes drug pick-up, regular screening, irregular visits for diabetes-related hospitalizations and complications. An expected consent rate of 90% is based on our previous experience and from the national survey of costs incurred by people with TB and their households in the Philippines.

Figure 5. flow of participants for assessing costs of TB and diabetes from the patient perspective



I expected that approximately 640 people with TB from the main study would be available for enrolment into this costing sub-study from November 2018 to February 2020. I excluded those with HIV and COVID-19 pneumonia (expected 3%) resulting in 620 potentially eligible participants. Assuming a consent rate of 90% for this costing study, I expected to enrol 558 people with TB with known diabetes status (expected 9-12% with diabetes [157]). Assuming that 90% of these were successfully followed up, I expected data on total TB patient costs to be available for 502 people with TB (**Figure 5**). The 90% retention rate was estimated from the treatment success rate for DS-TB (91% in 2016) in the Philippines. A sample size of 60 people with TB and diabetes and 120 people with TB only was powered at 90% to detect a minimum effect size of a 17% increase in total costs as a proportion of household income between TB-diabetes vs TB-non-diabetes. This assumed a mean of 18.5% of annual household income for non-diabetes TB from a study that assessed costs of people with diabetes and their households in Thailand [104,158].

The total costs over the full course of treatment were compared with results from a simulated cross-sectional approach. The simulated cross-sectional approach extrapolated the costs from a random sample of participants at the end of the intensive phase and the middle of the continuation phase. Each participant was randomly allocated to either the intensive phase or continuation phase group. The deterministic sensitivity analysis was conducted to determine which factors most affect potential over- or under-estimation of the total costs and incidence of catastrophic costs.

1.6.2 Objective 2. To identify the potential biases of the WHO recommended cross-sectional study design for TB catastrophic cost estimates and to explore optimal approaches for sampling and analysing cross-sectional cost data for the catastrophic cost estimates.

Longitudinal study design

Using longitudinal data collected for objective 1, it was first interpolated backwards for the period since the last interview using the data on costs incurred for the last visit by purpose of visits (i.e. hospitalization, directly observed therapy, medical follow-up and drug pick-up) and the frequency of each visit type during each phase. Then total costs were estimated by summing up the costs per phase. Catastrophic cost due to TB was defined as total costs, consisting of direct medical and non-medical costs and indirect costs, exceeding 20% of annual household income of people with TB following the WHO definition [117]. To be consistent with the method used for the Philippines national survey of costs incurred by people with TB and their households, this PhD project used the output approach as the primary method for estimating indirect cost (defined as the difference in self-reported household income before having TB symptoms and at the time of each data collection). Reported annual household income before having TB was used as a primary indicator for ability to pay (denominator for estimating catastrophic costs due to TB, output approach). For TB-affected households reporting zero income even before having TB, annual household income was imputed using a regression model based on household assets).

Simulating catastrophic cost estimates collected using cross-sectional design

To assess the difference in the cost estimates between the longitudinal and cross-sectional study designs, the total costs incurred by people with TB and their households over the full course of treatment were estimated also with a simulated cross-sectional design.

In the simulated cross-sectional method, the aim was to simulate data on incurred expenses captured only at one time point (either at the end of the intensive phase or in the middle of the continuation phase) per participant. Therefore, our samples collected in objective 1 were randomly allocated into two groups, either those for whom data would have been collected at the end of the intensive phase or those for whom data would have been collected in the middle of the continuation phase in accordance with WHO guidance. In order to assess the impact of the sampling balance from TB intensive and continuation phases, we replicated samples with different proportions of the sample in the intensive phase versus the continuation phase (i.e. 20%:80%, 35%:65%, 50%:50% for the proportion of samples in the intensive and continuation phases respectively). The selection of these different proportions was based on the most commonly reported proportions used in published

surveys of costs incurred by people with TB and their households conducted using the WHO recommended methodology [56,124,142,144-151,159,160].

The direct medical and non-medical costs of the other treatment phase were extrapolated based on the median costs estimated from the data of other participants in that treatment phase, following the WHO recommended extrapolation methods [117]. For example, to estimate the direct costs before TB diagnosis and during the intensive phase for participants who were in the middle of the continuation phase at the time of data collection, the median costs before TB diagnosis and during the intensive phase were taken from the participants who were in the intensive phase when data was collected from them. In this extrapolation process for the direct costs, differences in the costs by drug-resistance status and with/without hospitalization(s) were considered.

1.6.3 Objective 3. To assess the provider costs of diagnosing and managing diabetes for people with TB within TB services.

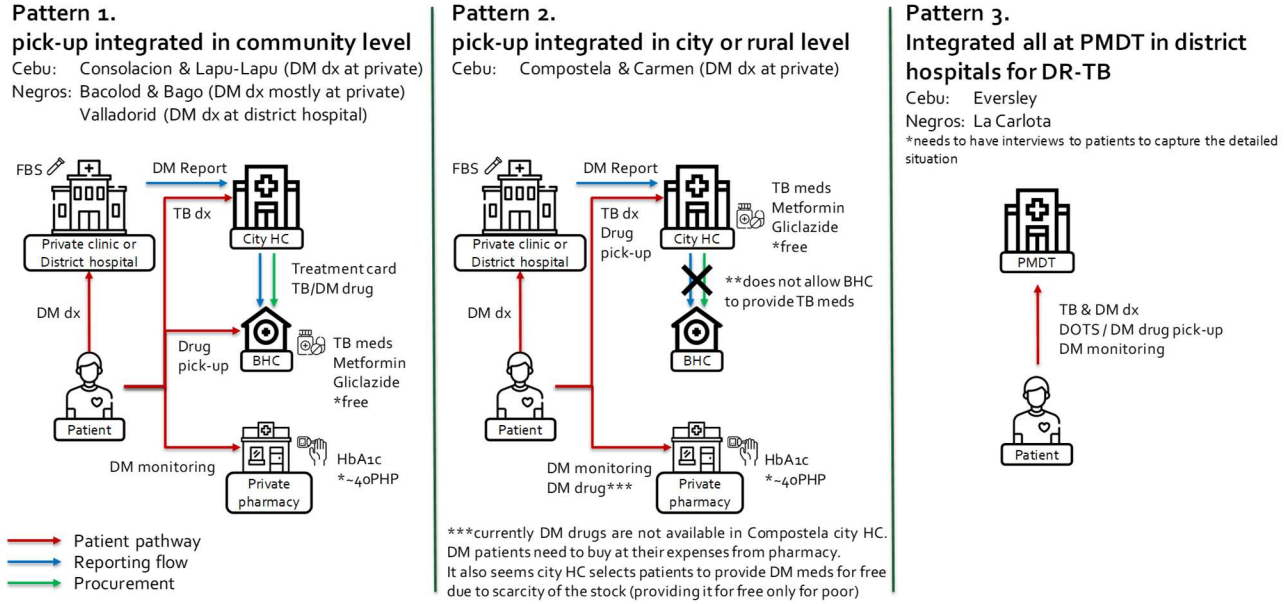
The current service integration for TB and diabetes services differs by area and level of facility, and three different patterns were identified in the study sites for TB and diabetes patient costs in the Philippines (**Figure 6**).

Pattern 1. Drug pick-up for TB and diabetes are integrated at community level (barangay health centre). However, diagnosis for TB and diabetes are provided at different levels of health facilities (diagnosis for TB is at the city/rural health unit and for diabetes it is at the district hospital). First screen and regular monitoring by Point of Care (POC) HbA1c or fasting blood glucose are not provided in public health facilities, and therefore people living with diabetes have to visit private pharmacies for these services.

Pattern 2. Drug pick-up for TB and diabetes are integrated at secondary health facility level (city or rural health unit). Some cities or rural health units do not allow TB medications to be provided at the community level, and therefore, for TB drug pick-up, people with TB and diabetes have to visit secondary health facility levels where diabetes medications are also available.

Pattern 3. All services for TB and diabetes are integrated in Programmatic Management of Drug-resistant TB (PMDT) facilities at district hospitals for people with DR-TB.

Figure 6. Patient pathway for TB and diabetes services



Data collection for diabetes provider costs was conducted in selected study city health centres in Negros and Cebu where the data collection for TB and diabetes patient costs was being conducted.

Costs included were:

Recurrent costs: consumables for diabetes risk score, POC FBS, RPG and HbA1c, and salaries of healthcare staff

Capital costs: building space and equipment

Micro-costing is useful for estimating the cost associated with community-based studies and the raw data includes not only medical supplies used for treatment but also personnel hours, building cost and equipment cost for health facilities [161]. This costing method is also useful for decision-making where the cost of production of the cost centre is allocated to each unit of service [134]. Micro-costing enumerates staff time, supplies and items used to provide a specific service and estimates their costs. The method needs to include all costs; cost of development, set-up, screening, supplies, and space, and also ideally non-wage labour cost such as social insurance expenditure or labour taxes and overhead cost. The biggest advantage of this method is accuracy, and it is often needed to find the cost of a service intervention. On the other hand, the method is too labour intensive to estimate all the health services and thus must be limited to activities most likely to be affected by the specific intervention [162]. The total cost is divided into recurrent and capital costs. Recurrent costs include consumables for diabetes screening such as POC HbA1c and also salaries for additional human resource, and capital costs include building space to provide diabetes services within DOTS facilities as well as equipment and training costs for providing diabetes screenings [134].

1.6.4 Objective 4. To assess cost-effectiveness of integrating diabetes services within the TB programme in the Philippines.

WHO is developing new guidance on diabetes management for people with TB, and it will be added to the operational handbook on tuberculosis: TB and comorbidities [48]. The current WHO guidance on managing comorbidities for people with TB recommends three different models of integrated care: stand-alone screening provided separately for TB and comorbidities, then referred for diagnosis and treatment (separate service delivery model); screening and diagnosis service provided by providers for TB and comorbidities located in the same premises, then referred for treatment (co-located services model); screening, diagnosis and treatment fully integrated and provided by a service provider (one-stop-shop model) [48,49]. WHO conducted a stakeholder consultation in October 2023 to discuss the latest evidence and the evidence gap on diabetes management for people with TB and to develop the operational handbook. Many evidence gaps were identified in the consultation meeting, such as the lack of evidence on optimal algorithms and timing of providing diabetes testing, association of early diabetes screening and case detection with improvement of TB treatment outcomes. The cost-effectiveness of early detection and management of diabetes in people with TB was also listed one of the topics with evidence gap.

In this PhD project, a simple decision tree was developed to estimate the incremental cost-effectiveness of providing diabetes screening and diagnosis as outpatient services for people with TB at their TB diagnosis. The intervention was defined as providing diabetes screening and diagnosis and the subsequent diabetes management for 90% of people diagnosed with TB who do not know their diabetes status at the time of TB diagnosis.

The cost and health outcomes were compared with the base case scenario which provides TB treatment only. The probability of diabetes screening and diagnostic results and TB treatment outcomes were extracted from the main study (St-Att study) [76,163]. Diabetes status was categorized into three: non-diabetes, unmanaged diabetes and managed diabetes. TB treatment outcomes had four categories: treatment success, loss-to-follow-up, treatment failure and death. The costs were assessed from the societal perspective using the patient cost data of TB and diabetes (objective 1) and the provider cost of diabetes outpatient services for people with TB (Objective 3) [164,165]. TB provider costs were extracted from the VALUE-TB study that assessed health system costs of TB interventions using a nationally representative sample of health facilities in the Philippines [152,153]. Health outcomes were assessed using disability-adjusted life years (DALYs) averted, and DALY weights for health states of TB and diabetes were extracted from the latest Global Burden of Disease study

[166]. Since no data were available for the transition between unmanaged and managed diabetes in lifetime, for simplicity, we assumed no transitions of TB- and diabetes-related health status after the completion of TB treatment.

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CHAPTER 2. COSTS INCURRED BY PEOPLE WITH CO-MORBID TUBERCULOSIS AND DIABETES AND THEIR HOUSEHOLDS IN THE PHILIPPINES

2.1 Preamble

This paper presented the results of a study that assessed costs incurred by people with TB-only and with concurrent TB and diabetes who received TB diagnosis and treatment at public health facilities in Cebu and Negros Occidental, the Philippines. At the time this research paper was written, there was no evidence on the financial burden faced by people with concurrent TB and diabetes, even though diabetes is one of risk factors of TB, and an estimated 0.37 million incident cases of TB was attributable to diabetes globally. The aim of this analysis was to assess the difference in health service utilization and patient costs between people with TB and diabetes (TB-DM) vs with TB-only.

This study was conducted as a nested study within a cohort study (St-Att study, the main study), which evaluated the effects of malnutrition and diabetes on TB treatment outcomes in Manila, Cebu and Negros Occidental, the Philippines. We collected costs, income, coping mechanisms and social consequences of TB and diabetes from care seeking until the end of TB treatment. Costs consisted of direct medical costs (including consultation fees, drugs, screening and diagnostic tests, and hospitalization), direct non-medical costs (including transportation, food and supplements, and accommodation), and indirect costs (income losses). The data collection tool was adapted to the longitudinal study design from the national TB patient cost survey in the Philippines and the WHO handbook for surveys of costs incurred by people with TB and their households. In order to assess the patient costs of diabetes, data collection items assessing direct medical costs (e.g. diabetes screening and diagnosis, diabetes medications, hospitalization for diabetes-related complications) non-medical costs (e.g. transportation, food, accommodation for visiting health facilities for diabetes care and nutritional supplement for diabetes) and indirect costs of diabetes were added in the data collection tool. The data collection was conducted in Cebu and Negros Occidental between November 2018 and October 2020. Catastrophic cost due to TB and diabetes was defined as total costs, consisting of direct medical and non-medical costs and indirect costs, exceeding 20% of ability to pay as per the WHO definition used in surveys of costs incurred by people with TB and their households.

We found that people with TB-diabetes faced a substantially higher burden in terms of health service utilization. However, this did not translate into higher total costs given the limited overall cost of medical expenses and transport costs in our patient populations. There was no significant difference

in the total costs between those with TB-DM (USD 1,178) and TB-only (USD 917) with a p-value of 0.208, and between those with TB-DM receiving diabetes management (TB-managed DM (USD 1,363) and TB-DM not receiving diabetes management (TB-unmanaged DM) (USD 841) with a p-value of 0.078. This study was able to enrol only a small sample of people with TB-DM (N=144), and our study participants did not have severe complications caused by diabetes. This might result in having a low financial impact of diabetes. Hence, further studies with a larger sample size of TB-DM are required to understand the economic impact of TB comorbid with diabetes in the Philippines.

This research paper was published in PLoS One in January 2024, and the paper was reproduced in this chapter with no revisions or adaptation from the published manuscript. Additional information section (**section 2.9**) was included to provide clarifications of methods, results and discussions for the purpose of the thesis development.

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2.2 Research paper cover sheet

The Research Paper Cover Sheet is enclosed on the following pages.

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RESEARCH PAPER COVER SHEET

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Thesis Title	Mitigating the economic impact of TB and diabetes in the Philippines		
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If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	PLoS One		
When was the work published?	25 January 2024		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	**No. Published as open access**	Was the work subject to academic peer review?	**Yes**

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	AV, TY and YL conceptualized the study. TY developed the study methods and obtained funding for this study. JPF, MCC and TY implemented the data collection. TY cleaned, validated and analysed study data with supervision from AV and YL. TY, AV and YL interpreted results. TY developed the draft of the paper. All authors reviewed and edited the paper.

SECTION E

Student Signature	[redacted]
Date	31 August 2024

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Date	31 August 2024

2.3 Abstract

Objective:

Diabetes is a risk factor for TB mortality and relapse. The Philippines has a high TB incidence with co-morbid diabetes. This study assessed the pre- and post-TB diagnosis costs incurred by people with TB and diabetes (TB-DM) and their households in the Philippines.

Methods:

Longitudinal data was collected for costs, income, and coping mechanisms of TB-affected households in Negros Occidental and Cebu, the Philippines. Data collection was conducted four times during TB treatment. The data collection tools were developed by adapting WHO's cross-sectional questionnaire in the Tuberculosis Patient Cost Surveys: A Handbook into a longitudinal study design. Demographic and clinical characteristics, self-reported household income, number of facility visits, patient costs, the proportion of TB-affected households facing catastrophic costs due to TB (>20% of annual household income before TB), coping mechanisms, and social support received were compared by diabetes status at the time of TB diagnosis.

Results:

530 people with TB were enrolled in this study, and 144 (27.2%) had TB-DM based on diabetes testing at the time of TB diagnosis. 75.4% of people with TB-DM were more than 45 years old compared to 50.3% of people with TB-only ($p<0.001$). People with TB-DM had more frequent visits for TB treatment (120 vs 87 visits, $p=0.054$) as well as for total visits for TB-DM treatment (129 vs 88 visits, $p=0.010$) compared to those with TB-only. There was no significant difference in the proportion of TB-affected households facing catastrophic costs between those with TB-DM (76.3%) and those with TB-only (68.7%, $p=0.691$).

Conclusion:

People with TB-DM in the Philippines face extensive health service use. However, this does not translate into substantial differences in the incidence of catastrophic cost. Further study is required to understand the incidence of catastrophic costs due to diabetes-only in the Philippines.

2.4 Introduction

In 2015, the World Health Organization (WHO) set the End TB Strategy, aiming "to ensure that no family is burdened with catastrophic expenses due to TB by 2020" [1]. To capture the situation of TB-associated household costs and monitor the progress toward achieving this target, WHO supports countries to conduct baseline and periodic TB patient cost surveys [2]. Their guideline prescribes conducting a national TB patient cost survey using a feasible and affordable cross-sectional design to assess direct costs (for medications, consultations, hospitalization, transportation, accommodation, and supplements) and indirect costs (such as income loss) [5, 6].

Diabetes increases the risk of progressing to active TB disease and may increase the risk of poor TB treatment outcomes, thus contributing to ongoing transmission, particularly where diabetes is poorly managed [3-6]. As such, the risk of death and the risk of relapse are also higher among people with TB and diabetes (TB-DM) [4]. Therefore, enhancing diagnosis and management of diabetes may improve the rate of decline of TB incidence. The WHO published a separate guideline to develop and implement collaborative actions aimed at reducing the dual burden of TB-DM. The guideline included bi-directional screening of TB in people living with diabetes and of diabetes in people with TB; as well as monitoring and evaluation of collaborative TB-DM activities [7,8].

Given this dual burden there is a concern that people with TB-DM may be more likely to suffer damaging levels of associated costs than those with TB alone, yet there is limited data available on how co-morbidity impacts household costs associated with TB. For HIV, another common comorbidity of TB, a study assessing patient costs for TB-only, HIV-only, and TB-HIV showed that people with TB-HIV visited health facilities more frequently (18.4 times per month) than those with TB-only (16.0 times) or HIV-only (2.2 times) due to fragmented services [9]. A similar situation is expected for the comorbidity of TB-DM, and therefore this study assesses the costs of diabetes diagnosis and treatment among people with TB-DM.

2.5 Methods

Study setting

The Philippines is classified by the WHO as one of the 30 high burden countries for both drug susceptible TB (DS-TB) and multidrug-resistant and rifampicin-resistant TB [10-12], with an estimated TB incidence of 650 per 100,000 in 2021 [11,12]. In the Philippines, the National Tuberculosis Control Program (NTP) conducted a nationwide TB patient cost survey in 2015–2017 using the WHO recommended method [2,13]. The results of the survey found 42.4% (95% confidence interval (95%

CI) 40.2%-44.6%) of TB-affected households faced catastrophic costs [12,14]. The Philippines has a high TB incidence with co-morbid diabetes (22,000 adult TB incident cases were attributable to diabetes in 2021) [12,15].

In the Philippines, costs for diabetes diagnosis and management are not fully covered by national insurance, the NTP or the non-communicable disease control programme, but direct medical costs for TB treatment and diagnosis are covered [16,17]. Social support is provided by the NTP for people with drug-resistant TB (DR-TB) with the purpose of improving treatment adherence and includes food packages and transportation fees for visiting health facilities [14,18,19]. Furthermore, The Department of Social Welfare and Development (DSWD) of the Philippines has a nationwide conditional cash transfer (CCT) programme for households living in poverty, and as of 2016, the CCT programme covered 4.4 million households, equivalent to 20% of the total population [20].

Patient costs for TB and diabetes were collected within an ongoing cohort study. The aim of the main cohort study was to measure the effects of malnutrition and diabetes on TB treatment outcomes in people with TB in Manila, Negros Occidental and Cebu, Philippines [21].

Study design

We collected cost data from people with TB, enrolled in the cohort study between November 2018 and October 2020. The aim was to assess the changes in costs incurred, income earned and coping mechanisms before TB diagnosis until completion of TB treatment, and also assess the difference in costs incurred by people with TB-DM and TB-only. People with pulmonary TB including DR-TB who were 18 years and over were eligible to participate in this study following the eligibility criteria of the main study. Although people with TB-HIV were included in the main study, they were excluded in this costing study to exclude the financial impact from TB-HIV coinfection.

This costing study used a sub-sample of 11 health facilities located in two regions of the Philippines: Negros Occidental and Cebu. After excluding people with HIV (expected 3%), 620 people with TB from the main study were expected to be eligible for this study from November 2018 to February 2020. Assuming a 90% consent rate and 91% treatment completion rate, we expected to collect patient cost data from a total of 502 people with TB. Given 9-12% of the cohort were estimated to have diabetes (45-60 people) [22], we estimated that our sample size of 502 people with TB was sufficiently powered to detect a minimum 17% increase in total costs [23,24].

Research nurses were based in each study site to recruit study participants from the main study into this study. The research nurses explained the purpose of this sub-study using a printed information sheet, in relevant local languages and English. People who agreed to participate in this research and signed the additional informed consent form were enrolled. Data collection for patient costs, household income and coping strategies was subsequently conducted by an in-person interview at each participant's home or by telephone during the period of COVID-19 lockdowns. To capture the total TB and diabetes-related costs incurred, patient interviews were conducted four times per patient; at the start of TB treatment for costs before TB diagnosis, at the end of the TB intensive phase for costs in TB intensive phase, and during the middle and end of the TB continuation phase for costs during the first half of the TB continuation phase and costs during the second half of the TB continuation phase. The enrolment of study participants was conducted from 11 November 2018 until 21 February 2020, and all the required follow-up data collection completed on 4 August 2020.

We used data collection tools derived from the national TB patient cost survey adapted for the Philippines [14] and used the same cost categories to estimate the costs incurred by those with TB-DM and with TB-only. These in turn are based on the WHO Tuberculosis Patient Cost Survey handbook [2,25]. Costs consisted of direct medical costs (including consultation fees, drugs, screening and diagnostic tests, and hospitalization), direct non-medical costs (including transportation, food and supplements, and accommodation), and indirect costs (income losses).

Costs per phase, which were collected at the start of TB treatment, at the end of the TB intensive phase, during the middle and at the end of the TB continuation phase, were interpolated using the data collected on costs at the last visit by visit types (i.e. hospitalization, directly observed therapy, medical follow-up and drug pick-up) and the frequency of each visit type during each phase. Then total costs were estimated by summing the costs per phase. Costs are considered as catastrophic when the total of direct medical, non-medical and indirect costs exceeded 20% of ability to pay (i.e. annual household income) following the WHO definition [2]. Reported annual household income before having TB was used as a primary indicator for ability to pay (output approach). The output approach is a measure of indirect cost and uses a difference in self-reported household income at each time point of data collection to estimate income changes during a TB episode. For TB-affected households reporting zero income before having TB, annual household income was imputed using a regression model based on household assets information **(Table 2).**

Table 2. Regression analysis for asset-based imputed household income

	Coefficients	Standard error	p-value
(constant)	32.4	36.7	0.377
Motorcycle/Tricycle	-45.5	31.6	0.151
Car/Jeep/Van	427.2	86.7	<0.001
Air conditioner	116.9	81.3	0.151
Stove with oven/Gas range	74.8	28.7	0.010
Refrigerator/Freezer	63.0	33.6	0.062
PC/tablet	171.7	52.5	0.001
Gold/jewellery	81.5	50.8	0.109
Number of rooms	29.2	12.6	0.021

Data cleaning and processing, statistical analyses, and data visualizations were performed using R4.2.0 (CRAN: Comprehensive R Archive Network). Mean with standard deviation (SD) and 95% CI, and median with interquartile range (IQR) were used for continuous data, and frequency with proportion (%) was presented for categorical data. All results were stratified by the diabetes status at the time of TB diagnosis. The diabetes screening (HbA1c and RPG: Random Plasma Glucose) and confirmatory (OGTT: Oral Glucose Tolerance Test) tests were provided in the main study. Those who had previously known diabetes, who had a blood sugar level >7.8 mmol/L by OGTT, and who had HbA1c >6.5% or RPG >200mg/dL at the time of TB diagnosis were categorized as people with TB and diabetes. Statistical differences between people with and without diabetes were tested using a chi-square test for categorical data and the t-test or Kruskal–Wallis test for continuous data. Statistical significance was defined as a p-value less than 0.05. Data on costs and incomes were collected in Philippine Pesos (Php) and later converted into United States dollars (USD) for analysis at the rate of Php 51.19 to USD 1 using the average UN Operational Rates of Exchange during the data collection period (November 2018-October 2020).

Ethical considerations

A written consent form was obtained from each participant prior to enrolment, explicitly stating that only the principal investigator (PI) and co-PIs were able to access the study dataset. Prior to obtaining a written informed consent, our data collectors explained the purpose of this research with a written information sheet during patients' waiting time at each study site. Following ethics committees approved the consent procedure.

The St. Cabrini Medical Center-Asian Eye Institute Ethics Review Committee (SCMC-AEI ERC) reviewed and provided a Philippine national ethics approval for the main study, including approval for this sub-study (ERC #2018-008). Ethics approvals were also obtained from the Ethics Review Committee of the WHO Regional Office for the Western Pacific (Ref: 2019.18.PHL.4.STB) and Ethics Review Committees at the London School of Hygiene & Tropical Medicine and Nagasaki University.

2.6 Results

Study population

A total of 530 adults with TB were enrolled at TB diagnosis. Of these, 386 (72.8%) had TB only and 144 (27.2%) had TB-DM according to the status of the known diabetes, the OGTT and the HbA1c or RPG tests at the time of TB diagnosis. Out of 144 participants who were categorized as TB-DM according to their status at the time of TB diagnosis, 48 (33.3%) knew their DM status, with 39 reported managing DM and 9 reported not managing DM. Most (79.4%) of the study participants completed TB treatment, while 15.6% had loss-to-follow-up, 1.2% had treatment failure, and 3.9% died during TB treatment. Of 530 participants, 445 completed every data collection point until the end of the continuation phase and were included in the analyses.

The majority (70.2%) of people with TB-DM were 45 years old or over, while only half of the people with TB-only were in that age group (p<0.001) (**Table 3**). The proportion with DR-TB was slightly higher amongst people with TB-DM (TB-DM: 15.7%, TB-only: 10.5%), but without a significant difference (p=0.179). Higher BMI (≥ 18.5) was observed amongst a greater proportion of people with TB-DM (TB-DM: 68.6%, TB-only: 52.6%, p=0.004), and the proportion with a high blood glucose level (HbA1c ≥5.7) was also greater amongst people with TB-DM (TB-DM: 96.6%, TB-only: 35.0%, p<0.001).

Table 3. Demographic and clinical characteristics of survey participants

	TB patients without diabetes*		TB patients with diabetes		All TB patients		P-value
	N	(%)	N	(%)	N	(%)	
Total	**324**		**121**		**445**		
Demographic characteristics							
Sex							
Female	92	28.4%	37	30.6%	129	29.0%	0.738
Male	232	71.6%	84	69.4%	316	71.0%	
Age group							
18–44	166	51.2%	36	29.8%	202	45.4%	<0.001
≥45	158	48.8%	85	70.2%	243	54.6%	
Education level							
No education/Primary	114	35.2%	34	28.1%	148	33.3%	0.164
High school	155	47.8%	58	47.9%	213	47.9%	
University or higher/Vocational	55	17.0%	29	24.0%	84	18.9%	
Insurance status							
No insurance	97	29.9%	32	26.4%	129	29.0%	0.724
PhilHealth	138	42.6%	56	46.3%	194	43.6%	
GSIS/SSS	89	27.5%	33	27.3%	122	27.4%	
Household size, median (interquartile range)	5 (1-12)		4 (1-14)		5 (1-14)		
Employment status before TB							
Employed (Formal)	65	20.1%	24	19.8%	89	20.0%	0.815
Employed (Informal)	127	39.2%	51	42.1%	178	40.0%	
Unemployed	105	32.4%	39	32.2%	144	32.4%	
Student/Retired	27	8.3%	7	5.8%	34	7.6%	
Primary income earner							
No	170	52.5%	57	47.1%	227	51.0%	0.368
Yes	154	47.5%	64	52.9%	218	49.0%	
Clinical characteristics							
Drug resistance status							
Drug susceptible-TB	290	89.5%	102	84.3%	392	88.1%	0.179
Drug resistant-TB	34	10.5%	19	15.7%	53	11.9%	
Treatment history							
New	212	66.0%	80	66.7%	292	66.2%	0.791
Relapse	98	30.5%	36	30.0%	134	30.4%	
Treatment after loss to follow up	7	2.2%	3	2.5%	10	2.3%	
Treatment after failure	3	0.9%	0	0.0%	3	0.7%	
Unknown	1	0.3%	1	0.8%	2	0.5%	
Body mass index							
<18.5 (kg/m^2)	153	47.4%	38	31.4%	191	43.0%	0.004
>=18.5 (kg/m^2)	170	52.6%	83	68.6%	253	57.0%	
Diagnostic delay (>4weeks)	221	68.2%	92	76.0%	313	70.3%	-
Duration of TB episode (weeks)							
Care seeking: Mean (SD)	11.3	17.5	11.2	13.4	11.3	16.5	0.942
Intensive phase: Mean (SD)	9.2	3.3	9.6	3.7	9.3	3.4	0.231
Continuation phase: Mean (SD)	16.8	2.4	17.0	2.6	16.9	2.4	0.526
Hospitalized due to TB	34	10.5%	9	7.4%	43	9.7%	0.429
Previously hospitalized in the current treatment phase	255	78.7%	90	74.4%	345	77.5%	-
Treatment supports in intensive phase							
Self-administered	241	74.4%	83	68.6%	324	72.8%	0.271
With treatment partner	83	25.6%	38	31.4%	121	27.2%	
Treatment supports in middle of continuation phase							
Self-administered	252	77.8%	87	71.9%	339	76.2%	0.242

With treatment partner	72	22.2%	34	28.1%	106	23.8%	
Treatment supports in end of continuation phase							
Self-administered	255	78.7%	90	74.4%	345	77.5%	0.398
With treatment partner	69	21.3%	31	25.6%	100	22.5%	
HbA1c							
HbA1c:<5.7	207	65.9%	4	3.3%	211	48.6%	<0.001
HbA1c:5.7-6.4	107	34.1%	19	15.8%	126	29.0%	
HbA1c:6.5+ or RPG:200+ (mg/dL)	0	0.0%	97	80.8%	97	22.4%	

Health service utilisation

Mean total number of visits for TB-DM services amongst all the participants was 92.2 visits per person, and of these, 90.5 visits were for TB services and 1.8 for diabetes services (**Table 4**). People with TB-DM compared to people with TB-only, had more frequent visits for TB treatment (TB-DM: 120.0, TB-only: 86.9, p=0.054) as well as more frequent aggregated visits for TB services and DM services (such as regular monitoring for blood sugar level and drug pickup) (TB-DM: 128.8, TB-only: 87.6, p=0.010). There were no significant differences in the number of visits for TB services by treatment phase and by visit type between people with TB-DM and TB-only, except for medical follow-up (that is for physician's consultation and follow-up tests) between the middle and the end of the continuation phase (TB-DM: 1.1, TB-only: 0.7, p=0.002).

Table 4. Health service utilizations, mean per person

	People with TB only		People with TB and diabetes		Overall		p-value
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	
For TB services							
Before TB diagnosis	**5.1**	**(4.9-5.3)**	**5.4**	**(4.8-5.9)**	**5.1**	**(4.9-5.3)**	**0.398**
Intensive phase							
Medical follow-up	1.0	(0.9-1.2)	1.1	(0.8-1.4)	1.0	(0.9-1.2)	0.532
Drug pickup	16.8	(13.5-20.2)	23.0	(12.4-33.7)	17.5	(14.3-20.7)	0.156
Directly observed therapy	21.0	(16.8-25.1)	28.9	(17.0-40.8)	21.8	(17.9-25.7)	0.085
Middle of continuation phase							
Medical follow-up	0.6	(0.5-0.6)	0.7	(0.4-0.9)	0.6	(0.5-0.6)	0.289
Drug pickup	9.8	(8.0-11.5)	13.0	(7.6-18.4)	10.1	(8.4-11.8)	0.276
Directly observed therapy	12.7	(10.1-15.4)	18.6	(11.1-26.0)	13.4	(10.9-15.9)	0.114
End of continuation phase							
Medical follow-up	0.7	(0.6-0.8)	1.1	(0.8-1.3)	0.7	(0.7-0.8)	0.002
Drug pickup	8.0	(6.6-9.4)	11.7	(6.5-16.9)	8.4	(7.0- 9.8)	0.178
Directly observed therapy	11.2	(8.8-13.7)	16.6	(9.1-24.0)	11.8	(9.5-14.2)	0.182
For diabetes services							
Intensive phase							
Monitoring	0.2	(0.1-0.3)	1.2	(0.8-1.5)	0.3	(0.2-0.4)	<0.001
Drug pickup	0.2	(0.06-0.3)	2.5	(1.6-3.3)	0.5	(0.3-0.6)	<0.001
Middle of continuation phase							
Monitoring	0.03	(0.007-0.06)	0.5	(0.1-0.9)	0.1	(0.04-0.2)	0.020
Drug pickup	0.2	(0.08-0.2)	2.4	(1.4-3.3)	0.5	(0.3-0.6)	<0.001
End of continuation phase							
Monitoring	0.03	(0.007-0.06)	0.3	(0.1-0.4)	0.1	(0.03-0.1)	0.003
Drug pickup	0.1	(0.05-0.2)	2.0	(1.4-2.7)	0.4	(0.2-0.5)	<0.001
Total							
TB total	86.9	(73.7-100.1)	120.0	(76.9-163.2)	90.4	(77.7-103.2)	0.054
Diabetes total	0.7	(0.5-1.0)	8.8	(6.8-10.9)	1.8	(1.4-2.2)	0.056
Total TB and diabetes	87.6	(74.4-100.8)	128.8	(85.1-172.6)	92.2	(79.4-105.0)	0.010

Costs incurred by TB-affected households

Overall, the mean total costs were estimated at USD 952 (

Table 5). Of these, TB costs accounted for USD 932 (97.9%), and the TB costs were mainly driven by income loss (86.1%), followed by direct non-medical costs (10.5%) and direct medical costs (3.5%).

Although the total costs among people with TB-DM were USD 1,178, which was 28% higher than that incurred by people with TB only (USD 917), no significant difference was observed (p=0.208). For TB services, while people with TB-DM incurred higher costs, there was no significant difference in TB costs between people with TB-DM and TB only (TB-DM: USD 1,053, TB only: USD 914, p=0.464). For

TB-DM patient costs, US$			**People with TB only**			**People with TB and diabetes**			**Overall**			**p-value**
			Mean	**%**	**(95% CI)**	**Mean**	**%**	**(95% CI)**	**Mean**	**%**	**(95% CI)**	
Pre-TB diagnosis	Direct medical costs		27.4	3.0%	(17.6-37.1)	37.3	3.5%	(25.8-48.8)	28.7	3.1%	(20.1-37.3)	0.197
	Direct non-medical costs		27.2	3.0%	(22.3-32.2)	41.1	3.9%	(25.6-56.7)	29.1	3.1%	(24.3-33.9)	0.096
	Income loss		205.7	22.5%	(148.1-263.4)	308.1	29.3%	(86.2-530.1)	219.3	23.5%	(161.2-277.4)	0.382
Post-TB diagnosis	Direct medical costs	Drug pickup	0.06	0.0%	(0.0-0.1)	0.0	0.0%	(0.0-0.0)	0.05	0.0%	(0-0.1)	0.101
		Directly observed therapy	0.0	0.0%	(0.0-0.0)	0.0	0.0%	(0.0-0.0)	0.0	0.0%	(0.0-0.0)	N/A
		Follow-up	1.8	0.2%	(0.8-2.7)	1.8	0.2%	(0.0-3.9)	1.8	0.2%	(0.9-2.6)	0.970
		Hospitalization	1.9	0.2%	(0.0-4.8)	0.8	0.1%	(0.0-2.4)	1.8	0.2%	(0-4.3)	0.527
		Total	3.7	0.4%	(0.7-6.8)	2.6	0.2%	(0.0-6.2)	3.6	0.4%	(0.9-6.3)	0.652
	Direct non-medical costs	Accommodation	0.05	0.0%	(0.0-0.1)	0.1	0.0%	(0.0-0.3)	0.06	0.0%	(0-0.1)	0.632
		Food	3.0	0.3%	(2.1-3.8)	7.6	0.7%	(2.8-12.5)	3.6	0.4%	(2.6-4.6)	0.065
		Travel	18.6	2.0%	(15.4-21.8)	22.7	2.2%	(14.6-30.8)	19.2	2.1%	(16.2-22.1)	0.360
		Nutrition supplement	39.5	4.3%	(34.0-45.0)	87.4	8.3%	(65.1-109.7)	45.8	4.9%	(40.0-51.7)	<0.001
		Total	61.1	6.7%	(53.4-68.8)	117.8	11.2%	(89.5-146.1)	68.6	7.4%	(60.8-76.5)	<0.001
	Income loss		588.3	64.4%	(489.7-687.0)	545.9	51.8%	(350.2-741.6)	582.7	62.5%	(493.3-672.1)	0.704
Total direct medical costs			31.1	3.4%	(20.9-41.3)	40.0	3.8%	(28.2-51.8)	32.3	3.5%	(23.3-41.3)	0.267
Total direct non-medical costs			88.4	9.7%	(78.4-98.3)	158.9	15.1%	(123.1-194.7)	97.7	10.5%	(87.6-107.8)	<0.001
Income loss			794.1	86.9%	(653.1-935.0)	854.0	81.1%	(519.9-1 188.1)	802.0	86.1%	(672.0-932.1)	0.746
Total cost (TB)			913.5	100%	(768.8-1 058.3)	1,052.9	100%	(709.3-1 396.4)	932.0	100%	(798.4-1 065.7)	0.464
For diabetes services												
Direct medical costs			2.7	73.0%	(0.6-4.7)	104.2	83.3%	(47.9-160.5)	16.1	81.3%	(7.8-24.4)	<0.001
Direct non-medical costs			1.1	29.7%	(0.5-1.7)	20.9	16.7%	(12.4-29.4)	3.7	18.7%	(2.3-5.1)	<0.001
Total (Diabetes)			3.7	100%	(1.2-6.3)	125.1	100%	(61.9-188.2)	19.8	100%	(10.4-29.3)	<0.001
Total cost												
Total cost (TB)			913.5	99.6%	(0.5-1.7)	1,052.9	89.4%	(709.3-1 396.4)	932.0	97.9%	(2.3-5.1)	0.464
Total cost (Diabetes)			3.7	0.4%	(1.2-6.3)	125.1	10.6%	(61.9-188.2)	19.8	2.1%	(10.4-29.3)	<0.001
Total cost (TB-diabetes)			917.3	100%	(772.3-1 062.3)	1,177.9	100%	(800.0-1 555.8)	951.8	100%	(816.2-1 087.5)	0.208

diabetes costs, people with TB-DM incurred significantly higher costs (TB-DM: USD 125) since people with TB-only incurred a minimal amount of costs (USD 4, $p<0.001$) for diabetes-related services, mainly for diabetes screening during TB treatment.

Among the three main cost categories for TB services (direct medical, direct non-medical, and income loss), a significant difference was shown only in direct non-medical costs between people with TB-DM and TB-only (TB-DM: USD 159, TB-only: USD 88, $p<0.001$), which was specifically for nutritional supplements and additional food (TB-DM: USD 87, TB-only: USD 40, $p<0.001$).

Table 5. Detail of costs incurred per TB-affected households by TB treatment phase (mean, percentage, 95%CI), by diabetes status at the time of TB diagnosis

Costs data was converted to United States Dollars (US$) from Philippines Peso (Php) using the average UN Operational Rates of Exchange during data collection period (Nov 2018-Oct 2020) of US$1 = Php 51.193375 (https://treasury.un.org/operationalrates/OperationalRates.ph

N/A: Not available

Costs incurred by TB-DM affected households

TB-DM patient costs, US$			People with TB only			People with TB and diabetes			Overall			p-value
			Mean	%	(95% CI)	Mean	%	(95% CI)	Mean	%	(95% CI)	
Pre-TB diagnosis	Direct medical costs		27.4	3.0%	(17.6-37.1)	37.3	3.5%	(25.8-48.8)	28.7	3.1%	(20.1-37.3)	0.197
	Direct non-medical costs		27.2	3.0%	(22.3-32.2)	41.1	3.9%	(25.6-56.7)	29.1	3.1%	(24.3-33.9)	0.096
	Income loss		205.7	22.5%	(148.1-263.4)	308.1	29.3%	(86.2-530.1)	219.3	23.5%	(161.2-277.4)	0.382
Post-TB diagnosis	Direct medical costs	Drug pickup	0.06	0.0%	(0.0-0.1)	0.0	0.0%	(0.0-0.0)	0.05	0.0%	(0-0.1)	0.101
		Directly observed therapy	0.0	0.0%	(0.0-0.0)	0.0	0.0%	(0.0-0.0)	0.0	0.0%	(0.0-0.0)	N/A
		Follow-up	1.8	0.2%	(0.8-2.7)	1.8	0.2%	(0.0-3.9)	1.8	0.2%	(0.9-2.6)	0.970
		Hospitalization	1.9	0.2%	(0.0-4.8)	0.8	0.1%	(0.0-2.4)	1.8	0.2%	(0-4.3)	0.527
		Total	3.7	0.4%	(0.7-6.8)	2.6	0.2%	(0.0-6.2)	3.6	0.4%	(0.9-6.3)	0.652
	Direct non-medical costs	Accommodation	0.05	0.0%	(0.0-0.1)	0.1	0.0%	(0.0-0.3)	0.06	0.0%	(0-0.1)	0.632
		Food	3.0	0.3%	(2.1-3.8)	7.6	0.7%	(2.8-12.5)	3.6	0.4%	(2.6-4.6)	0.065
		Travel	18.6	2.0%	(15.4-21.8)	22.7	2.2%	(14.6-30.8)	19.2	2.1%	(16.2-22.1)	0.360
		Nutrition supplement	39.5	4.3%	(34.0-45.0)	87.4	8.3%	(65.1-109.7)	45.8	4.9%	(40.0-51.7)	<0.001
		Total	61.1	6.7%	(53.4-68.8)	117.8	11.2%	(89.5-146.1)	68.6	7.4%	(60.8-76.5)	<0.001
	Income loss		588.3	64.4%	(489.7-687.0)	545.9	51.8%	(350.2-741.6)	582.7	62.5%	(493.3-672.1)	0.704
Total direct medical costs			31.1	3.4%	(20.9-41.3)	40.0	3.8%	(28.2-51.8)	32.3	3.5%	(23.3-41.3)	0.267
Total direct non-medical costs			88.4	9.7%	(78.4-98.3)	158.9	15.1%	(123.1-194.7)	97.7	10.5%	(87.6-107.8)	<0.001
Income loss			794.1	86.9%	(653.1-935.0)	854.0	81.1%	(519.9-1 188.1)	802.0	86.1%	(672.0-932.1)	0.746
Total cost (TB)			913.5	100%	(768.8-1 058.3)	1,052.9	100%	(709.3-1 396.4)	932.0	100%	(798.4-1 065.7)	0.464
For diabetes services												
Direct medical costs			2.7	73.0%	(0.6-4.7)	104.2	83.3%	(47.9-160.5)	16.1	81.3%	(7.8-24.4)	<0.001
Direct non-medical costs			1.1	29.7%	(0.5-1.7)	20.9	16.7%	(12.4-29.4)	3.7	18.7%	(2.3-5.1)	<0.001
Total (Diabetes)			3.7	100%	(1.2-6.3)	125.1	100%	(61.9-188.2)	19.8	100%	(10.4-29.3)	<0.001
Total cost												
Total cost (TB)			913.5	99.6%	(0.5-1.7)	1,052.9	89.4%	(709.3-1 396.4)	932.0	97.9%	(2.3-5.1)	0.464
Total cost (Diabetes)			3.7	0.4%	(1.2-6.3)	125.1	10.6%	(61.9-188.2)	19.8	2.1%	(10.4-29.3)	<0.001
Total cost (TB-diabetes)			917.3	100%	(772.3-1 062.3)	1,177.9	100%	(800.0-1 555.8)	951.8	100%	(816.2-1 087.5)	0.208

People with TB and known diabetes that were already under management incurred much higher diabetes costs (TB-known and managed DM: USD 209, TB-unmanaged DM: USD 23, p<0.001), while there was no significant difference in the total TB-DM costs (TB-known and managed DM: USD 1363, TB-unmanaged DM: USD 841, p<0.078) (**Table 6**).

Table 6. Detail of costs incurred per TB-DM affected households (mean, percentage, 95%CI), by diabetes management status at the time of TB diagnosis

TB and diabetes patient costs, US$			TB patients with known and managed diabetes*			TB patients with unmanaged diabetes*			p-value
			Mean	%	(95% CI)	Mean	%	(95% CI)	
Pre-TB diagnosis	Direct medical costs		34.7	3.0%	(19.9-49.4)	27.6	3.4%	(19.4-35.8)	0.412
	Direct non-medical costs		44.6	3.9%	(21.7-67.5)	26.0	3.2%	(17.6-34.3)	0.138
	Income loss		309.6	26.8%	(0.0-643.7)	214.9	26.3%	(111.2-318.6)	0.596
Post-TB diagnosis	Direct medical costs	Drug pickup	0.0	0.0%	(0.0-0.0)	0.0	0.0%	(0.0-0.0)	N/A
		Directly observed therapy	0.0	0.0%	(0.0-0.0)	0.0	0.0%	(0.0-0.0)	N/A
		Follow-up	2.8	0.2%	(0.0-6.4)	1.0	0.1%	(0.2-1.8)	0.355
		Hospitalization	1.5	0.1%	(0.0-4.5)	0.1	0.0%	(0.0-0.4)	0.363
		Total	4.3	0.4%	(0.0-10.8)	1.2	0.1%	(0.3-2.0)	0.350
	Direct non-medical costs	Accommodation	0.2	0.0%	(0.0-0.6)	0.0	0.0%	(0.0-0.0)	0.314
		Food	9.8	0.8%	(1.2-18.4)	3.2	0.4%	(1.7-4.6)	0.137
		Travel	28.2	2.4%	(14.6-41.8)	19.4	2.4%	(14.2-24.6)	0.240
		Nutrition supplement	103.0	8.9%	(69.8-136.2)	44.0	5.4%	(31.9-56.2)	0.001
		Total	141.2	12.2%	(98.0-184.5)	66.6	8.1%	(51.9-81.4)	0.002
	Income loss		619.2	53.7%	(378.9-859.6)	481.4	58.9%	(341.2-621.7)	0.334
Total direct medical costs			39.0	3.4%	(23.7-54.3)	28.7	3.5%	(20.2-37.3)	0.254
Total direct non-medical costs			185.8	16.1%	(133.5-238.1)	92.6	11.3%	(73.5-111.7)	0.001
Income loss			928.8	80.5%	(492.3-1 365.4)	696.3	85.2%	(484.8-907.9)	0.349
Total cost (TB)			1,153.6	100%	(697.1-1 610.1)	817.7	100%	(601.0-1 034.3)	0.195
For diabetes services									
Direct medical costs			181.2	86.5%	(85.4-276.9)	15.1	65.7%	(6.0-24.1)	0.001
Direct non-medical costs			28.4	13.5%	(14.6-42.2)	7.9	34.3%	(4.5-11.3)	0.005
Total (diabetes)			209.6	100%	(102.0-317.2)	23.0	100%	(11.4-34.5)	0.001
Total cost									
Total cost (TB)			1,153.6	84.6%	(14.6-42.2)	817.7	97.3%	(4.5-11.3)	0.195
Total cost (diabetes)			209.6	15.4%	(102.0-317.2)	23.0	2.7%	(11.4-34.5)	0.001
Total cost (TB and diabetes)			1,363.2	100%	(832.2-1 894.2)	840.7	100%	(619.1-1 062.2)	0.078

*Study participants who reported known diabetes and also were already taking diabetes management at the study enrolment were categorized as TB patients with managed diabetes.

Household income, catastrophic cost, and social support schemes

Overall, the mean reported monthly household income before having TB was USD 183 (95%CI: 155-210), with no significant differences between people with TB-DM (USD 189, 95%CI: 140-238) and TB-only (USD 182, 95%CI: 151-212), declining during TB diagnosis (USD 80, 95%CI: 68-92) and at the end of the intensive phase of TB treatment (USD 9, 95%CI: 6-11) (**Table 7**). It increased towards the middle

of the continuation phase (USD 195, 95%CI: 164-227) and was sustained to the end of that phase (USD 197, 95%CI: 165-228). No significant differences were observed for the mean reported monthly household income between people with TB-DM and TB-only except at the end of the intensive phase (TB-DM: USD 3 (95%CI: 1-5), TB-only: USD 10 (95%CI: 7-12), p<0.001).

In line with the changes in income, the proportion of households living below the international poverty line was greatest at the end of the intensive phase but with no statistically significant difference between people with TB-DM and TB-only.

The proportion of TB-affected households spending more than 20% of their annual household income on TB -related services was 69.0% (95%CI: 64.7-73.3%), and there was no statistically significant difference between people with TB-DM (68.7%, 95%CI: 64.0-73.3%) and TB-only (71.2%, 95%CI: 59.3-83.1%), with a p-value of 0.691 (**Figure 7**). Unsurprisingly, the proportion of households incurring costs greater than 20% of their annual household income for TB and DM-related services was higher for people with TB-DM (76.3%, 95%CI: 65.1-87.5%), while there was no significant difference compared to people with TB-only (p=0.207).

Cash from the CCT programme was received by 16.0% (95%CI: 12.8-19.7%) of TB-affected households before TB diagnosis, and the proportion remained constant throughout TB treatment (**Table 7**). Similarly, the social support package was received by 13.3% (95%CI: 16.8-10.4%) of TB-affected households during the TB intensive phase and remained at the same level during the TB continuation phase. There was no significant difference in the proportion of households receiving the social support package between people with TB-DM and TB-only during TB treatment. Social consequences of TB were summarised in **Table 8.**

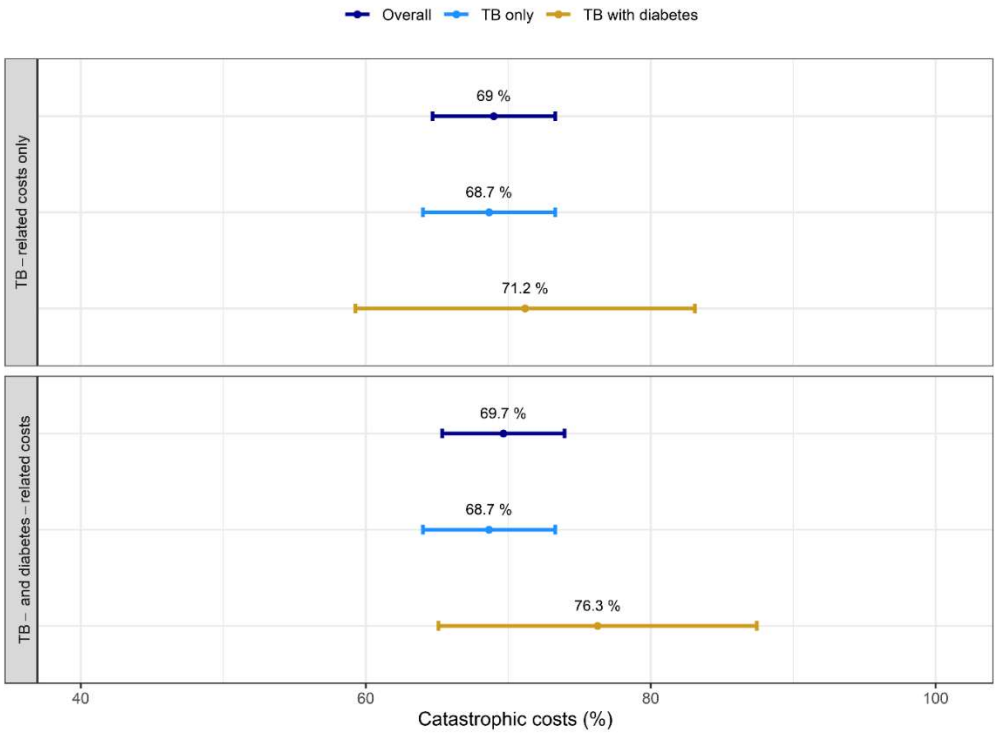
Table 7. Reported household income and social support received by TB-affected households

	People with TB only		People with TB and diabetes		Overall		p-value
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	
Self-reported monthly household Income (in US$)							
Before onset of TB symptoms	181.8	(151.3-212.3)	188.9	(140.3-237.5)	182.7	(155.4-210.0)	0.810
At the time of TB diagnosis	79.1	(66.6-91.6)	88.2	(51.5-124.8)	80.3	(68.4-92.1)	0.647
At the end of intensive phase	9.5	(6.7-12.2)	2.9	(0.6-5.3)	8.6	(6.2-11.0)	<0.001
At the middle of continuation phase	196.4	(160.7-232.1)	187.8	(139.4-236.2)	195.3	(163.6-226.9)	0.780
At the end of continuation phase	195.3	(160.4-230.1)	205.0	(152.4-257.7)	196.5	(165.5-227.6)	0.761
	%	**95% CI**	**%**	**95% CI**	**%**	**95% CI**	
Impoverishment: TB-affected households below international poverty line, percentage (95% CI)							
Before onset of TB symptoms	47.7	(43.2-52.3)	46.4	(34.6-58.4)	47.5	(43.3-51.8)	0.835
At the time of TB diagnosis	74.0	(69.9-77.9)	75.4	(64.4-84.9)	74.2	(70.3-77.8)	0.806
At the end of intensive phase	87.9	(84.7-90.7)	91.3	(83.4-96.8)	88.3	(85.4-90.9)	0.210
At the middle of continuation phase	35.4	(31.0-39.8)	33.3	(22.6-45.0)	35.1	(31.1-39.2)	0.678
At the end of continuation phase	33.8	(29.6-38.2)	30.4	(20.0-42.0)	33.4	(29.4-37.5)	0.482
Conditional cash transfer for poor							
Before TB diagnosis	16.8	(13.4-20.9)	10.2	(4.6-21.2)	16.0	(12.8-19.7)	0.194
Intensive phase	16.6	(13.2-20.6)	8.5	(3.5-19.1)	15.5	(12.4-19.2)	0.110
Middle of continuation phase	17.9	(14.4-22.0)	10.2	(4.6-21.2)	16.9	(13.6-20.6)	0.142
End of continuation phase	15.8	(12.5-19.8)	8.5	(3.5-19.1)	14.8	(11.8-18.5)	0.141
Social supports for TB people							
Before TB diagnosis	2.8	(1.6-5.1)	1.7	(0.2-11.5)	2.7	(4.7-1.5)	0.611
Intensive phase	12.7	(9.7-16.4)	16.9	(9.2-29.0)	13.3	(16.8-10.4)	0.370
Middle of continuation phase	15.3	(12.0-19.2)	16.9	(9.2-29.0)	15.5	(19.2-12.4)	0.743
End of continuation phase	14.0	(10.9-17.8)	18.6	(10.5-30.9)	14.6	(18.2-11.6)	0.347

Table 8. Social consequences of TB and diabetes

	TB people without diabetes		TB people with diabetes		Overall	
	%	**(95% CI)**	**%**	**(95% CI)**	**%**	**(95% CI)**
Social consequences						
Before TB diagnosis						
Food insecurity	3.6	(2.2-6.0)	1.7	(0.2-11.5)	3.4	(2.0-5.5)
Divorce/separation	0.3	(0.04-1.8)	-	0.0	0.2	(0.03-1.6)
Job loss	47.4	(42.4-52.4)	37.3	(25.7-50.5)	46.1	(41.5-50.7)
Interrupted schooling	0.5	(0.1-2.1)	-	0.0	0.4	(0.1-1.8)
Social exclusion	13.5	(10.4-17.3)	8.5	(3.5-19.1)	12.8	(10.0-16.3)
End of intensive phase						
Food insecurity	8.0	(5.7-11.2)	5.1	(1.6-14.9)	7.6	(5.5-10.5)
Divorce/separation	-	N/A	-	N/A	-	N/A
Job loss	40.7	(35.9-45.7)	42.4	(30.2-55.5)	40.9	(36.4-45.6)
Interrupted schooling	0.8	(0.2-2.4)	1.7	(0.2-11.5)	0.9	(0.3-2.4)
Social exclusion	4.7	(3.0-7.3)	5.1	(1.6-14.9)	4.7	(3.1-7.1)
Middle of continuation phase						
Food insecurity	6.2	(4.2-9.1)	3.4	(0.8-12.9)	5.8	(4.0-8.5)
Divorce/separation	-	N/A	-	N/A	-	N/A
Job loss	25.9	(21.8-30.5)	22.0	(13.1-34.7)	25.4	(21.6-29.7)
Interrupted schooling	0.3	(0.04-1.8)	1.7	(0.2-11.5)	0.4	(0.1-1.8)
Social exclusion	3.4	(2.0-5.7)	6.8	(2.5-17.0)	3.8	(2.4-6.1)
End of continuation phase						
Food insecurity	4.4	(2.7-7.0)	3.4	(0.8-12.9)	4.3	(2.7-6.6)
Divorce/separation	-	N/A	-	N/A	-	N/A
Job loss	14.2	(11.1-18.1)	15.3	(8.0-27.1)	14.4	(11.4-18.0)
Interrupted schooling	0.3	(0.04-1.8)	-	0	0.2	(0.03-1.6)
Social exclusion	1.0	(0.4-2.7)	1.7	(0.2-11.5)	1.1	(0.5-2.7)

Figure 7. Percentage of TB-affected households facing catastrophic costs > 20%



2.7 Discussion

We found high costs due to TB-DM, with an overall mean total cost of USD 952, and catastrophic costs in a high proportion of households (69%). We did not however find any significant difference in costs incurred or levels of catastrophic costs between those with TB-only and with TB-DM. Both groups were found to have similar levels of income before the start of the study and similar levels of income loss during TB treatment. While on average those with TB-DM incurred slightly more non-medical expenses and income loss, this was not substantially higher than those with TB-only. Those with TB-DM did face a substantially higher burden in terms of health care usage, but this did not translate into higher total costs given the limited overall cost of medical expenses and transport costs in our patient populations. Also, diabetes costs were much higher among those who were already receiving diabetes management at the time of TB diagnosis, while this also did not translate into higher total costs for TB-DM due to the limited number of samples in our study.

The unemployment rate of our study participants before having TB was already high at 34.5%, and approximately half (47%) of our participants were living under the international poverty line even before having TB. Those with TB-DM incurred a substantial amount of additional direct costs due to diabetes during the TB episode (USD 125). However, the total incurred costs for TB (USD 914 in TB-only, USD 1153 in TB-DM) had a far greater financial impact in affected households given their financial vulnerability due to high baseline unemployment and poverty rates. Therefore, in our study, the additional costs due to diabetes did not translate into a higher incidence of catastrophic costs and impoverishment during their TB episode.

This study was unable to capture costs for diabetes-related complications and hospitalizations in the sample of 144 people with TB-DM since the study was only assessing costs during a discrete period of a TB episode and not over the course of DM disease. Also, not all of them were taking DM management throughout the episode of TB. Therefore, our findings are not generalisable in describing the financial burden of diabetes. Lack of access to diabetes diagnosis and treatment usually result in the development of earlier, more frequent and severe complications such as blindness, kidney disease, coronary heart disease, cerebrovascular disease and stroke, and those complications lead to premature disability and death which incur a higher financial burden in affected households [26,27]. A previous study that assessed direct and indirect costs of diabetes in Kenya in 163 people showed that the total annual costs for diabetes services was USD 673, with 10% and 12% of study participants reporting costs for hospitalizations and irregular facility visits, respectively [28]. In that study, more than 50% of diabetes-affected households faced catastrophic costs (using a threshold of 20% of annual

household income). Another study assessing 6,359 people in China showed that hospitalizations accounted for 73% of total diabetes costs, and the incidence of catastrophic costs was 24%, even with a higher threshold (40%) of annual household income [29]. Hence, another study with a larger sample size of people with diabetes is required to understand the entire picture of patient costs, incidence of catastrophic costs, and impoverishment due to diabetes in the Philippines.

In our study sites, integrated services for TB and diabetes were provided only in health facilities with programmatic management of drug resistant TB, and therefore most of the study participants with drug susceptible TB had to have separate facility visits for diabetes services. For example, the initial screening and regular monitoring for diabetes by point of care HbA1c or fasting blood glucose were not always provided in public health facilities, and therefore people living with diabetes had to visit private pharmacies and laboratories for these services. This study found that people with TB-DM had 40 extra visits to health facilities and/or treatment partners (e.g. facility and/or community DOT) compared with those with TB only. Therefore, the reduction in visits to healthcare providers and related costs (e.g. travel and food costs in direct non-medical costs) might be achieved by integrated care for TB and diabetes. However, given the high incidence of catastrophic costs regardless of diabetes status in this study, it is unlikely that catastrophic costs can be mitigated only by ensuring the health service integration.

TB-affected households in this study lost almost 95% of their monthly household income at the end of the intensive phase, and this highlighted that TB-affected households may become financially vulnerable and require social and/or financial support during the TB intensive phase. However, only around 15% of the participants received financial support from the nationwide CCT programme for households living under poverty. It did not increase throughout TB treatment, even though their household income was considerably reduced at the time of TB diagnosis and at the end of the TB intensive phase. A similar situation was observed in the national TB patient cost survey in the Philippines, however, an even lower proportion of survey participants (1.3%) were receiving the nationwide CCT programme provided by the DSWD of the Philippines [12,14]. The national survey recommended that enhanced cooperation between NTP and DSWD is necessary for TB-affected households to benefit from financial support from the CCT programme. Our findings support the findings and recommendation from the national survey, and timely social protection and support are indispensable to avert catastrophic costs among TB-affected households in the Philippines.

This study had several limitations. First, it was conducted at 11 health facilities located in urban (Cebu) and rural (Negros) settings in the Philippines, and therefore, the results and findings cannot be generalized. Second, this study was able to enrol only a small sample of people with TB-DM (N=144). Thus, further studies with a larger sample that assesses the financial impact of TB-DM is necessary. Third, although the longitudinal study design allowed multiple interviews during a TB episode with less recall bias compared to a cross-sectional study, this study assessed costs from the onset of TB symptoms until the completion of TB treatment. Therefore, costs due to TB-related sequelae and/or prolonged social consequences after TB treatment were not investigated in this study. Fourth, approximately 15% of the enrolled participants were not able to complete all the data collection points due to dropout either from our study or TB from treatment. Therefore, results of catastrophic cost estimates might be affected by attrition bias. Fifth, the costs were estimated from participants who completed interviews for four times and the sample size was N=445, which did not reach the intended sample size of N=502 due to unexpectedly high proportion of loss-to-follow-up (15.6%). Therefore, our sample size might be not powered enough to detect cost differences between TB-DM and TB-only.

2.8 Conclusion

People with TB-DM in the Philippines face extensive health service use and incur higher costs to receive diabetes related health services. However, this does not translate into substantial differences in the incidence of catastrophic cost due to the baseline poverty in TB-affected households. Further study is required to understand the incidence of catastrophic costs due to diabetes-only in the Philippines.

2.9 Additional information

Asset-based imputation used as the denominator of catastrophic total costs due to TB

Asset-based imputed household income was used to replace the annual household income for those who reported zero household income before TB and used in the calculation of catastrophic cost estimates, otherwise the calculation returns infinity. This method is consistent with the WHO recommended analytical approach for national TB patient cost surveys (https://github.com/GTB-PCS), rather than other approaches e.g. minimum wage, to take the financial characteristics of population with TB into account [2]. The selection of assets used for the income imputation was done by univariate logistic regression analysis was conducted to identify predictor variables for household income from the sample population with non-zero household income and then conducted multivariate backward stepwise logistic regression to identify the final selection of asset items (**Table 2**) based on the Akaike information criterion (AIC).

Complete case analysis

This analysis used complete case analysis, excluding observations who missed one or more interview of. This is because the imputation of data, e.g. in the continuation phase from the reported data in the intensive phase, was not feasible due to the change in costs and income by TB treatment phase. This might have incurred attrition bias of the study results as discussed in the discussion section.

Household income at the end of the TB intensive phase

The reported monthly household income in people with concurrent TB and diabetes was lower (US$ 2.9) compared to those with TB-only (US$ 5.8) with p-value <0.001 (**Table 7**) which could be due to additional health facility visits for diabetes care (**Table 4**).

Statistical tests in cost estimates

This chapter used Kruskal–Wallis test to examine the statistical significance in cost estimates, and my study was not able to detect a statistically significant difference in costs incurred by people with concurrent TB and diabetes versus those with TB-only. However, this does not mean that the higher total costs incurred by people with concurrent TB and diabetes than those with TB-only (US$ 1,178 vs US$ 917) is negligible since the focus in health economics should be on economic significance in decision-making, rather than a statistical significance [30,31].

To summarize the results of cost estimates, I used means, instead of medians, since means provide the total economic burden and aggregated resource use which can be used in cost-effectiveness analyses (in **Chapter 5**), while medians can provide a typical cost estimate incurred by individual.

Recall bias

While the longitudinal study design of this allowed multiple interviews during a TB episode with less recall bias compared to a cross-sectional study design used for the WHO recommended methods for national TB patient cost surveys, the recall period still existed in this study (1 week to 1 month).

Characteristic	Longitudinal study (our study)	Cross-sectional study (surveys of costs incurred by people with TB and their households)
Recall bias	1 week to 1 month for the recall period	maximum 3-9 months for the recall period for income before TB diagnosis

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CHAPTER 3. COMPARING DISEASE SPECIFIC CATASTROPHIC COST ESTIMATES USING LONGITUDINAL AND CROSS-SECTIONAL DESIGNS: THE EXAMPLE OF TUBERCULOSIS

3.1 Preamble

This research paper presented the comparison of the proportion of TB affected households facing catastrophic costs between the longitudinal study design and the WHO recommended cross-sectional study design. At the time this paper was written, there were no studies that assessed the differences in TB catastrophic cost estimates between the longitudinal and cross-sectional study designs. The aim of this analysis was to identify the potential biases of the WHO recommended cross-sectional study design for TB catastrophic cost estimates and to explore optimal approaches for sampling and analysing cross-sectional cost data for the catastrophic cost estimates.

As with paper 1, this study was conducted as a nested study within a cohort study (St-Att study, the main study), which evaluated the effects of malnutrition and diabetes on TB treatment outcomes in Manila, Cebu and Negros Occidental, the Philippines. As a part of the cohort study, we conducted our study in Cebu and Negros Occidental and collected costs, income, coping mechanisms and social consequences of TB from care seeking until the end of TB treatment. The data collection tool was adapted to the longitudinal study design from the national TB patient cost survey in the Philippines and the WHO handbook for surveys of costs incurred by people with TB and their households. The data collection was conducted between November 2018 and October 2020.

Catastrophic cost due to TB was defined as total costs, consisting of direct medical and non-medical costs and indirect costs, exceeding 20% of ability to pay (i.e. annual household income of people with TB) as per the WHO definition. Using longitudinal data, total costs were estimated by summing the costs per phase, i.e. prior to TB diagnosis, the intensive phase, until the midpoint of the continuation phase and until the endpoint of the continuation phase. To achieve the simulated cross-sectional study design, we randomly sampled and allocated our samples into two groups; either those for whom data would have been collected at the end of the intensive phase and or at the midpoint of the continuation phase in accordance with WHO guidance. We then produced different samples for different proportions of patients in the intensive and continuation phases, i.e. 20%:80%, 35%:65%, 50%:50%.

We found that while with the longitudinal study design the catastrophic cost estimate was 69%, with the simulated cross-sectional study design, the estimate ranged from 40% to 55% depending on the sampling proportion of the intensive and continuation phases. Also, our analysis highlighted an inconsistency in the inclusion of indirect costs before TB diagnosis in the WHO recommended surveys of costs incurred by people with TB and their households. The results of this paper contributed to improvements in the recommendations and guidelines provided by the WHO Task Force for implementing surveys of costs incurred by people with TB and their households.

This research paper was published in Social Science and Medicine in February 2024 and the paper was reproduced in this chapter with no revisions or adaptation from the published manuscript. Additional information section (**section 3.9**) was included to provide additional clarifications of methods, results and discussions for the purpose of the development of the thesis.

Citation

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3.2 Research paper cover sheet

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Thesis Title	Mitigating the economic impact of TB and diabetes in the Philippines		
Primary Supervisor	Dr Anna Vassall		

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	AV, TY and YL conceptualized the study. TY developed the study methods and obtained funding for this study. JPF, MCC and TY implemented the data collection. TY cleaned, validated and analysed study data with supervision from AV and YL. TY, AV and YL interpreted results. TY developed the draft of the paper. All authors reviewed and edited the paper.

SECTION E

Student Signature	[redacted]
Date	31 August 2024

Supervisor Signature	[redacted]
Date	31 August 2024

3.3 Abstract

Background:

There has been an increasing interest in assessing disease-specific catastrophic costs incurred by affected households as part of economic evaluations and to inform joint social/health policies for vulnerable groups. Although the longitudinal study design is the gold standard for estimating disease-specific household costs, many assessments are implemented with a cross-sectional design for pragmatic reasons. We aimed at identifying the potential biases of a cross-sectional design for estimating household cost, using the example of tuberculosis (TB), and exploring optimal approaches for sampling and interpolating cross-sectional cost data to estimate household costs.

Methods:

Data on patient incurred costs, household income and coping strategies were collected from TB patients in Negros Occidental and Cebu in the Philippines between November 2018 and October 2020. The data collection tools were developed by adapting WHO Tuberculosis Patient Cost Surveys: A Handbook into a longitudinal study design. TB-specific catastrophic cost estimates were compared between longitudinal and simulated cross-sectional designs using different random samples from different times points in treatment (intensive and continuation phases).

Results:

A total of 530 adult TB patients were enrolled upon TB diagnosis in this study. Using the longitudinal design, the catastrophic cost estimate for TB-affected households was 69% using the output approach. The catastrophic cost estimates with the simulated cross-sectional design were affected by the reduction and recovery in household income during the episode of TB care and ranged from 40-55%.

Conclusion:

Using longitudinally collected costs incurred by TB-affected households, we illustrated the potential limitations and implications of estimating household costs using a cross-sectional design. Not capturing changes in household income at multiple time points during the episode of the disease and estimating from inappropriate samples may result in biases that underestimates catastrophic cost.

3.4 Introduction

Tuberculosis (TB) is a chronic disease that requires a minimum of 6 months treatment [1]. The risk of TB infection and disease is associated with poverty, together with poor care-seeking behaviour, delay in diagnosis, and poor treatment adherence and the development of drug-resistant TB (DR-TB) [2-4]. Despite free TB services available in public health facilities, TB patients usually incur large costs for care seeking, diagnosis, and treatment. The costs include not only out-of-pocket (OOP) payments for direct medical costs, but also direct non-medical costs such as transportation, food or nutritional supplements and indirect costs such as income loss [5-7]. TB also impacts poverty as it can reduce the physical ability to work, and as a result lead to income loss [4-6]. In addition, households being affected by long-term diseases such as TB usually mobilize their money for treatments by dissaving, selling assets, or taking loans, making them poorer and trapped in the cycle of poverty [8], which can have a long-term economic impact on TB patients and their households [9].

In 2013, the World Health Organization (WHO) set the End TB Strategy, and one target of the strategy is “to ensure that no family is burdened with catastrophic expenses due to TB” [10]. To capture the current situation of TB associated household costs and monitor the progress to toward achieving this target, WHO supports countries to conduct baseline and periodic TB patient cost surveys [11]. National TB patient cost surveys have already been conducted so far in 31 countries [12].

In 2015, WHO produced a generic protocol and data collection tool (field testing version) which was later refined and published as a handbook in 2017 [11]. This handbook has also been adapted for use in other disease specific studies assessing societal and catastrophic costs. The WHO recommended using a cross-sectional design for the estimation of this target, given that it is commonly measured using population wide surveys. WHO then applied different approaches to estimate total costs incurred for TB services compared to that used for “catastrophic health expenditure” in the general population [11]. All the national surveys were designed and conducted as cross-sectional studies due to feasibility and practicality; smaller survey budget required, shorter duration of data collection, and no follow-up interviews required, compared to longitudinal designs. TB treatment has two phases, the intensive and continuation phase, which are treated with different regimens and different frequency of monitoring by providers. The estimation of direct costs (i.e. direct medical and non-medical costs) is based on an assumption that the frequency of health service utilization and expenditure within a treatment phase is consistent. Direct costs for the last facility visit by visit type (i.e. collection of TB drugs, directly observed therapy (DOT), follow-up by clinicians) were being captured, and then scaled up to the entire duration of the phase using the frequency of health service utilization. The direct costs

for the treatment phase that are not captured directly are extrapolated based on the median costs estimated from the data of other patients in that treatment phase [11].

Indirect costs are estimated through two different methods: the output approach and human capital approach [11]. The output approach relies on self-reported household income before and during the TB episode, while the human capital approach uses reported time spent for care seeking and treatment during a TB episode multiplied by an individual hourly income estimated from reported income and working hours.

This study aims to assess the differences in the costs using the output approach between the longitudinal and cross-sectional methods, and to identify methodological improvements in the WHO recommended surveys of costs incurred by people with TB and their households. We compare estimates of total costs and the prevalence of catastrophic costs between the longitudinal and cross-sectional designs. Our analysis aims at highlighting limitations and implications of the current guideline for assessing catastrophic costs due to TB using a cross-sectional design, which can also inform methods for other diseases.

3.5 Methods

Study setting and population

The estimated TB incidence in the Philippines was 650 per 100,000 in 2021 [13,14], and The Philippines has been classified by the WHO as one of the 30 high TB burden countries for both drug-susceptible TB (DS-TB) and multidrug-resistant and rifampicin resistant TB (MDR/RR-TB) [13-15]. The National Tuberculosis Control Program (NTP) conducted a nationwide TB patient cost survey in the Philippines between 2015–2017 using the WHO recommended cross-sectional design and cost extrapolation method [11,16]. The results of the survey found 42.4% (95% confidence interval (95% CI) 40.2-44.6%) of TB patients' households faced catastrophic costs [14,17,18].

Our study was conducted as a nested sub-study of an ongoing longitudinal study aimed to measure the effects of malnutrition and diabetes in patients with TB in Manila, Negros Occidental and Cebu, the Philippines, and to investigate associations with treatment outcome through potential effects on treatment compliance, drug side effects, glycaemic control, weight gain and nutrition during treatment and cell-mediated immune responses (Appendix 1). Part of our nested sub-study was to assess the change in costs, income and coping mechanisms before TB diagnosis through to completion of TB treatment, and to assess the difference in costs incurred by TB patients with and without

diabetes [19]. It was conducted in Negros Occidental and Cebu in the Philippines. Negros Occidental is a province in the Western Visayas Region, located in the south-eastern area of the Philippines and categorized as a rural area with a population size of 2.6 million. Cebu is a province of the Central Visayas Region with the second largest city (Cebu city) in the Philippines and categorized as an urban area. We used a sub-sample of 11 health facilities and hospitals located in those two regions. All study sites in Cebu (urban setting) and Negros Occidental (rural setting) used for the main study were also used in our sub-study. The main objective of this sub-study was to compare patient costs incurred by TB patients (and their households) with versus without comorbid diabetes. Assuming a 90% consent rate and 91% treatment completion rate, we expected to collect patient cost data from a total of 502 people with TB. Given 9-12% of the cohort were estimated to have diabetes (45-60 people) [20], we estimated that our sample size of 502 people with TB was sufficiently powered to detect a minimum 17% increase in total costs, based on a 2011 diabetes patient cost study in Thailand [21,22].

The eligibility criteria of the main study were pulmonary TB patients aged 18 years or older. Although HIV positive TB patients were included in the main study, they were excluded in this sub-study to exclude the financial impact from TB-HIV coinfection. Therefore, costing study participants were TB patients from the main study enrolled between November 2018 and March 2020, and all the data collection was completed by October 2020.

Study design and data collection

We collected data on patient incurred costs, income, health service utilization, coping mechanisms and social consequences of TB at four time points as part of the ongoing main study [23]. The patient was interviewed at: 1) the start of TB treatment, 2) the end of the TB intensive phase (month 2 for DS-TB and month 4 for DR-TB), 3) the midpoint of the TB continuation phase (month 4 for DS-TB and month 7.5 for DR-TB), and 4) the end of the TB continuation phase (month 6 for DS-TB and month 9 for DR-TB). For DS-TB and DR-TB, the TB continuation phase lasts longer (4 months and 7 months) than the TB intensive phase (2 months and 4 months), respectively, and patients usually return to work during the TB continuation phase due to physical recovery and resolution of TB symptoms. This informed the two timepoints for data collection in the TB continuation phase of our study.

Research nurses were based at each study site as interviewers to recruit study participants from the main study into this patient cost study. Prior to being deployed to each study site, research nurses received a five-day training on the survey instrument, process of informed consent, TB infection control measures, ethical considerations, and pilot data collection. While patients from the main study at each study site were waiting to be seen, a research nurse explained the purpose of the patient cost

study and shared an information sheet. Patients who agreed to participant in the research and signed the informed consent form were enrolled. Data collection for patient costs, household income and coping strategies was conducted by the trained research nurses via 30-45 minute in-person interviews at each participant's home and by telephone during the period of COVID-19 lockdowns when it was difficult to have face-to-face interviews.

The data collection tool was adapted from the national TB patient cost survey in the Philippines [17], and this in turn was based on the WHO guideline for surveys of costs incurred by people with TB and their households [11]. Costs consisted of direct medical costs (e.g. medical consultation fees, and costs for drugs, diagnostic tests before starting treatment, monitoring tests, hospitalization, and DOT), direct non-medical costs (e.g. costs for transportation, food and supplements, and accommodation), and indirect costs (e.g. income losses due to illness when too unwell to work and costs for a care giver). The data collection included household income and assets, health service utilization, coping mechanisms and social consequences of TB. Other socio demographic and clinical information such as age, sex, education level, TB diagnosis, and body mass index (BMI) were extracted from the main study.

Data analysis

Data were collected and entered at the time of the interviews via tablet-based questionnaires using Open Data Kit (ODK) and ODK collect. Data cleaning and processing, statistical analyses, and data visualizations were performed using R4.2.0. Data monitoring and validation were performed on a weekly basis, and identified missing data was collected by follow-up phone calls and entered into the database using R coding. Mean with standard deviation (SD) and 95% confidence intervals (CI), and median with inter-quartile range (IQR) were used for continuous data, and frequency and proportions (%) were used for categorical data. All results were stratified based on diabetes status at the time of TB diagnosis. Statistical differences between patients with DS-TB and DR-TB were tested using a chi-square test for categorical data such as demographic and clinical characteristics and the t-test or Kruskal–Wallis's test for continuous data such as income, health service utilization and cost data. Fisher's exact test was performed for statistical differences in the proportion of catastrophic costs between the longitudinal and cross-sectional designs. Statistical significance was defined as a p-value less than 0.05. Data on costs and income were collected in Philippine Pesos (Php) and later converted into US$ for analysis at the rate of Php 51.19 per US$ 1, which was the average UN Operational Rate of Exchange during the data collection period (November 2018-October 2020).

Catastrophic cost estimates using the longitudinal study design

Using longitudinal data, costs per phase were first interpolated backwards for the period since the last interview using the data on costs incurred for the last visit by purpose of visits (i.e. DOT, medical follow-up and drug pick-up) multiplied by the frequency of each visit type during each phase. Only for hospitalizations, the duration, reasons and incurred costs for each hospitalization were collected separately considering the individuality of costs of hospitalizations. Then total costs were estimated by summing the costs per phase. Catastrophic cost due to TB was defined as total costs, consisting of direct medical and non-medical costs and indirect costs, exceeding 20% of ability to pay (i.e. annual household income of TB patients) as per the WHO definition [11]. Following the method used for the Philippines national TB patient cost survey, our study used the output approach as the primary method for estimating indirect cost (differences in self-reported household income before having TB symptoms and at the time of each data collection). A secondary approach, estimating indirect costs using the human capital approach, was used and the results of the two approaches compared (see further details in Appendix 2). Reported annual household income prior to TB diagnosis was used as a primary indicator for ability to pay (denominator for estimating catastrophic costs due to TB, output approach). For TB-affected households reporting zero income before having TB, annual household income was imputed using a regression model based on household assets, and the imputed value was used as the denominator for catastrophic costs.

Simulating catastrophic cost estimates collected using the cross-sectional design

The total longitudinal patient costs over the full course of treatment were compared with results from a simulated cross-sectional design.

In the simulated cross-sectional method, the aim was to simulate incurred expenses per patient at one time point only (either end of intensive phase or middle of continuation phase). To achieve this, we randomly sampled patients from our sample and allocated them to two groups; either those for whom data would have been collected at the end of the intensive phase and or in the middle of the continuation phase in accordance with WHO guidance. We then produced different samples for different proportions of patients in the intensive and continuation phases, respectively (i.e. 20%:80% (proportion 1), 35%:65% (proportion 2), 50%:50% (proportion 3)). The selection of these proportion combinations was based on the most commonly reported proportions used in published surveys of costs incurred by people with TB and their households conducted using the WHO recommended methodology (Appendix 4) [17,24-35]. Proportion 1 was adopted to replicate the sampling of the Philippines national TB patient cost survey. Proportion 2 was adopted to present the ideal proportion of patients in the cross-sectional design given that the majority of TB patients have DS-TB, which has

a 2-month TB intensive phase (33.3%) and 4-month TB continuation phase (66.6%), which results in the ratio of 33.3%:66.6%. Proportion 3 was adopted to replicate some national surveys that applied a higher proportion of patients in the TB intensive phase (e.g. Mongolia survey purposively applied 50%:50% in the sampling) (Appendix 4).

Thereafter the direct medical and non-medical costs of the non-sampled treatment phase were extrapolated based on the median costs estimated from other patients in that treatment phase, following the methodology used for national patient cost surveys [11]. In this extrapolation process for the direct costs, differences in the costs by drug-resistance status and with/without experience of hospitalization were considered.

Ethical considerations

Ethical approval for the main study, including approval for this sub-study, was obtained from the St. Cabrini Medical Center-Asian Eye Institute Ethics Review Committee (SCMC-AEI ERC) (ERC #2018-008). Ethical approvals were also obtained from the Ethics Review Committee of the WHO Regional Office for the Western Pacific (Ref: 2019.18.PHL.4.STB) and the Ethics Review Committee at the London School of Hygiene and Tropical Medicine and Nagasaki University. In addition to the ethics approvals, we obtained an endorsement letter from National TB Control Programme, Department of Health, the Philippines, to conduct this study. A written consent form was obtained from all participants before the commencement of the interview. The informed consent signed by all participants explicitly stated that only the principal investigator (PI) and co-PIs would have access to the study dataset.

3.6 Results

Study population

A total of 530 adult TB patients were enrolled upon TB diagnosis in this study. Of these, 443 patients (83.6%) were enrolled in the first-line TB treatment (DS-TB patients) and 87 patients (16.4%) were enrolled in MDR/RR-TB treatment (DR-TB patients) (**Table 9**). Most of the study participants completed TB treatment (79.4%) while 15.6% had loss-to-follow-up, 1.2% had treatment failure, and 3.9% died during TB treatment. Therefore, data from all four data collection timepoints were obtained for 445 participants (84%) (**Table 10**), which has been the basis for the analysis in **Table** 11 onwards.

The proportion of participants with no education was less among DR-TB patients (DS-TB: 34.1%, DR-TB: 21.8%, p=0.041). The proportion of participants receiving treatment support (facility or community DOT) while in DR-TB treatment was higher throughout TB treatment (intensive phase: DS-TB 17.3%,

DS-TB: 97.0%; middle of continuation phase: DS-TB 14.9%, DR-TB: 88.1%; end of continuation phase: DS-TB 13.0%, DR-TB 92.5%; p<0.001) (**Table 9**).

Households for both DS-TB and DR-TB patients reported a substantial decline in household income at the time of TB diagnosis and during TB treatment. For DS-TB patients, the mean reported monthly household income before having TB symptoms was USD 183 (95%CI: USD 152-215), and it reduced to USD 77 (95%CI: USD 64-89) at TB diagnosis and USD 8 (95%CI: 6-10) at the end of the intensive phase. The reported household income increased to USD 194 (95%CI: USD 159-229) and USD 189 (95%CI: USD 155-223) during the middle and at the end of the continuation phase, respectively. For DR-TB patients, the mean reported monthly household income before having TB symptoms was USD 250 (USD 182-319), decreasing to USD 99 (USD 64-134) at TB diagnosis and USD 13 (USD 2-23) at the end of the intensive phase. The reported household income increased to USD 204 (USD 149-259) and USD 250 (USD 182-319) during the middle and at the end of the continuation phase, respectively (**Table 9**).

The proportion of patients receiving the social support package was higher in DR-TB patients throughout TB treatment (intensive phase: DS-TB 3.3%, DR-TB: 86.8%; middle of continuation phase: DS-TB 4.8%, DR-TB: 94.3%; end of continuation phase: DS-TB 3.6%, DR-TB 96.2%; p<0.001 at all the time points). There was no statistical significance between the proportion of DS-TB and DR-TB patients receiving the conditional cash transfer (CCT) programme. The CCT programme was received by 16.0% (95%CI: 12.8-19.7%) of TB-affected households before TB diagnosis, and the proportion remained constant throughout TB treatment (TB diagnosis: 15.5% (95%CI: 12.4-19.2%), the end of intensive phase: 16.9% (95%CI: 13.6-20.6%), the middle of continuation phase: 15.5% (95%CI: 19.7-12.8%), the end of continuation phase: 14.6% (95%CI: 11.8-18.5%)) (**Table 9**).

The mean total number of visits for TB services amongst all participants was 90.5 visits, with 5.1 visits occurring for care seeking before TB diagnosis. People with DR-TB had more frequent visits in total (DR-TB: 418.0, DS-TB: 47.1, p<0.001) compared to people with DS-TB (**Table 9**). There were significant differences (p<0.001) in the number of visits for TB services by treatment phase and by purpose of visit between people with DR-TB and DS-TB.

Among the three main cost categories for TB services, the costs were predominantly driven by indirect costs throughout a TB episode. For DS-TB patients, the proportion of income loss out of total costs incurred before TB diagnosis was 73.8%, 94.4% in the intensive phase, 81.4% and 84.9% in the middle and end of the continuation phase. For DR-TB patients, the proportion was 51.0% before TB diagnosis,

89.1% in the intensive phase, 76.9% and 72.1% in the middle and end of the continuation phase, while the proportion of direct medical costs was also high at 31.0%.

Table 9. Demographic, clinical, and economic characteristics of study participants in Negros Occidental and Cebu, the Philippines by drug resistance status

		Drug-susceptible TB		Drug-resistant TB		All TB patients		p-value
		N	(%)	N	(%)	N	(%)	
Total		**443**	**83.6%**	**87**	**16.4%**	**530**	**100%**	
Demographic characteristics								
Sex	Female	133	30.0%	21	24.1%	154	29.1%	0.329
Age group	18–24	69	15.6%	10	11.5%	79	14.9%	0.092
	25–34	74	16.7%	15	17.2%	89	16.8%	
	35–44	61	13.8%	17	19.5%	78	14.7%	
	45–54	85	19.2%	25	28.7%	110	20.8%	
	55–64	82	18.5%	13	14.9%	95	17.9%	
	≥65	72	16.3%	7	8.1%	79	14.9%	
Education level	No education/Primary	151	34.1%	19	21.8%	170	32.1%	0.041
	High school	213	48.1%	45	51.7%	258	48.7%	
	University or higher/Vocational	79	17.8%	23	26.4%	102	19.3%	
Insurance status	No insurance	125	28.2%	28	32.2%	153	28.9%	0.479
	PhilHealth	194	43.8%	32	36.8%	226	42.6%	
	GSIS/SSS (insurance for formal employment)	124	28.0%	27	31.0%	151	28.5%	
Household size		5(1-14)		4(1-14)		5(1-14)		
Employment status before TB	Employed (Formal)	88	19.9%	23	26.4%	111	20.9%	0.140
	Employed (Informal)	171	38.6%	29	33.3%	200	37.7%	
	Unemployed	150	33.9%	33	37.9%	183	34.5%	
	Student/Retired	34	7.7%	2	2.3%	36	6.8%	
Primary income earner	Yes	209	47.2%	46	52.9%	255	48.1%	0.393
Clinical characteristics								
Diabetes status at TB diagnosis	With diabetes	112	25.3%	32	36.8%	144	27.2%	0.038
Treatment history	New	322	73.4%	24	27.6%	346	65.8%	<0.001
	Relapse	111	25.3%	46	52.9%	157	29.9%	
	Retreatment	5	1.1%	10	11.5%	15	2.9%	
	Unknown	0	0.0%	5	5.8%	5	1.0%	
Body mass index (kg/m^2)	>=18.5	254	57.5%	44	50.6%	298	56.3%	0.286
Diagnostic delay (>4weeks)		308	69.5%	69	79.3%	377	71.1%	0.087
Duration of TB treatment (weeks)	Intensive phase: Mean, SD	8	1.2	18	2.8	10	3.9	<0.001
	Continuation phase: Mean, SD	16	1.5	22	2.0	17	2.4	<0.001
Hospitalized due to TB		39	8.8%	13	14.9%	52	9.8%	0.118
Treatment supports in intensive phase	Self-administered	340	82.7%	2	3.0%	342	71.6%	<0.001
	With treatment partner	71	17.3%	65	97.0%	136	28.5%	
Treatment supports in middle of continuation phase	Self-administered	338	85.1%	7	11.9%	345	75.7%	<0.001
	With treatment partner	59	14.9%	52	88.1%	111	24.3%	
Treatment supports in end of continuation phase	Self-administered	341	87.0%	4	7.6%	345	77.5%	<0.001
	With treatment partner	51	13.0%	49	92.5%	100	22.5%	
Financial status		**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	

Self-reported monthly household Income (in US$)	Before onset of TB symptoms	183.4	(151.7-215.2)	179.0	(139.2-218.8)	182.7	(155.4-210.0)	0.865
	At the time of TB diagnosis	76.7	(64.3-89.1)	98.6	(63.8-133.5)	80.3	(68.4-92.1)	0.245
	At the end of intensive phase	8.0	(5.8-10.1)	12.5	(1.8-23.2)	8.6	(6.2-11.0)	0.420
	At the middle of continuation phase	194.0	(158.6-229.4)	203.8	(148.9-258.8)	195.3	(163.6-226.9)	0.768
	At the end of continuation phase	189.3	(155.4-223.2)	250.2	(181.5-318.9)	196.5	(165.5-227.6)	0.120
Social supports for TB patients	Before TB diagnosis	0.3	(0.04-1.8)	20.8	(11.7-34.1)	2.7	(4.7-1.5)	<0.001
	Intensive phase	3.3	(1.9-5.6)	86.8	(74.4-93.7)	13.3	(16.8-10.4)	<0.001
	Middle of continuation phase	4.8	(3.1-7.5)	94.3	(83.5-98.2)	15.5	(19.2-12.4)	<0.001
	End of continuation phase	3.6	(2.1-6.0)	96.2	(85.7-99.1)	14.6	(18.2-11.6)	<0.001
Conditional cash transfer for poor	Before TB diagnosis	16.3	(13.0-20.3)	13.2	(6.3-25.6)	16.0	(19.7-12.8)	0.561
	Intensive phase	15.6	(12.3-19.5)	15.1	(7.6-27.8)	15.5	(19.2-12.4)	0.930
	Middle of continuation phase	16.8	(13.4-20.9)	17.0	(8.9-29.9)	16.9	(20.6-13.6)	0.979
	End of continuation phase	15.1	(11.8-19.0)	13.2	(6.3-25.6)	14.8	(18.5-11.8)	0.723
Health service utilization (times of facility visits)		**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	
Before TB diagnosis	Care seeking	5.1	(4.9-5.3)	5.8	(5.1-6.6)	5.1	(4.9-5.3)	0.033
Intensive phase	Medical follow-up	0.7	(0.7-0.8)	3.2	(2.3-4.1)	1.0	(0.9-1.2)	<0.001
	Drug pickup	6.9	(6.3-7.6)	97.0	(83.1-110.8)	17.5	(14.3-20.7)	<0.001
	Directly observed therapy	9.1	(6.9-11.3)	117.7	(109.2-126.1)	21.8	(17.9-25.7)	<0.001
Middle of continuation phase	Medical follow-up	0.4	(0.4-0.5)	1.8	(1.5-2.0)	0.6	(0.5-0.6)	<0.001
	Drug pickup	5.7	(5.2-6.2)	43.5	(33.6-53.3)	10.1	(8.4-11.8)	<0.001
	Directly observed therapy	7.3	(5.5-9.1)	59.4	(50.0-68.8)	13.4	(10.9-15.9)	<0.001
End of continuation phase	Medical follow-up	0.6	(0.6-0.7)	1.7	(1.4-2.0)	0.7	(0.7-0.8)	<0.001
	Drug pickup	5.3	(5.0-5.6)	31.7	(22.5-41.0)	8.4	(7.0-9.8)	<0.001
	Directly observed therapy	5.9	(4.3-7.6)	56.2	(47.7-64.8)	11.8	(9.5-14.2)	<0.001
Total (before TB diagnosis until end of continuation phase)		47.1	(41.6-52.6)	418.0	(383.8-452.1)	90.5	(77.7-103.2)	<0.001

Diagnostic delay: Duration from start having TB symptoms until TB diagnosis

Table 10. Characteristics of longitudinal versus cross-sectional study design for patient cost data collection

Characteristic	Longitudinal study (our study)	Cross-sectional study (surveys of costs incurred by people with TB and their households)
Sample population	Patients newly diagnosed with TB	Patients receiving TB treatment (at least initial 14 days of the current treatment phase)
Duration of study	Enrolment period plus follow-up period (at least 6 months for DS-TB and 9 months for DR-TB)	Depending on TB burden in study sites, on average 4-6 months
Example for length of data collection	2 years for the sample size of 530	3-6 months for the sample size of 500-1300
Number of data collection points	At least 4 times per patient to assess changes in income, costs, and coping mechanisms over time. (e.g. at TB diagnosis, during intensive phase, and during continuation phase)	Single time point per patient, interviewed during either intensive phase (costs before and during TB diagnosis, and during intensive phase) or continuation phase (costs during continuation phase).
Missing data	More due to dropout (84% completion rate for 4 interviews, >90% of participants without missing data at each time point) (e.g. refuse to participate, moveout from study areas, death, loss to follow-up) during follow-up period.	Less (>90% of participants without missing data) (have missing data only to specific questions for which participants refuse to answer)
Recall bias	1 week to 1 month for the recall period	maximum 3-9 months for the recall period for income before TB diagnosis
Estimation of total costs	Interpolation of costs in each treatment phase based on data from same patient over period of TB episode.	Extrapolation of reported costs to estimate costs incurred during the phase in which patients were not interviewed. (e.g. costs incurred during continuation phase for patients who were in intensive phase at the time of interview)

Comparison of total costs between longitudinal and simulated cross-sectional designs

With the output approach, using longitudinal data, the mean total cost was estimated as USD 932 (95%CI: USD 798-1066). However, the mean total costs estimated using the cross-sectional design was based on the proportion of patients in the intensive and continuation phases. It was USD 680 (95%CI: USD 566-794) for proportion 1, USD 928 (95%CI: USD 710-1146) for proportion 2, and USD 1113 (95%CI: USD 878-1348) for proportion 3 (**Table** 11). Income loss was the main contributor to differences between the longitudinal and cross-sectional designs. Income loss was estimated at USD 802 (95%CI: USD 672-932) with the longitudinal method, while the cross-sectional methods estimated

USD 550 (95%CI: USD 440-660), USD 788 (95%CI: USD 573-1002) and USD 975 (95%CI: USD 744-1206) for proportions 1, 2 and 3 respectively (**Table 11**).

Table 11. Detail of costs incurred per TB-affected households, by design, mean (95%CI), output approach

TB patient costs, US$			Longitudinal			Cross-sectional								
						Proportion of patients in intensive and continuation phases								
						20:80			35:65			50:50		
			Mean	(95% CI)	%	Mean	(95% CI)	%	Mean	(95% CI)	%	Mean	(95% CI)	%
Pre-TB diagnosis	Direct medical costs		28.7	(20.1-37.3)	3.1%	13.9	(12.4-15.3)	2.0%	16.1	(14.3-17.9)	1.7%	16.7	(14.9-18.4)	1.5%
	Direct non-medical costs		29.1	(24.3-33.9)	3.1%	18.4	(17.1-19.6)	2.7%	20.3	(17.8-22.9)	2.2%	23.4	(19.6-27.1)	2.1%
	Income loss		219.3	(161.2-277.4)	23.5%	125.8	(89.6-161.9)	0.0%	179.7	(126.9-232.5)	0.0%	263.7	(180.6-346.9)	0.0%
Post-TB diagnosis	Direct medical costs	Drug pickup	0.05	(0-0.1)	0.0%	0.002	(0-0.006)	0.0%	0.004	(0-0.009)	0.0%	0.01	(0.001-0.02)	0.0%
		Directly observed therapy	0.0	(0.0-0.0)	0.0%	0.0	(0.0-0.0)	0.0%	0.0	(0.0-0.0)	0.0%	0.0	(0.0-0.0)	0.0%
		Follow-up	1.8	(0.9-2.6)	0.2%	1.5	(0.5-2.5)	0.2%	2.1	(0.9-3.2)	0.2%	1.2	(0.2-2.2)	0.1%
		Hospitalization	1.8	(0-4.3)	0.2%	2.7	(0-6.3)	0.4%	2.2	(0-5.7)	0.2%	2.0	(0-4.8)	0.2%
	Direct non-medical costs	Accommodation	0.06	(0-0.1)	0.0%	0.5	(0.2-0.8)	0.1%	0.3	(0.2-0.4)	0.0%	0.4	(0.2-0.7)	0.0%
		Food	3.6	(2.6-4.6)	0.4%	7.6	(4.0-11.1)	1.1%	7.6	(3.6-11.6)	0.8%	6.9	(3.5-10.4)	0.6%
		Travel	19.2	(16.2-22.1)	2.1%	33.2	(24.7-41.7)	4.9%	32.7	(22.0-43.3)	3.5%	34.7	(22.6-46.7)	3.1%
		Nutritional supplement	45.8	(40.0-51.7)	4.9%	52.1	(44.3-59.8)	7.7%	59.0	(49.9-68.1)	6.4%	52.4	(44.6-60.2)	4.7%
	Income loss		582.7	(493.3-672.1)	62.5%	424.2	(341.9-506.5)	62.4%	607.9	(434.1-781.7)	65.5%	711.3	(534.7-887.8)	63.9%
Total direct medical costs			32.3	(23.3-41.3)	3.5%	18.1	(13.7-22.5)	2.7%	20.3	(16.0-24.7)	2.2%	19.9	(16.5-23.3)	1.8%
Total direct non-medical costs			97.7	(87.6-107.8)	10.5%	111.7	(97.0-126.4)	16.4%	119.9	(101.7-138.1)	12.9%	117.9	(0-135.9)	10.6%
Total income loss			802.0	(672.0-932.1)	86.1%	550.0	(439.5-660.4)	80.9%	787.7	(572.9-1002.4)	84.9%	975.0	(743.9-1206.1)	87.6%
Total cost			932.0	(798.4-1065.7)	100.0%	679.8	(565.8-793.7)	100.0%	927.9	(710.0-1145.7)	100.0%	1112.8	(877.7-1347.8)	100.0%

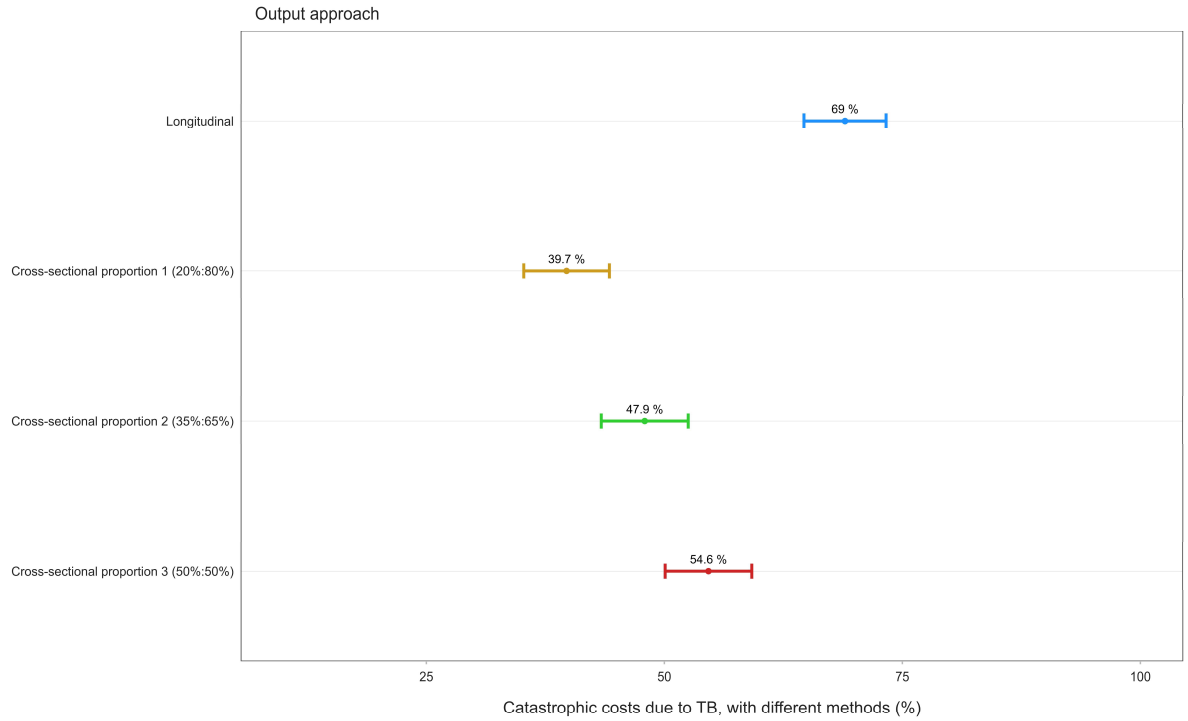
Comparison of TB-affected households facing catastrophic costs

Using the output approach and longitudinal method, 69.0% (95%CI: 64.7-73.3%) of TB-affected households incurred costs >20% of annual household income (**Figure 8**).

With the cross-sectional method, 39.7% (95%CI: 35.2-44.2%) of TB-affected households faced catastrophic costs for proportion 1, which was lower than that for proportion 2 (47.9%, 95%CI: 43.4-52.5%) and for proportion 3 (54.6%, 95%CI: 50.1-59.2%). Statistically significant differences ($p<0.001$) were observed between the catastrophic costs using the longitudinal and cross-sectional designs for

proportions 1, 2 and 3 and also within the cross-sectional design (between proportions 1 and 2, and proportions 2 and 3).

Figure 8. Percentage of TB-affected households facing catastrophic costs (> 20% of annual household income)

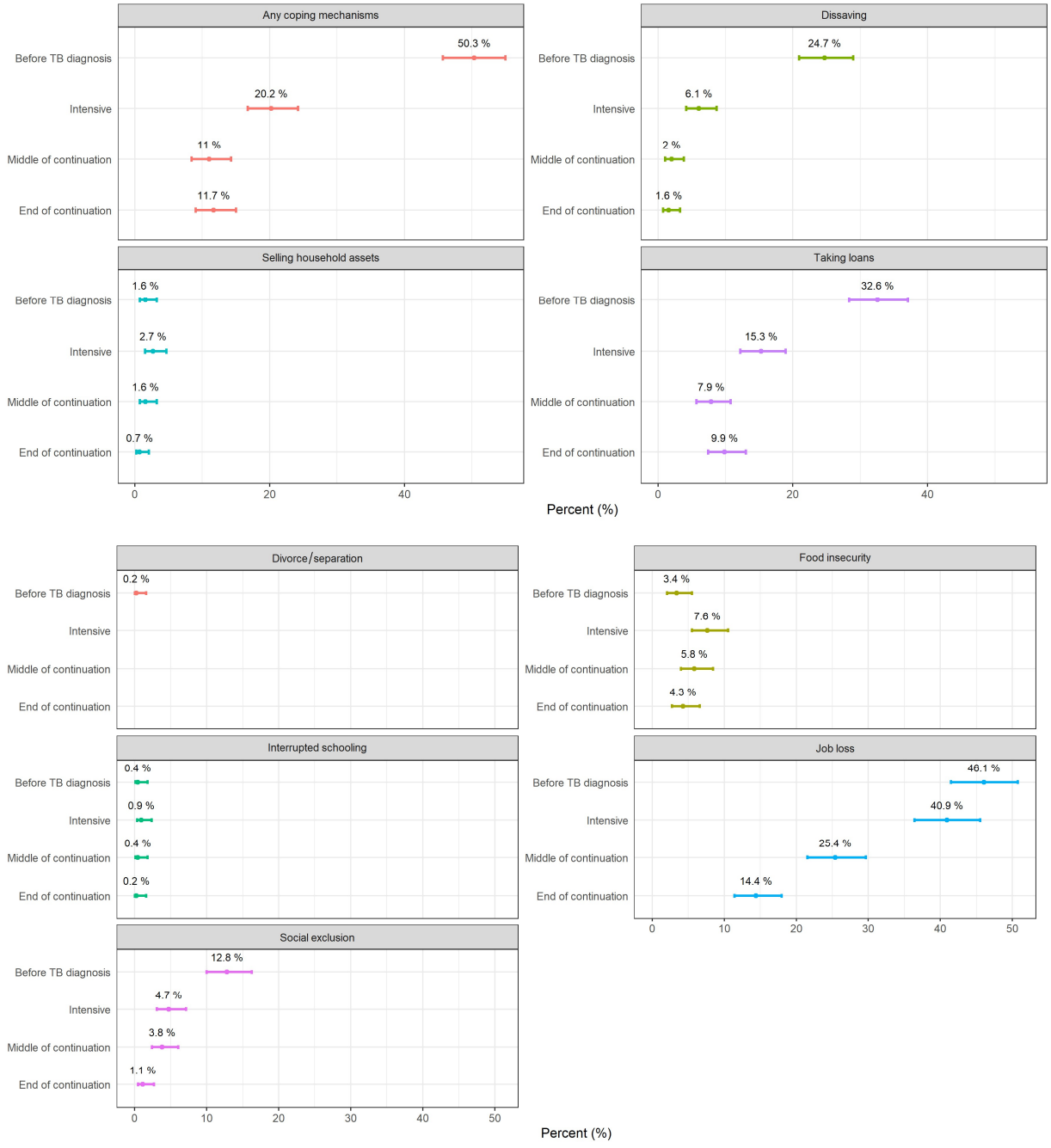


Coping mechanisms and social consequences

Half (50.3%) of TB-affected households relied on either dissaving, loans, or selling household assets to cope with the financial burden prior to TB diagnosis (**Figure 9**). The proportion decreased to 20.2% in the intensive phase and 11.0% and 11.7% during the middle and at the end of the continuation phase. Among the three coping mechanisms, taking loans was the most common, at 32.6% before TB diagnosis, 15.3% in the intensive phase, and 7.9% and 9.9% during the middle and at the end of the continuation phase, respectively.

Job loss was the most encountered social consequence of TB, with nearly half of households experiencing job loss before TB diagnosis (46.1%) and during the intensive phase (40.9%). Food insecurity was greatest amongst households during the intensive phase (7.6%), but social exclusion was greatest before TB diagnosis (12.8%).

Figure 9. Coping mechanisms and social consequences due to TB



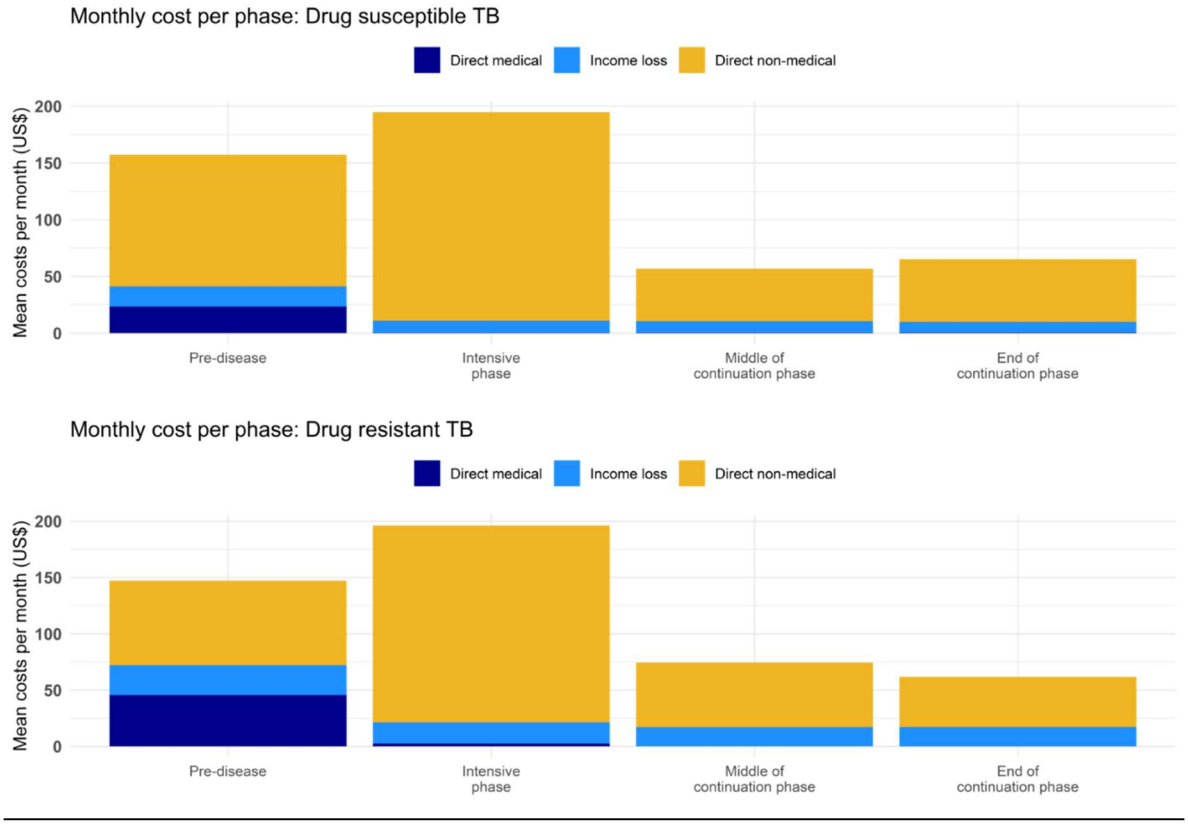
*interrupted schooling includes both children in households and patients themselves

Monthly costs incurred by TB-affected households, by drug-resistance status, output approach

There were no substantial differences in the mean monthly costs between DS-TB and DR-TB patients (**Figure 10**). Both categories incurred high costs before TB diagnosis (DS-TB: USD 157, DR-TB: USD 147 per month) and in the intensive phase (DS-TB: USD 195, DR-TB: USD 196 per month). The monthly

costs decreased to USD 57 (DS-TB) and USD 74 (DR-TB) per month at the middle of the continuation phase and to USD 65 (DS-TB) and USD 62 (DR-TB) per month at the end of the continuation phase.

Figure 10. Monthly mean costs by TB drug resistance status, treatment phase and cost category, output approach



3.7 Discussion

Key findings

Our analysis highlighted the potential bias of estimating disease-specific catastrophic costs using a cross-sectional design. We found that catastrophic cost estimates of TB were underestimated with the cross-sectional approach compared to the longitudinal approach. The catastrophic cost estimates with the cross-sectional approach were considerably affected by the proportion of patients taken from each treatment phase. Our analysis with a simulated cross-sectional approach showed that the catastrophic cost estimates ranged from 40% to 55% according to the proportion of patients selected in the intensive versus continuation phase. This is due to an inherent failure in the cross-sectional design to capture changes in household income during a TB episode because the changes experienced during the intensive phase are typically reduced by 95% but increased by 7%-8% during the continuation phase, compared to household income prior to TB symptoms.

Redesigning surveys of costs incurred by people with TB and their households for robust evaluation of indirect costs

In the longitudinal approach, the changes in household income (and incurred income loss) can be captured by having multiple data collection points. However, in the WHO recommended cross-sectional design, the changes cannot be captured as the income loss during TB treatment is calculated based on the difference in income between before having TB symptoms and at the time of TB diagnosis [11]. In our study, TB-affected households were more financially vulnerable during pre-diagnosis and the TB intensive phase, with their household income recovering in the TB continuation phase to that of the level before having TB symptoms. In line with the changes in household income, the proportions of households using savings and taking loans were also high during these periods. In this situation, with the cross-sectional design, income loss is overestimated for those in the TB intensive phase and underestimated for those in the continuation phase.

However, there is a trade-off with these inaccurate estimates and using a longitudinal design which requires a longer duration for study implementation, more frequent data collection, and a larger budget. In resource-limited settings, it is not always feasible to estimate catastrophic costs using the longitudinal design and the cross-sectional design must be used. Our findings indicate that care should be taken when interpretating cross-sectional patient cost surveys. Indirect costs were the main cost driver in 13 surveys of costs incurred by people with TB and their households out of 31 completed [12], which highlights why robust evaluation of indirect costs is essential in assessing TB patient costs. One option for the cross-sectional design is to enrol TB patients while in the TB continuation phase only to allow an assessment of household income before TB, during TB diagnosis, in the TB intensive and continuation phases, even though this increases the risk of recall bias. A study in Nepal that compared the results of TB patient cost between the longitudinal and cross-sectional approaches suggested that in resource-constrained settings where a longitudinal study design is not feasible, one-time data collection in the TB continuation phase would provide more accurate cost estimates [36]. Another option is to consider surveys of costs incurred by people with TB and their households using a feasible longitudinal design. Although the longitudinal approach requires additional time and financial resources and may increase the risk of attrition bias, it provides a more robust evaluation of costs and income per person across an episode of TB [37,38]. Our study conducted data collection at four time points during an episode of TB, and another longitudinal TB patient cost study (TB Sequel) collected data at 0, 2, 6, 12 and 24 months, which is likely not feasible in resource-limited settings [37]. Therefore, WHO guidelines for conducting surveys of costs incurred by people with TB and their

households could explore a more feasible option for a longitudinal approach, such as two data collection timepoints: once in each of the intensive and continuation phases.

Required recommendations for sampling

The absence of an official recommendation about the sample proportions to be obtained in the TB intensive and continuation phases for national surveys using the cross-sectional design resulted in large differences, varying from 19% in the Philippines to 53% in Solomon Islands [11]. This may have resulted in under or overestimation of indirect costs. Given the majority of TB patients globally have DS-TB and the treatment requires 2 months for the intensive phase and 4 months for the continuation phase [1,14], the appropriate proportion of patients in the intensive phase would be around 33.3%. And given that 2.5% of global TB notifications are DR-TB, with shorter treatment regimens typically lasting 4 months for the intensive phase and 5 months for the continuation phase, the appropriate proportion is 33.6% [39]. For the WHO-recommended surveys, since the proportion of patients with DR-TB varies by country, it can be recommended that the ideal sampling proportion needs to be defined using the latest statistics around TB notifications (https://worldhealthorg.shinyapps.io/tb_profiles/). In the case of the Philippines, out of 444,987 total cases notified in 2022, 9916 cases (2.2%) were MDR/RR-TB, and therefore, the ideal proportion of patients in the intensive phase is estimated as 33.6% assuming all MDR/RR-TB patients are on treatment with the shorter 9-month regimen. For countries with a large number of (pre-)extensively drug-resistant TB (XDR-TB) and/or extrapulmonary TB, the proportion of notifications may need to be considered as the treatment for (pre-)XDR-TB and extrapulmonary TB takes longer than that for pulmonary DS-TB. Our findings suggests that the catastrophic cost estimates in studies that enrolled more than 33.6% of participants from the intensive phase and applied the output approach (i.e. 50% or more in Kenya, Solomon Islands, Uganda, Vietnam, and Zimbabwe) might have been overestimated (**Table 12**). Surveys that under-sampled patients in the intensive phase (i.e. 19% in the Philippines) may have underestimated the catastrophic costs. Hence our study findings highlight the need for an official recommendation by WHO.

Table 12. List of national patient cost surveys and proportion of cross-sectionally enrolled participants in intensive and continuation phases

Country	Year of data collection	Sampling in cross-sectional design		Method for indirect costs*	Inclusion of indirect costs before diagnosis	Authors, year of publication	Reference
		Intensive phase	Continuation phase				
Democratic Republic of the Congo	2019	49.1%	50.9%	Human capital approach	Yes	Kaswa M, 2021	[34]
Ghana	2016	33.6%	66.4%	Output approach	No	Pedrazzoli D, 2018	[28]
Kenya	2017	50.7%	49.3%	Human capital approach	Yes	Kirubi B, 2021	[27]
Lao People Democratic Republic	2018	37.2%	62.8%	Output approach	No	Chittamany P, 2020	[25]
Mali	2021	37.5%	62.5%	Human capital approach	Yes	Traore M, 2022	[31]
Myanmar	2015	39.1%	60.9%	Output approach	No	Aung ST, 2021	[33]
Philippines	2016-2017	19.4%	80.6%	Output approach	No	Florentino JL, 2022	[17]
Papua New Guinea	2018	34.2%	65.8%	Output approach	No	Aia P, 2022	[29]
Solomon Islands	2017-2019	53.0%	47.0%	Output approach	No	Viney K, 2021	[24]
Timor-Leste	2016-2017	39.8%	60.2%	Output approach	No	Viney K, 2019	[35]
Tanzania	2018	39.0%	61.0%	Human capital approach	Yes	Kilale AM, 2022	[30]
Uganda	2017	47.5%	52.5%	Human capital approach	Yes	Muttamba W, 2020	[32]
Vietnam	2016	49.0%	51.0%	Output approach	No	Nhung NV, 2018	[40]
Zimbabwe	2018	43.6%	56.4%	Output approach	No	Timire C, 2021	[26]

*Human capital approach: indirect costs were estimated from lost time multiplied by hourly wage that were the national average or estimated from self-reported income and working hours of survey participants. Output approach: indirect costs were estimated from the difference in self-reported household income before having TB symptoms and at the time of interview in the survey.

Inconsistency between recommendations and implementations

We found that the mean total costs incurred by TB-affected households was USD 932, and of these costs 24% (USD 219) was indirect costs borne during care seeking before TB diagnosis. More than 70% of our study participants took four weeks or more from the onset of TB symptoms until the diagnosis of TB, and therefore the long duration of care seeking and the consequent delay in TB diagnosis resulted in income loss even before diagnosis of the disease. This result is consistent with a previous systematic review of TB patient cost studies showing that indirect costs before TB diagnosis accounted for 26% of total costs [6]. The WHO recommendation clearly stated, *"Use self-reported household income at three points in time (before the onset of TB symptoms, at the time of diagnosis and during the "current" treatment phase) to estimate income change before and during the TB episode"*. However, the implementation is being conducted differently for surveys using the output approach. As we summarize in **Appendix 4**, the majority of national surveys used the output approach for estimating indirect costs, but none of them included income loss before TB diagnosis [17,24-26,28,29,33,35,40]. This inconsistency between the recommendation and the implementation can be also observed in a recent WHO publication *"National surveys of costs faced by tuberculosis patients and their households 2015-2021" [41]*. In part 2, 20 country profiles are presented, and for those using the output approach, the publication was unable to present income loss before TB diagnosis. The exclusion of indirect costs before TB diagnosis may have a considerable impact on catastrophic cost estimates since it lowers the catastrophic cost estimates. Yet of 14 publications of surveys of costs incurred by people with TB and their households implemented using a cross-sectional design, nine surveys applied the output approach as a method for estimating indirect costs [17,24-26,28,29,33,35,40]. Our analyses re-highlights the impact of indirect costs before TB diagnosis and the need to correct the inconsistency between the recommended method and what is implemented in surveys of costs incurred by people with TB and their households.

Limitations

This study had several limitations. First, this study was conducted using 11 health facilities located in urban (Cebu) and rural (Negros) settings in the Philippines, and therefore, the results and findings cannot be generalized. Changes in household income, coping mechanism, and social consequences of a disease could be markedly different by country and local contexts. Although the reduction and recovery in household income and in social consequences in our findings are observed in a longitudinal study in Vietnam, the pattern was not identified in another longitudinal study that assessed the catastrophic cost estimates for TB in Nepal [42,43]. Second, in this study, 16% of participants were not able to complete four data collection time points due to drop out from TB treatment or study

participation, and therefore, results of catastrophic cost estimates might be affected by attrition bias. Also, the dropout rate in the longitudinal design will be an issue if the study design is applied to a national survey since the WHO recommended national surveys require a much larger sample size (i.e. around 800-1,000 or more), and a high dropout rate may result in extension of survey duration. The issue needs to be carefully considered especially for countries with mobile populations. Third, although the longitudinal study design allowed multiple interviews during a TB episode with less recall bias compared to a cross-sectional study, this study assessed costs from the onset of TB symptoms to the completion of TB treatment. Therefore, financial loss due to TB-related sequalae and/or prolonged social consequences after TB treatment were not investigated in this study. Fourth, self-reported income was used as the ability to pay measure in the catastrophic cost estimates in this study. However, the use of self-reported income can induce the underestimation of the catastrophic cost compared to methods with the asset linking approach or income estimates using the national average [44]. Furthermore, though household consumption/expenditure is considered the gold standard for estimating ability to pay [45,46], we did not explore this method. Further studies developing and validating a consumption/expenditure-based measure will contribute to the improvement of the measurement of ability to pay in the catastrophic cost estimates.

3.8 Conclusion

Using longitudinal data of costs incurred by TB-affected households, we illustrated the potential limitations and implications of estimating indirect costs using a cross-sectional design and the output approach in the catastrophic cost estimates. Excluding possible changes in household income during the treatment of the disease and an inappropriate sampling balance from the different treatment phases will potentially underestimate catastrophic costs. Our findings can contribute to improvements in the recommendations and guidelines provided by the WHO Task Force for conducting surveys of costs incurred by people with TB and their households to assess TB-specific catastrophic costs.

3.9 Additional information

Data collection and extrapolation used for the simulated cross-sectional design

While in the longitudinal design, the total costs were calculated from the data collected at four timepoints; in the simulated cross-sectional design, the costs of e.g. the continuation phase were extrapolated using medians by purpose of visits (i.e. drug pick-up, DOT, medical follow-up and hospitalization) from the samples from the continuation phase (**Table 13**).

Table 13. Difference in cost estimation between the longitudinal and simulated WHO cross-sectional design

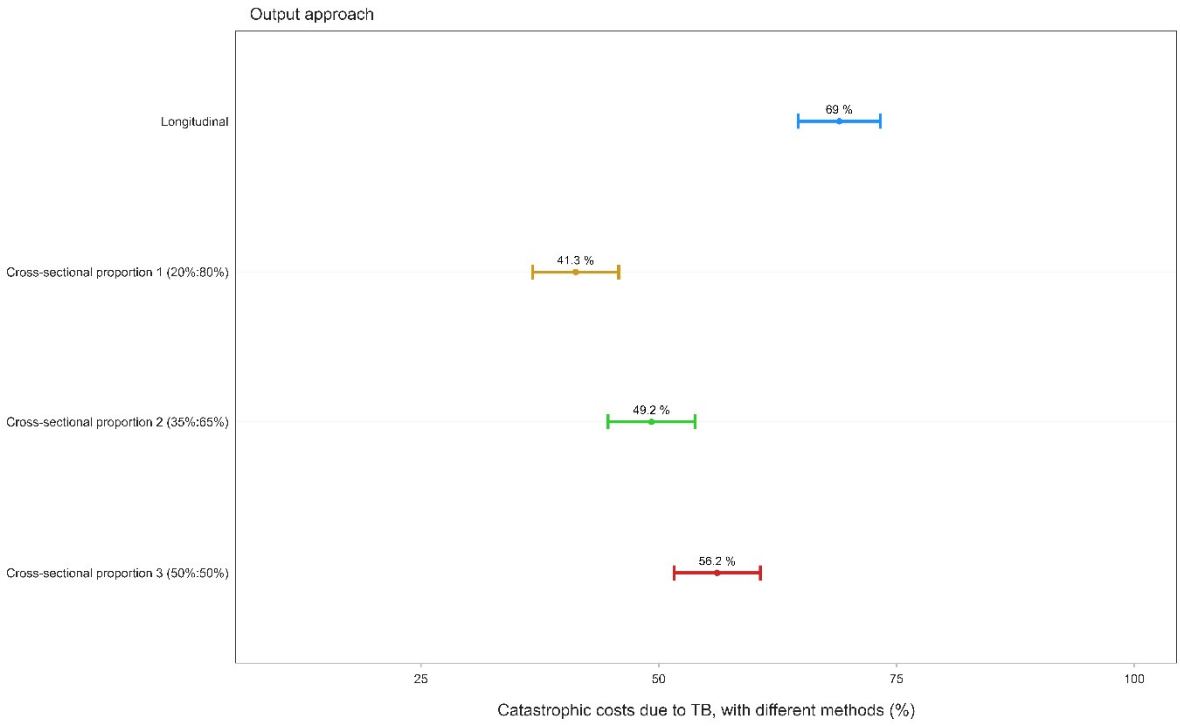
#	Category of people with TB	Cost before TB diagnosis	Cost during intensive phase	Cost from start to middle of continuation phase	Cost from middle to end of continuation phase
Simulated WHO cross-sectional design					
1	**Sampled from the dataset at end of intensive phase**	Calculated from the data collected at enrolment	Calculated from the data collected at end of intensive phase	Extrapolated using the median costs from the sample population 2	
2	**Sampled from the dataset at middle of continuation phase**	Extrapolated using the median costs from the sample population 1		Calculated from the data collected at middle of continuation phase	Inflated from the data collected at middle of continuation phase
Longitudinal design					
-	**All study participants**	Calculated from the data collected at enrolment (at 0 month of TB treatment)	Calculated from the data collected at end of intensive phase (at 2nd month of DS-TB treatment, at 6.5th month of DR-TB treatment with 9-months regimens)	Calculated from the data collected at middle of continuation phase (at 4th month of DS-TB treatment, at 6.5th month of DR-TB treatment with 9-months regimens)	Calculated from the data collected at end of continuation phase (at 6th month of DS-TB treatment, at 9th month of DR-TB treatment with 9-months regimens)

Use of means, not medians in the cost extrapolations in the simulated cross-sectional design

As described above, in the WHO recommended methods for national TB patient cost surveys, medians are used in the cost extrapolation. In this additional analysis, the impact of using means instead of medians in the cost extrapolation was assessed, and the analysis showed that the results using means increased the total cost estimates and the catastrophic cost estimates e.g. with 20:80, the catastrophic cost estimates increased from 39.7% in ***Figure 8*** to 41.3% in ***Figure 11***.

Hence, the use of means vs medians in the cost extrapolations may also need to be considered in the revision of WHO guidance on national TB patient cost surveys.

Figure 11. Percentage of TB-affected households facing catastrophic costs (> 20% of annual household income), using means for cost extrapolations



Potential under and overestimation of income loss in the cross-sectional design

The longitudinal design allowed this study to capture the changes in household income and the dynamics of income loss during an episode of TB (***Figure 12***). In the cross-sectional design with the current WHO recommended method, the data on household income is available only at the time of the data collection, and the method assumes that the collected household income data is applicable to the other treatment phase. This assumption may result in overestimation (***Figure 13***) and underestimation (***Figure 14***) of indirect costs when the sampling was unbalanced between the intensive and continuation phases. Also, the pattern of changes in household income could influence the over-/under-estimation of indirect costs i.e., whether household income considerably decreases during TB care seeking and the intensive phase, whether household income recovers during the continuation phase to the level of before having TB.

Figure 12. Income loss estimation in the longitudinal design (based on reported household income in Table 9)

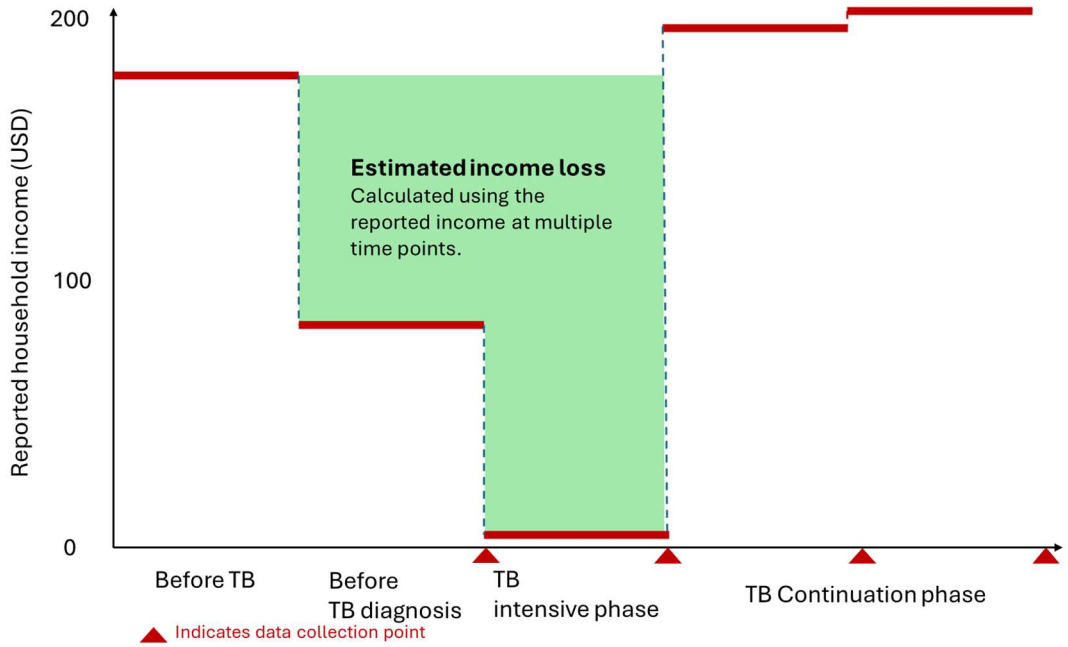
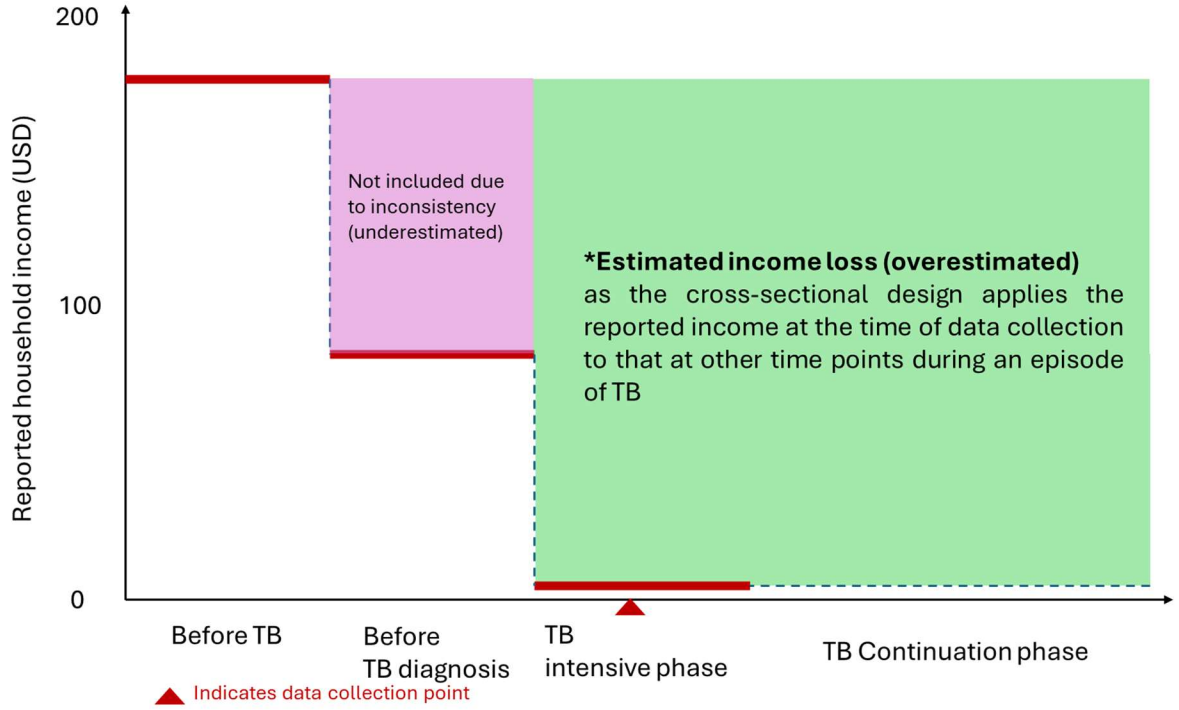
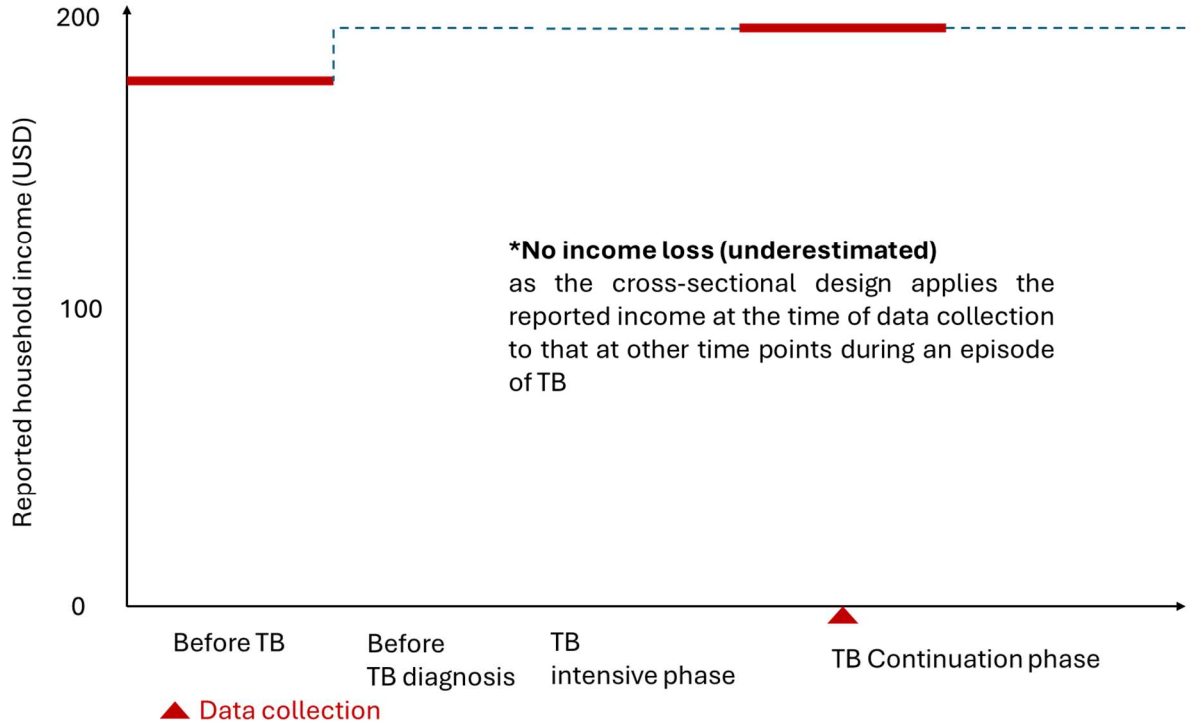


Figure 13. Income loss estimation for the sample population in the intensive phase in the cross-sectional design (based on the current practice in the national TB patient cost surveys)



* This figure assumes that the income changes in this study is applicable as a nationally representative result.

Figure 14. Income loss estimation for the sample population in the continuation phase in the cross-sectional design (based on the current practice in the national TB patient cost surveys)



* This figure assumes that the income changes in this study is applicable as a nationally representative result.

Asset-based imputation used as the denominator of catastrophic total costs due to TB

To avoid obtaining infinity in the catastrophic cost calculation, asset-based imputed household income was used to replace the annual household income for those who reported zero household income before TB . This method is consistent with the WHO recommended analytical approach for national TB patient cost surveys (https://github.com/GTB-PCS), rather than other approaches e.g. minimum wage, to take the financial characteristics of population with TB into account [11]. The selection of assets used for the income imputation was done by univariate logistic regression analysis was conducted to identify predictor variables for household income from the sample population with non-zero household income and then conducted multivariate backward stepwise logistic regression to identify the final selection of asset items (**Table 2**) based on the Akaike information criterion (AIC).

Periodic measurement of the percentage of TB-affected households facing catastrophic total costs due to TB

In the WHO handbook for national TB patient cost surveys, the periodic measurement of the catastrophic cost indicator was recommended (i.e. every five years) [11]. WHO needs to address the

methodological issues raised in this chapter and publish the revised guidance on national TB patient cost surveys. At the time of writing this thesis, the updated guidance is under development.

Output approach and human capital approach in estimating indirect costs

The output approach measures income loss and uses self-reported household income to measure the difference in income at different points in time before TB, at TB diagnosis and during TB treatment, while the human capital approach measures productivity loss and uses self-reported time spent for care seeking and TB treatment, multiplied by an individual hourly income. The output approach captures loss of income in households for any reasons, not only for seeking or receiving health services, during an episode of TB. However, this approach may underestimate the economic value of self-employed or informal worker's indirect costs. The human capital approach includes the economic value of lost time in households to seek or receive care for TB, which may overestimate costs in informal labour sector, especially in high unemployment settings.

Impact of post TB treatment costs

Economic consequences and sequalae of TB were not included in the scope of the data collection and analysis which was one of limitations of this study. The potential post TB treatment costs may include costs for visiting health facilities for TB sequalae, continuous income loss after the completion of TB treatment, or interest payment for the loans taken during an episode of TB.

Sample size calculation

Assuming a consent rate of 90% for this costing study, I expected to enrol 558 people with TB with known diabetes status (expected 9-12% with diabetes [20]). Assuming that 90% of these were successfully followed up, I expected data on total TB patient costs to be available for 502 people with TB. This means that 10% were expected to have death due to TB, loss-to-follow-up during TB treatment or treatment failure. The 90% retention rate was estimated from the treatment success rate for DS-TB (91% in 2016) in the Philippines. A sample size of 60 people with TB and diabetes and 120 people with TB only was powered at 90% to detect a minimum effect size of a 17% increase in total costs as a proportion of household income between TB-diabetes vs TB-non-diabetes. This assumed a mean of 18.5% of annual household income for non-diabetes TB from a study that assessed costs of people with diabetes and their households in Thailand [21,22].

3.10 Reference

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CHAPTER 4. HEALTH SYSTEM COST OF OUTPATIENT CARE FOR DIABETES IN PEOPLE WITH TUBERCULOSIS: ESTIMATES FROM THE PHILIPPINES

4.1 Preamble

This research paper presented the costs of providing integrated diabetes outpatient services within the TB programme, from the provider perspective. Both costs and cost-effectiveness of providing diabetes services for people with TB were identified as a gap in WHO guidance development group for managing TB and diabetes. At the time this paper was written, there were no comprehensive evidence on the costs of diabetes services for people with TB, which can be used for the cost effectiveness analysis of providing diabetes services for people with TB. The aim of this analysis was to assess the costs of providing diabetes outpatient services such as diabetes screening and diagnostics and the subsequent routine diabetes management that can be integrated into TB services in order to inform policymakers of the health system costs of implementing TB and diabetes service integration.

This study was conducted as a cross-sectional study in 11 health facilities that provide diabetes outpatient services in Negros Occidental, the Philippines. We enrolled a total of 60 health professionals who provide diabetes care, and we sought to conduct five to six interviews with key informants including one medical doctor, two nurses or midwives, one laboratory technician and one staff member in charge of procurement and/or finance at each site. In order to assess the cost of diabetes outpatient services, the WHO ‘‘Costing Guidelines for Tuberculosis Interventions’’ was adapted. The bottom-up approach was adopted to collect unit cost of diabetes drugs, consumables and equipment using a semi-structured interview guide. For staff time, both the bottom-up and top-down approaches were adopted using semi-structured interviews and staff timesheets. The data collection was conducted between October 2021 and June 2022.

We found that risk assessment, screening and diagnosis with fasting blood glucose (FBS) or random plasma glucose (RPG), drug prescription, consultation visits and referral services to other facilities for diagnostics and complications were the most common practices in outpatient diabetes services. Screening with the HbA1c test and diagnosis with oral glucose tolerance test (OGTT) were only provided in one private hospital. The cost per case detected with different diagnostic algorithms ranged from USD 17.43 (RPG+FBS) to USD 25.41 (HbA1c+FBS). The total monthly costs per patient were estimated at USD 8.95 (medicines and drug prescription only) to USD 12.36 (medicines, drug

prescription, monitoring and consultation visits). The results of this paper contributed to fill the evidence gap identified in the stakeholder consultation for WHO operational handbook tuberculosis module 6: Tuberculosis and Diabetes.

This research paper was published in IJTLD Open in March 2024 and the paper was reproduced in this chapter with minor revisions of figure and table structures from the published manuscript, but without any changes results. Additional information section (**section 4.9**) was included to provide clarifications of methods, results and discussions for the purpose of the thesis development.

Citation

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4.2 Research cover sheet

The Research Paper Cover Sheet is enclosed on the following pages.

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Surname/Family Name	Yamanaka		
Thesis Title	Mitigating the economic impact of TB and diabetes in the Philippines		
Primary Supervisor	Dr Anna Vassall		

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Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	AV, TY and YL conceptualized the study. TY developed the study methods and obtained funding for this study. JPF, MCC and TY implemented the data collection. TY cleaned, validated and analysed study data with supervision from AV and YL. TY, AV and YL interpreted results. TY developed the draft of the paper. All authors reviewed and edited the paper.

SECTION E

Student Signature	[redacted]
Date	31 August 2024

Supervisor Signature	[redacted]
Date	31 August 2024

4.3 Abstract

Background

Diabetes is a known risk factor for active TB. A key activity in the Philippines is to integrate TB services with other disease programmes, with a target of diabetes screening in 90% of TB cases. However, costs of providing diabetes outpatient services for TB patients are not well known.

Methods

We estimated the costs of providing integrated diabetes outpatient services within TB services, from the health system perspective. Resources for outpatient diabetes services were valued using the bottom-up approach for capital goods, staff time and consumables. Resource quantities were obtained by interviewing 60 healthcare professionals in 11 health facilities in the Philippines.

Results

Mean cost per service ranged from USD 0.53 for diabetes risk assessment to USD 23.72 for oral glucose tolerance test. The cost per case detected for different algorithms varied from USD 17.43 to USD 80.81. The monthly cost per patient was estimated at USD 8.95 to USD 12.36.

Conclusion

Our study provides the first estimates of costs for providing diabetes outpatient services in a low- and middle-income country integrated into TB care. The costs of diabetes detection in TB patients suggests that it may be useful to further investigate the cost-effectiveness and affordability of service delivery.

4.4 Introduction

Diabetes causes a substantial financial burden for patients, their households and health systems as well as disabilities and mortality [1-3]. Diabetes is known to increase the risk of progressing to active TB disease [4-6]. The Philippines has a high TB incidence occurring with comorbid diabetes [7]. Estimated TB incidence in the Philippines was 638 per 100,000, and 22,000 adult TB incident cases were attributable to diabetes in 2022 [8]. Diabetes not only increases the risk of developing TB but also has adverse effects on TB treatment outcomes particularly if diabetes is not properly managed [4-6]. Increasing early diagnosis and improving management of diabetes may accelerate the decline of TB incidence and unfavourable treatment outcomes thus contributing to ongoing transmission [4,6,9]. Considering the disease burden of TB comorbid with diabetes, WHO published a guideline to develop and implement collaborative actions aimed at reducing the double burden of TB and diabetes. The guideline included bi-directional screening of TB in people with diabetes and of diabetes in TB patients [10]. Despite increased political and public health awareness of diabetes management within TB services, there is a lack of evidence to promote policy for TB patients with comorbid diabetes. In the Philippines, the current TB national strategic plan includes integrating TB with other health programs including non-communicable diseases as a key activity, targeting 90% of TB cases to be screened for diabetes by 2022 [11,12]. This requires further understanding of the cost of providing diabetes screening and diagnostic services for TB patients and the subsequent costs to provide routine diabetes services such as for drug prescriptions, and regular monitoring for blood sugar level.

There is a recent systematic review for diabetes provider costs that included 52 publications and investigated costs per outpatient visit and annual inpatient, laboratory, and drug costs [13-17]. None of these studies assessed costs of diabetes services for TB patients. In the Philippines, only one study assessed provider costs and availability of diabetes services. However, the study is outdated and only assessed unit cost for diabetes medications [18]. Other cost categories such as for screening, human resources and equipment costs have not yet been investigated. Therefore, this study aimed to assess the costs of providing diabetes outpatient services that can be integrated into TB services.

4.5 Methods

Scope, study sites, timing and population

We estimated the provider costs for delivering 11 services as part of an algorithm integrating diabetes services into TB services from the health system perspective, including risk assessment, screening and diagnosis, drug prescription, consultation. Unit costs of diabetes services were estimated using data collected from sites not currently integrating services but providing both services. We estimated unit costs excluding overhead and start-up costs. A cross-sectional study was conducted in health facilities that provide diabetes outpatient services in Negros Occidental, the Philippines. Health professionals who provide diabetes care were identified in each study site, and we sought to conduct five to six interviews with key informants including one medical doctor, two nurses or midwives, one laboratory technician and one staff in charge of procurement and/or finance in each site. A total of 60 respondents were purposively selected and enrolled in our study. Our study was a nested study within an on-going cohort study assessing effects of malnutrition on TB treatment outcomes in Manila, Negros Occidental and Cebu in the Philippines and the study sites of our nested study were selected from the main cohort study [19,20]. Other study sites in Manila and Cebu were not included in our study due to difficulties to commence data collections during COVID-19 disruptions. Data collections were conducted between October 2021 and June 2022, and all the data were collected retrospectively for 2021.

Health system of TB and diabetes services in the Philippines

In the Philippines, costs for diabetes diagnosis and management are not fully covered by national insurance, the NTP or the non-communicable disease control programme, but direct medical costs for TB treatment and diagnosis are covered [21,22]. Social support is provided by the NTP for people with drug-resistant TB (DR-TB) with the purpose of improving treatment adherence and includes food packages and transportation fees for visiting health facilities [23-25]. Furthermore, The Department of Social Welfare and Development (DSWD) of the Philippines has a nationwide conditional cash transfer (CCT) programme for households living in poverty, and as of 2016, the CCT programme covered 4.4 million households, equivalent to 20% of the total population [26].

The current situation for the provision of TB and diabetes services differs by area and the level of facility. No diabetes outpatient services, except for drug pick-up at community level, are integrated within the TB programme. We identified two different patterns for providing TB and diabetes services in our study sites in the Philippines.

Pattern 1.

Drug pick-up for TB & diabetes: provided at the community level (barangay health centre (BHC)).

*BHC is classified as community level (Level 0 facility) for TB care in the Philippines [27].

Diagnosis of and prescription for TB and diabetes: Not integrated. Provided at different levels of health facilities (diagnosis for TB is at city/rural health centres and diabetes is at district hospitals).

*Urban/rural health centre including city health centre is classified as primary-care level (level 1 facility), and district hospitals as primary-care level with specialized health services (level 2 facility) for TB care in the Philippines [27].

Diabetes screening and monitoring: 1st screening and regular monitoring by Point of Care (POC) HbA1c or fasting blood glucose are not provided in public health facilities, and therefore people living with diabetes have to visit private pharmacies.

Pattern 2.

Drug pick-up for TB & diabetes: provided at the secondary health facility level (city or rural health unit). Some cities or rural health units do not allow TB medications to be provided at community level, and therefore, for TB drug pick-up, patients have to visit secondary health facility level where diabetes medications are also available. However, TB services and diabetes services are provided separately.

Diagnosis of TB and diabetes: Not integrated. Provided at different levels of health facilities (diagnosis for TB is at city/rural health centres and diabetes is at district hospitals).

Diabetes screening and monitoring: 1st screening and regular monitoring by Point of Care (POC) HbA1c or fasting blood glucose are not provided in public health facilities, and therefore people living with diabetes have to visit private pharmacies.

Data collection

The WHO ''Costing Guidelines for Tuberculosis Interventions'' was adapted for the data collection, analysis, and reporting to assess the cost of diabetes outpatient services in this study [28-31]. Data were collected using a combination of interviews, timesheets and the extraction of data from financial and administrative documents obtained from the finance and human resource departments in each health facility, and resource quantity data were obtained from interviews with healthcare professionals who performed for diabetes outpatient services. In addition, general information, such as facility size in square meters, catchment population and service utilisation, including number of outpatient visits, diabetes screening and diagnosis tests performed, and people on diabetes management, was also obtained from facility records. The bottom-up (BU) approach was adopted to collect unit cost of diabetes drugs, consumables and equipment using a semi-structured interview guide. For staff time, both the BU and top-down (TD) approaches were adopted using semi-structured interviews and staff timesheets.

Bottom-up (BU) costing is an approach to estimate costs that involves detailed assessment and/or measurement of all materials and resources being used for providing health care services. The BU approach captures all the inputs utilized and consumed for a specific health service, by interviews, observations and/or reviewing work records/logs, then multiplies these input quantities by the unit cost of each input. Conversely, the top-down (TD) approach starts from total health expenditures/budgets, and the costs are estimated by allocating the total expenditures based on the utilization of each heath service [31].

Prior to interviews with healthcare professionals, we conducted an interview with the head of each health facility to obtain permission to conduct interviews and identify key informants who can provide necessary data and information on facility infrastructure, finance and human resources and types of diabetes outpatient services provided in the facility. Key informant interviews were performed to estimate resource utilization and time consumed in the previous month, and staff timesheets were used to determine time spent from self-reported working schedule in a week.

Annual salaries for staffs were estimated from monthly salary and allowances per staff collected from records of human resources (**Table 14**). The value of the buildings in each study site was estimated using the size of the facility and the government official construction costs. Useful life of capital goods were 30 years for building and 5 years for equipment [32]. A five percent wastage rate was applied for medical consumables and drugs (**Table 15**). All the cost data were collected in Philippines Pesos (PHP) and converted to US Dollars (USD) using UN Operation Exchange Rate across the data collection period from October 2021 to June 2022 (1USD = 52.1 PHP).

Table 14. Mean salary of healthcare workers involved in providing diabetes care in sampled facilities in the Philippines in 2022 USD (USD1 = PHP52.1)

Title	N*	Annual salary	
		Mean	SD
Medical doctor	18	18,362	2,845
Nurse	68	8,862	1,676
Midwife	94	5,456	382
Nursing assistant	2	3,754	N/A
Medical technologist	24	5,989	2,351
Pharmacist	1	7,512	N/A
Laboratory aid	3	2,427	153
Other (warehouse, inventory, purchasing)	9	3,514	1,065

* N is the number of healthcare professionals providing diabetes services across 11 health facilities.

USD: United States dollars, PHP: Philippine peso, SD: Standard deviation

Medical doctors or medical officers, nurses, midwives, and medical technologists were the healthcare professionals who most commonly provided diabetes outpatient services (**Table 14**). The mean estimated annual salary, including allowances, was USD 18,362 (SD 2,845) for medical doctors, USD 8,862 (SD 1,676) for nurses, USD 5,456 (SD 382) for midwives, and USD 5,989 (SD 2,351) for medical technologists. In three facilities, there were also auxiliary and administrative staff including nursing assistants (USD 3,754), pharmacists (USD 7,512), laboratory aids (USD 2,427), and procurement/inventory staff (USD 3,514).

Table 15. Price sources and methods for estimating unit costs by input

Cost type	Assumed useful life (years)	Price source	Allocation method	Key assumptions
Buildings	30	Facility documents, government construction costs	Service statistics (outpatient visits)	
Medical equipment	5	Facility procurement price	Service statistics (outpatient visits)	
Other equipment, furniture	5	Facility procurement price	Service statistics (outpatient visits)	
Clinical staff	-	Human resource documents	Time sheet, interview	
Support staff	-	Human resource documents	Time sheet, interview	
Medical supplies	-	Facility procurement price	Service statistics (outpatient visits)	Wastage assumed 5%
Other supplies	-	Facility procurement price	Service statistics (outpatient visits)	Wastage assumed 5%
Drugs	-	Facility procurement price	Service statistics (outpatient visits)	
Maintenance	-		Not included	
Utilities	-		Not included	
Transport	-		Not included	
Food	-		Not included	
Training	-		Not included	

Data analysis

Collected data were entered, checked for reasonableness and cleaned using Microsoft Excel for each study site, and then merged and imported into R Statistical Software (v4.2.0) for further analysis. Costs were calculated separately for consumables, drugs, equipment, building, and staff for each diabetes service, and then combined to estimate the unit cost per diabetes services. Mean and standard deviation (SD) were used to summarize the unit cost per diabetes service. Results with median and interquartile range were summarized in supplementary information.

Cost per diabetes case detected among TB patients was calculated as the total costs of diabetes screening and diagnosis for a specified population using a particular screening and diagnostic algorithm divided by the total number of cases identified [33]. The screening and diagnostic testing approaches and algorithms available in each study site were obtained from interviews with nurses and laboratory technicians providing those services at the respective facilities. The cost per diabetes case detected was then estimated for five different algorithms with combination of glycated haemoglobin (HbA1c) test, Random Plasma Glucose (RPG), Fasting Blood Sugar (FBS) and Oral Glucose Tolerance Test (OGTT). This included the diagnostic algorithms comprised of 1 stage (confirmatory test) or 2 stages (screening test and confirmatory test). Furthermore, results were stratified by all age group and age group >45 years as a high-risk population having diabetes [34].

Since there were no integrated diabetes services for TB patients in our study sites, the proportion of TB patients who tested positive for diabetes screening and confirmatory tests were extracted from the main cohort study (**Table 16**) [19,20]. The participants of the main study were initially screened for diabetes using either HbA1c or RPG; those with an HbA1c>5.7% or RPG>11.1 mmol/L, OGTT was provided as a confirmatory test for diabetes. The sensitivity and specificity of each test and the estimated prevalence of diabetes were taken from available literature as assumptions for calculating the positive predictive values of each test (**Table 16, Table 17**) [35-39].

Table 16. Assumptions used for estimating cost per case detected

Test	% exceeded cut-off		Prevalence of diabetes		Sensitivity	Specificity	Positive predictive value	
	All age	Age > 45	All age	Age > 45			All age	Age > 45
HbA1c > 5.7%	47.5%	59.8%	22.6%	32.0%	92.3%	48.5%	34.4%	45.8%
RPG > 7.8mmol/l	47.5%[1]	59.8%[1]	22.6%	32.0%	93.0%	59.0%	39.8%	51.6%
OGTT for those with HbA1c > 5.7% or RPG > 7.8mmol/l	39.0%	48.6%	22.6%	32.0%	100.0%	100.0%	100.0%	100.0%
FBS for those with HbA1c > 5.7% or RPG > 7.8mmol/l	39.0%[1]	48.6%[1]	22.6%	32.0%	56.0%	97.9%	88.6%	92.6%

[1] Since there are no available data of positivity rate with RPG > 7.8 mmol/l and FBS > 7.0 mmol/l in TB patients in the Philippines, the proportion with HbA1c > 5.7% and diagnosed as diabetes with OGTT in the main study was used for that of RPG > 7.8 mmol/l and FBS > 7.0 mmol/l respectively.

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose, mmol/l: millimoles per litre

Table 17. Number of people screened, and cases detected based on the assumptions

Group	Algorithm Stage 1	Stage 2	Number screened	Case detected
All age group	HbA1c > 5.7%	-	100,000	16,318
	RPG[2] > 7.8mmol/l	OGTT	100,000	18,003
	RPG[2] > 7.8mmol/l	FBS[1] > 7.0mmol/l	100,000	12,077
	HbA1c > 5.7%	OGTT	100,000	18,003
	HbA1c > 5.7%	FBS[1] > 7.0mmol/l	100,000	12,077
Age > 45	HbA1c > 5.7%	-	100,000	18,901
	RPG[2] > 7.8mmol/l	OGTT	100,000	29,063
	RPG[2] > 7.8mmol/l	FBS[1] > 7.0mmol/l	100,000	25,373
	HbA1c > 5.7%	OGTT	100,000	29,063
	HbA1c > 5.7%	FBS[1] > 7.0mmol/l	100,000	25,373

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose, mmol/l: millimoles per litre

The monthly cost of treating each patient was estimated using the cost data of diabetes outpatient services that are periodically performed for people with diabetes.

Ethics considerations

The Asian Eye Institute Ethics Review Committee reviewed and provided the Philippines national ethics approval (2021-010). Approvals were also obtained from London School of Hygiene and Tropical Medicine (25149) and Nagasaki University (NU_TMGH_2021_153_1). A written consent form was obtained from all participants before the commencement of the interview. The informed consent signed by all participants explicitly stated that only the principal investigators can access the study dataset.

4.6 Results

Facility characteristics

The total number of outpatient visits at the 11 study sites ranged from 1,376 to 4,782 in 2021, and of these, outpatient visits for diabetes services accounted for 3% to 13% of total outpatient visits (**Table 18**).

Table 18. Characteristics and outpatient visits at 11 sampled health facilities in Negros Occidental, the Philippines

Facility	Facility level	Ownership	Locality	Total outpatient visits (2021)	Outpatient visits for diabetes (2021)	Outpatient visits for TB (2021)	Diabetes diagnostic algorithms
Bacolod Health Centre	Health centre	Government	Rural	4,383	436	1,864	RPG+FBS
Bago Health Centre	Health centre	Government	Rural	3,184	274	1,263	RPG+FBS
Bago Hospital	Primary hospital	Government	Rural	1,609	N/A	N/A	RPG+FBS
Don Salvador Rural Health Unit	Health centre	Government	Rural	1,376	86	358	RPG+FBS
Dr. Pablo O. Torre Memorial Hospital	Tertiary hospital	Private	Rural	3,187	93	257	HbA1c, HbA1c+OGTT, HbA1c+FBS
EB Magalona Rural Health Unit	Health centre	Government	Rural	4,782	425	2,370	RPG+FBS
La Carlota Health Centre	Health centre	Government	Rural	2,333	180	1,021	RPG+FBS
Pontevedra Rural Health Unit	Health centre	Government	Rural	4,431	N/A	2,319	RPG+FBS
San Enrique Rural Health Unit	Health centre	Government	Rural	2,803	210	1,248	RPG+FBS
Silay City Health Office	Health centre	Government	Rural	3,621	176	1,620	RPG+FBS
Valladolid Health Centre	Health centre	Government	Rural	1,857	243	580	RPG+FBS

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose, N/A: Not available

Unit cost for diabetes care

Risk assessment, screening and diagnosis with FBS or RPG, drug prescription, consultation visits and referral services to other facilities for diagnostics and complications were the most commonly provided outpatient services during diabetes visits. Screening with the HbA1c test and diagnosis with

OGTT were only provided in one private hospital. OGTT had the highest cost per patient at USD 23.72, while costs for risk assessment were only USD 0.53 (SD 0.20) (**Table 19**). Diabetes outpatient screening and monitoring were provided predominantly with FBS or RPG. Screening and diagnosis by FBS with chemistry analyser had a higher cost at USD 2.99 (SD 0.75) compared to that with glucometer (USD 1.67, SD 0.83). Using the proportion of people taking each type of diabetes medicine in each facility, the weighted mean monthly drug cost per patient was estimated at USD 7.67 per month. Staff was the main cost driver for diabetes outpatient visits where testing was not done in a laboratory (i.e., consultation visits, drug prescriptions, risk assessments), ranging from 70% to 92%. Consumables were the main driver for screening and diagnosis services, ranging from 52% to 90% (**Figure 15**).

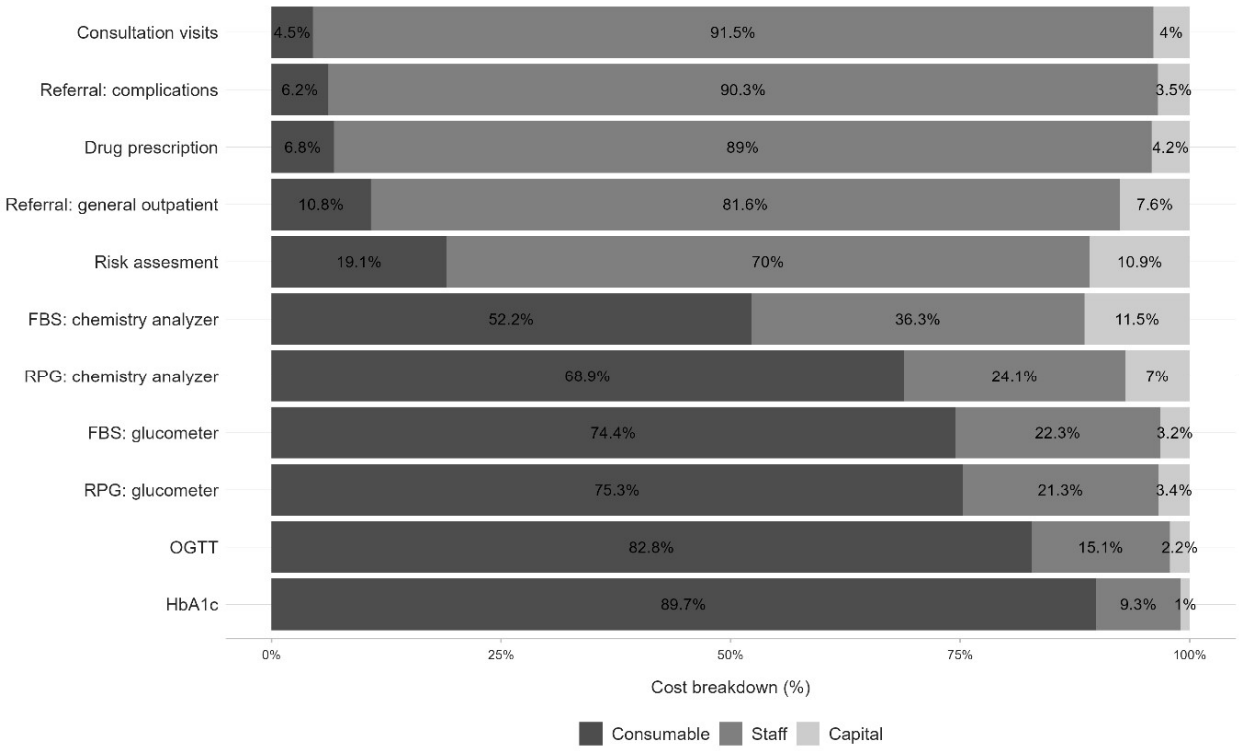
Table 19. Unit costs for diabetes interventions in sampled facilities

				Cost breakdown by input type			Cost per patient	
Intervention			**n**	**Consumable**	**Staff**	**Capital**	**Mean**	**SD**
Risk assessment			10	0.10	0.37	0.06	0.53	0.20
Screening and monitoring	FBS	Glucometer	10	1.24	0.37	0.05	1.67	0.83
	RPG	Glucometer	11	1.00	0.28	0.04	1.32	0.65
	HbA1c		1	2.61	0.27	0.03	2.91	N/A
Diagnosis/confirmation	FBS	Chemistry analyser	9	1.56	1.08	0.34	2.99	0.75
	RPG	Chemistry analyser	1	2.26	0.79	0.23	3.28	N/A
	OGTT		1	19.63	3.57	0.51	23.72	N/A
Drug prescription			11	0.09	1.15	0.05	1.29	0.43
Consultation visits			11	0.09	1.73	0.08	1.89	0.84
Referral service	General		10	0.08	0.64	0.06	0.78	0.39
	Complication		10	0.10	1.44	0.06	1.60	0.67

* N is the number of health facilities providing each type of diabetes outpatient services.

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose, USD: United States Dollar, PHP: Philippine Peso, SD: standard deviation, N/A: Not applicable

Figure 15. Cost drivers for providing diabetes outpatient services



*Proportions are based on the mean unit cost per diabetes outpatient service

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose

Cost per diabetes case detected in TB patients

Amongst the five diagnostic algorithms, one consisted of only a screening blood test, while the remaining four algorithms consisted of a screening blood test and a confirmatory blood test. The diagnostic algorithms with the lowest cost per case detected were a) HbA1c, b) screening by RPG and diagnosing by FBS, or c) screening by HbA1c and diagnosing by FBS (**Table 20**).

The cost per case detected for these three algorithms ranged from USD 17.43 (RPG+FBS) to USD 25.41 (HbA1c+FBS). When the target population is limited to people aged 45 years and over, the cost was lowered to USD 11.73 (RPG+FBS) to USD 16.17 (HbA1c+FBS) per case detected.

Table 20. Estimated cost per case detected for diabetes among TB patients

Group	#	Algorithm		Cost per case detected			
		Stage 1	Stage 2	Mean	SD	Median	Interquartile range
All age group	I	HbA1c > 5.7%	-	17.80	N/A	17.80	N/A
	II	RPG[2] > 7.8mmol/l	OGTT	80.81	N/A	80.81	N/A
	III	RPG[2] > 7.8mmol/l	FBS[1] > 7.0mmol/l	17.43	5.30	15.06	13.59-22.89
	IV	HbA1c > 5.7%	OGTT	78.72	N/A	78.72	N/A
	V	HbA1c > 5.7%	FBS[1] > 7.0mmol/l	25.41	N/A	25.41	N/A
Age > 40	I	HbA1c > 5.7%	-	10.62	N/A	10.62	N/A
	II	RPG[2] > 7.8mmol/l	OGTT	60.09	N/A	60.09	N/A
	III	RPG[2] > 7.8mmol/l	FBS[1] > 7.0mmol/l	11.73	3.46	10.19	9.35-15.23
	IV	HbA1c > 5.7%	OGTT	58.80	N/A	58.80	N/A
	V	HbA1c > 5.7%	FBS[1] > 7.0mmol/l	16.17	N/A	16.17	N/A

[1] testing cost with chemistry analyser was used for the estimation of cost per case detected.

[2] screening cost with glucometer was used for the estimation of cost per case detected.

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose, SD: Standard deviation USD: United States Dollar, PHP: Philippine Peso, mmol/l: millimoles per litre, SD: standard deviation; N/A: not applicable

Unit cost for diabetes drugs

The levels of diabetes medicines prescribed varied considerably across our study sites. Among oral medicines, Metformin and Gliclazide were most prescribed. The mean monthly cost per patient for Metformin (500mg) was USD 2.11 (SD 0.75), and for Gliclazide, depending on the dose, the mean monthly cost per patient ranged from USD 2.92 (30mg) to USD 3.22 (80mg) (**Table 21**).

For injectable drugs, the brand available and its cost also varied by health facility. The mean monthly cost per patient ranged from USD 13.58 to USD 43.01. Biphasic Isophane Human Insulin was most prescribed, and the mean monthly cost per patient was USD 29.45 (SD 6.34).

Table 21. Mean unit costs for diabetes drugs in sampled facilities in 2022 USD (USD1 = PHP52.1)

Type	n	Monthly cost per patient		Proportion of patients taking drugs	Monthly cost per patient	
		Mean	SD		Median	Interquartile range
Oral medicine						
Metformin (500 mg)	11	2.11	0.75	95.6%	2.24	1.86-2.52
Metformin HCL + Gliclazide (500mg / 80 mg)	1	10.08	N/A	0.1%	10.08	N/A
Dapagliflozin/Metformin HCL 10/1000 mg	1	36.99	N/A	5.3%	36.99	N/A
Metformin-sitagliptin 100/1mg	1	39.38	N/A	1.8%	39.38	N/A
Gliclazide (80mg)	3	3.22	1.50	2.1%	3.94	1.13-4.6
Gliclazide (60mg)	2	2.80	0.84	0.4%	2.80	N/A
Gliclazide (30mg)	5	2.92	1.36	8.4%	2.05	1.8-4.49
Glimepiride 4mg	1	10.80	N/A	8.0%	10.80	N/A
Glimepiride 3mg	1	6.30	N/A	0.1%	6.30	N/A
Glimepiride 2mg	5	7.99	0.48	3.7%	8.19	7.5-8.38
Injectable medicine						
Biphasic Isophane Human Insulin (Insuget 70/30)	7	29.45	6.34	2.2%	27.60	24.87-35.28
Scilin N 100IU/ml	2	32.00	11.00	0.1%	32.00	N/A
Scilin M30 70/30	1	43.01	N/A	1.4%	43.01	N/A
Regular Insulin Human u-100	1	33.52	N/A	0.1%	33.52	N/A
Humulin 70/30	2	13.58	9.62	0.3%	19.74	N/A
Humulin I 100 IU/ml	4	15.75	7.92	0.4%	19.74	9.14-20.37

* N is the number of health facilities providing each type of diabetes medicine.

HCL: Hydrochloride, SD: Standard deviation, USD: United States Dollar, PHP: Philippine Peso, SD: standard deviation, IU/ml: International units per millilitre, mg: milligram, N/A: Not applicable

Monthly costs per outpatient

The total monthly costs per patient were estimated at USD 8.95 (medicines and drug prescription only) to USD 12.36 (medicines, drug prescription, monitoring and consultation visits) (**Table 22**).

Table 22. Estimated monthly costs per patient (N=11)

Monthly services				Mean	SD	Median	Interquartile range
Diabetes medicine	Drug prescription	-	-	8.95	0.43	8.79	8.71-9.39
Diabetes medicine	Drug prescription	Monitoring by RPG (glucometer)	-	10.28	0.84	10.14	9.67-10.99
Diabetes medicine	Drug prescription	Monitoring by FBS (glucometer)	-	10.47	1.12	10.22	9.67-11.77
Diabetes medicine	Drug prescription	Monitoring by RPG (glucometer)	Consultation	12.17	1.37	11.46	11.12-12.74
Diabetes medicine	Drug prescription	Monitoring by FBS (glucometer)	Consultation	12.36	1.63	11.46	10.99-14.29

FBS: Fasting blood glucose, RPG: Random plasma glucose, USD: United States Dollar, PHP: Philippine Peso, SD: Standard deviation

4.7 Discussion

The aim of our study was to estimate the cost per diabetes case detected in TB patients in a low- and middle-income country: the Philippines. The cost per case detected with feasible and affordable algorithms (that is, using HbA1c, RPG and/or FBS) ranged from USD 17.43 to USD 25.41. The monthly outpatient cost per patient for diabetes drugs and outpatient services was estimated at USD 8.95 to USD 12.36. We provided the most recent evidence on costs of providing diabetes outpatient services and the cost per diabetes case detected amongst TB patients in the Philippines. Our results will help with planning, budgeting and assessing the cost-effectiveness of providing integrated diabetes outpatient care within the TB programme.

A recent systematic review showed that costs of diabetes outpatient services from the health system perspective, which were assessed using the same BU approach as our study, ranged from USD 4-5 (Thailand, Brazil) to USD 22 (Argentina) per outpatient visit, USD 5 (Iran) to USD 152 (Argentina) for annual laboratory costs, and USD 26 (Thailand) to USD 91 (Brazil) for drugs annually [13-17]. Results of our study for outpatient visits and drugs were also in this range. In our study, unit cost per diabetes outpatient service ranged from USD 0.53 for risk assessment to USD 23.72 for diagnosis with OGTT. Monthly drug cost per patient varied from USD 2.11 to USD 43.01.

In a previous study that assessed costs of diabetes medicine in the Philippines in 2009, the monthly costs of oral and injectable medicines per patient was estimated at USD 16 while it was USD 7.67 in our study [18]. The difference in the cost estimates could be due to the difference in study design and population. The previous study had interviews with people with diabetes and healthcare professionals in 30 hospitals across the capital city and four provinces. The study assessed costs of purchasing diabetes drugs from patient perspective and included private practitioners (e.g. private pharmacies). Therefore, the costs might have been overestimated due to the selling price or the price difference between public and private service providers.

Representativeness of our analysis

The subnational disease burden data for TB has not been fully assessed or understood in the Philippines. The latest TB prevalence survey was conducted in 2016, and the survey assessed TB prevalence at subnational level, by allocating 17 regions into four strata. The prevalence with bacteriologically confirmed TB was 1,159 (95% CI: 1.016-1,301) per 100,000 population, and it ranged at subnational level from 856 (95% CI: 686-1,026) in stratum 4 (Mindanao) to 1,358 (95% CI: 1,103-1,612) in stratum 1 (Metro Manila) per 100,000 population. The prevalence in stratum 2, which

includes Negros Occidental Region where our study was conducted, was 1,234 (95% CI: 873-1,594) per 100,000 population [40], which is not significantly different from the national prevalence of TB.
The availability of the prevalence of diabetes among TB patients at subnational level is very limited in the Philippines, and only one study assessed the prevalence of comorbidities including diabetes among TB patients at TB diagnosis [20]. The study assessed the prevalence of diabetes among TB patients in three different areas of the Philippines (i.e. Metro Manila, Negros Occidental, and Cebu). The study showed that the overall prevalence of diabetes was 22.6% (N=881). Although Negros Occidental, where our study was conducted, had a high prevalence point estimate (25.5%) compared to the other two areas (20.1% and 20.9%), the study did not find a statistical significance (p=0.24). The overall prevalence (22.6%) was used for the analysis of cost per case detected in our analysis.
As a sensitivity analysis, we assessed the range of cost per case detected when the prevalence of diabetes ranged from 20.1% to 25.5% for the algorithm with RPG (screening) + FBS (diagnosis). The cost per case ranged from USD 17.14 to USD 17.75 for all age group.

Our study has several limitations. First, the study was conducted in purposively selected public health facilities in one region in the Philippines, and therefore only represent settings in the public sector in rural areas in the Philippines. Second, the study did not include cost components such as overhead costs and training costs. In the VALUE-TB study in the Philippines, which assessed provider costs for TB services, overhead cost was one of main contributors to TB services. The proportion of overheads costs was 40-50% of the cost of outpatient screening, monitoring, diagnostic and treatment visits [28]. Therefore, estimated costs for diabetes services could also be higher when overhead costs are included. Third, data on the proportion of suspected diabetes and that of confirmed diabetes in TB patients were only available by HbA1c at 5.7% (screening) and OGTT (diagnosis) provided in the main study. Therefore, our study had to assume the proportion of population screened as suspected diabetes with RPG (>7.8mmol/l) and FBS (>7.0mmol/l) in TB patients using the values from HbA1c (>5.7%) and OGTT. Also, although diabetes risk assessment by scoring before blood tests is in practice in the Philippines, the risk assessment data for TB patients was not available and therefore we were unable to include diabetes risk assessment in the estimation of cost per diabetes case detected in TB patients. Fourth, the scope of this study was to estimate the provider costs for diabetes outpatient services that can be integrated into TB care. For those applying our results it is important to note that we did not look at costs of managing diabetes in the longer term (e.g. for diabetes related complications, or inpatient care), nor costs from the patient perspective [41], which both need to be considered when assessing affordability or cost-effectiveness.

4.8 Conclusion

Our study provided the most recent cost of providing diabetes outpatient services for TB patients. The results will help with planning, budgeting and assessing the cost-effectiveness of providing integrated diabetes outpatient care within the TB programme. Further studies are required to obtain more robust evidence around diabetes screening and diagnosis in TB patients, and to understand the costs of providing diabetes inpatient services and costs from the patient perspective.

4.9 Additional information

Cost per case detected for diabetes among TB patients

The algorithms in **Table 20** and the cost estimates are based on the availability of testing equipment in each study site, and therefore, for the algorithms with HbA1c, SDs are N/A as only one study site provided testing with HbA1c. The results by mean and by median are similar as the algorithms with HbA1c (and OGTT) were provided in only one study site.

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CHAPTER 5. COST-EFFECTIVENESS OF DIABETES SCREENING AND DIAGNOSIS SERVICES FOR PEOPLE WITH TB IN THE PHILIPPINES

5.1 Preamble

This research paper assessed the cost-effectiveness of providing integrated diabetes outpatient services within the TB programme, from the provider perspective and the societal perspective. While the Philippines national strategic plan for TB control aimed at providing diabetes screening to 90% of TB cases, at the time of writing this paper, there was no evidence on the cost-effectiveness of providing diabetes services for people with TB.

In this study, the intervention was defined as 90% of people newly diagnosed with TB with an unknown diabetes status receiving diabetes screening using the random plasma glucose (RPG) and diagnosis using the fasting blood sugar (FBS) tests. Health outcomes (DALYs averted) and costs were compared with a scenario providing TB treatment only (baseline scenario). A decision tree was developed to estimate the incremental cost-effectiveness of providing diabetes screening and diagnosis at the time of TB diagnosis in the Philippines. The probabilities used in the decision tree were extracted from a cohort study (St-Att study, the main study) that assessed the effects of malnutrition and diabetes on TB treatment outcomes in the Philippines. DALY weights for health states of TB and diabetes were extracted from the latest Global Burden of Disease study. Costs were estimated from the societal perspective, using the data of and patient costs of TB and diabetes (chapter 3) and provider costs of diabetes services (chapter 4) in the Philippines. Costs of TB services were extracted from the VALUE-TB study that assessed health system costs of TB interventions using a nationally representative sample of health facilities in the Philippines. The cost effectiveness of the intervention was assessed in five different target populations; people aged ≥18 years, aged >45 years, with BMI >18.5 kg/m^2, with drug-resistant TB, and males aged ≥18 years.

We found that the intervention is cost-saving from both provider and societal perspectives, saving USD 147 per person from the provider perspective and USD 187 per person from the societal perspective. The results of the cost-effectiveness were highly sensitive to the cost of diabetes complications in the population with unmanaged diabetes, time (years) to developing diabetes-related complications, and the proportion with diabetes-related complications in the population with unmanaged diabetes. At a willingness to pay threshold per DALY of 50% of GDP per capita, the probability of the intervention being cost-effective was 99% both from the provider perspective and from the societal perspective in the target population of people aged ≥18 years.

The results of this paper will contribute to planning and budgeting of providing integrated diabetes outpatient care within the TB programme.

This research paper was submitted to Diabetes Research and Clinical Practice in September 2024 and published in March 2025. The research paper was reproduced in this chapter with minor revisions of texts from the published manuscript for the purpose of the thesis development, but without any changes results. Additional information section (**section 5.9**) was included to provide additional sensitivity analysis.

Citation

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5.2 Research paper cover sheet

The Research Paper Cover Sheet is enclosed on the following pages.

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Surname/Family Name	Yamanaka		
Thesis Title	Mitigating the economic impact of TB and diabetes in the Philippines		
Primary Supervisor	Dr Anna Vassall		

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SECTION E

Student Signature	[redacted]
Date	**14 March 2025**

LSHTM Supervisor Signature	[redacted]
Date	**14 March 2025**

5.3 Abstract

Aim: Tuberculosis (TB) remains a leading cause of death in low- and middle-income countries, and diabetes is a known risk factor for progression to active TB disease. While the Philippines national strategic plan for TB aims to screen 90% of TB cases for diabetes, the cost-effectiveness of screening is not well known.

Methods: We constructed a decision tree model to assess the cost-effectiveness of providing diabetes testing for 90% of people with an unknown diabetes status at their TB diagnosis and subsequent routine diabetes care, compared to the scenario of providing TB treatment only. Cost-effectiveness of the intervention was assessed from the provider and societal perspectives.

Results: The intervention was cost saving. At a willingness to pay threshold per disability-adjusted-life-year of 50% of gross domestic product per capita, the probability of the intervention being cost saving was 99% from the provider and societal perspectives in people aged ≥18 years. The probability was highest in people with BMI >18.5kg/m^2 and in those aged >45 years.

Conclusion: Our findings suggest that providing diabetes care for people with TB will be cost saving, and the intervention is likely to be most cost saving in people with BMI >18.5kg/m^2 or those aged >45 years.

5.4 Introduction

Tuberculosis (TB) remains one of the major public health concerns globally. In many low- and middle-income countries, TB has reached epidemic proportions, with a third of the world's population being infected [1]. TB ranked second as cause of death from a single infectious agent after COVID-19 in 2022; a global estimate of 10.6 million people fell ill with TB and there were 1.3 million deaths due to TB [2]. Diabetes is a known risk factor for the progression of active TB disease and may increase the risk of poor TB treatment outcomes [3-5]. Diabetes not only increases the risk of developing TB but also has adverse effects on TB outcomes especially if diabetes is not well managed [4]. Therefore, increasing diagnosis and improving diabetes management may contribute to the decline of TB incidence, which suggests that diabetes may amplify TB transmission [6]. The estimated number of incident cases of TB attributable to diabetes globally was 0.37 million in 2022 [2].

WHO has developed a new guidance on diabetes management for people with TB, and it was added to the operational handbook on tuberculosis: TB and comorbidities [7]. The current WHO guidance for managing comorbidities in people with TB recommends three different models of integrated care: stand-alone screening provided separately for TB and comorbidities, followed by referral for diagnosis and treatment (separate service delivery model); screening and diagnosis provided by service providers for TB and for comorbidities located in the same premises, followed by referral for treatment (co-located services model); and screening, diagnosis and treatment fully integrated and provided by a single service provider (one-stop-shop model) [7-9]. However, there are many evidence gaps identified in the guidance including optimal algorithms and timing for diabetes testing, and an association of early diabetes screening and case detection with improvement of TB treatment outcomes. The cost-effectiveness of providing diabetes screening in populations with a high prevalence of diabetes other than TB has been suggested as well as the cost-effectiveness of early screening and diagnosis of diabetes [10-12]. A systematic review concluded that diabetes screening in high-risk populations e.g. people aged 50 years or above or with a high BMI is cost-saving or cost-effective [13]. However, little is known about the cost-effectiveness of early detection and management of diabetes in people with TB.

In line with WHO guidance [14], the Philippines TB national strategic plan aims to screen 90% of TB cases for diabetes [15,16]. However, there is a lack of evidence to accelerate the implementation of the policy, specifically the cost-effectiveness of providing diabetes screening and diagnostic services for people with TB. Hence, to inform the Philippines National TB Control Programme (NTP) and policy makers around the need to implement diabetes screening for people with TB in the Philippines, this

study aimed to assess the cost-effectiveness of providing diabetes screening and diagnostic services for people with TB including the subsequent costs of routine diabetes services, namely diabetes medications, consultations with clinicians and regular blood sugar monitoring.

5.5 Methods

Study setting

The Philippines is classified as a high TB burden country both for drug susceptible TB (DS-TB) and multidrug-resistant TB (MDR-TB) [2]. WHO estimations of TB prevalence and incidence in the Philippines were 1,159 and 554 per 100,000 in 2016 (3rd highest incidence), and the number of rifampicin-resistant TB (RR-TB) cases was estimated as 20,000 persons [17,18]. The latest WHO estimate of TB incidence in the Philippines was 638 per 100,000 in 2022 [2], showing an increasing trend. The Philippines also has a high TB incidence occurring with comorbid diabetes [19], with 22,000 adult TB incident cases attributable to diabetes in 2022 [2]. In the Philippines, costs for diabetes diagnosis and management are not fully covered by national insurance, the NTP or the non-communicable disease control programme; only direct medical costs for TB diagnosis and treatment are covered [20,21].

Population, Interventions, Comparators and Timeframe

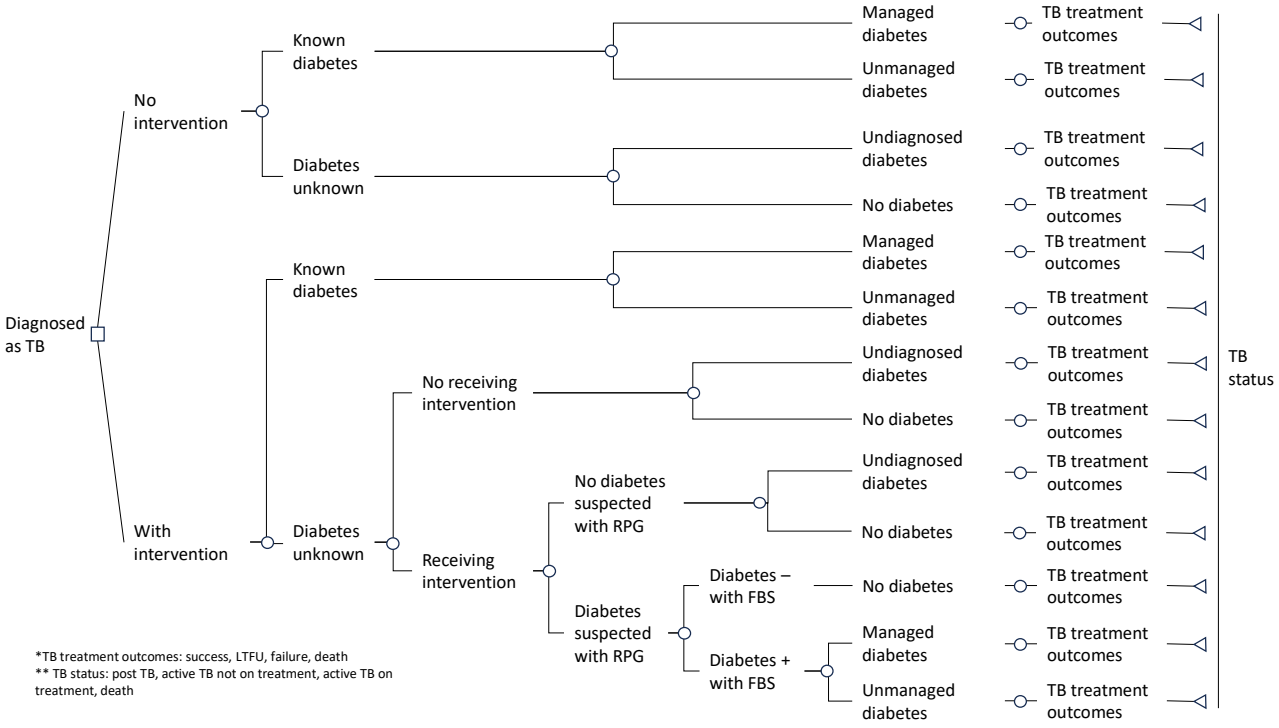
We defined our intervention as ensuring that 90% of people diagnosed with TB with an unknown diabetes status receive diabetes screening using the random plasma glucose (RPG) and diagnosis using the fasting blood sugar (FBS) tests. People diagnosed with diabetes start diabetes management during their TB treatment. The proportion screened and diagnosed with diabetes and initiating diabetes management were detailed in **Table 23**. The difference in TB treatment outcomes by diabetes status at TB diagnosis was also considered in the model. For those who initiated diabetes treatment, we assumed that routine monthly monitoring and management with diabetes drugs, consultations and testing for blood sugar were provided. The costs of diabetes drugs were estimated based on weighting the proportion receiving oral medications (Metformin, Gliclazide etc) and injectables (Insulin) [22]. In the model, RPG was used for screen testing and for routine monitoring of diabetes status following the national guidelines and also due to the unavailability of OGTT and HbA1c tests in public health facilities especially at community and primary levels [22-24]. Health outcomes and costs were compared with the do-nothing scenario (baseline scenario). We conducted analysis for three health status (people without diabetes, with unmanaged diabetes and with managed diabetes) for their lifetime costs and health outcomes based on assumptions of life expectancy [25-29].

Model structure

A decision tree was developed to estimate the incremental cost-effectiveness of providing diabetes screening and diagnosis at the time of TB diagnosis in the Philippines (**Figure 16**). The decision tree simulated the progression of people diagnosed with TB who receive either screening and diagnosis

for diabetes (intervention scenario) or no diabetes screening (baseline scenario). In the baseline scenario, we assumed that only people with already known diabetes receive routine diabetes management. In the intervention scenario, diabetes screening with RPG is provided for 90% of those who do not know their diabetes status at their TB diagnosis. Then, those with suspected diabetes receive a diabetes confirmatory test using FBS. TB treatment is provided for all in both scenarios. For simplicity, we assumed no transition of TB- or diabetes-related health status after the completion of TB treatment (e.g. recurrence of TB, transition from non diabetes to unmanaged/managed diabetes, new initiation of diabetes management, dropout from diabetes management), given that models and data that incorporate TB and diabetes lifetime transitions are not yet fully understood and developed [30,31]. Outcomes in the decision tree were based on four treatment outcomes; success, loss-to-follow-up (LTFU), failure, and death, with DALYs averted applied to each of these outcomes.

Figure 16. Decision tree for diabetes screening and diagnosis for people with TB



FBS: fasting blood glucose, LTFU: loss to follow up, RPG: random plasma glucose

Model inputs

The probabilities used in the decision tree were based on the results of an cohort study (the main study), which was conducted to measure the effects of malnutrition and diabetes on TB treatment outcomes in the Philippines, with a sub-study that estimated TB and diabetes costs [32-34]. The parameters used for this analysis were extracted from the main study and also from sub-studies that

were conducted within the main study and assessed the costs incurred by people with TB and diabetes and their households and the provider costs of diabetes outpatient services for people with TB [22,33]. Given that no national data is available on diabetes screening for people with TB at this time, the proportion of people with TB who tested positive for diabetes using screening and confirmatory tests was also obtained from the main study. The participants of the main study were initially screened for diabetes using either HbA1c or RPG. Those with an HbA1c >5.7% or RPG >11.1 mmol/L, were administered the Oral Glucose Tolerance Test (OGTT) as a diabetes confirmatory test. Since there are no available data for the positivity rate with RPG >7.8 mmol/l and FBS >7.0 mmol/l in people with TB, the proportion in the main study with HbA1c >5.7% and OGTT confirmed diabetes was used for that of RPG >7.8 mmol/l and FBS >7.0 mmol/l respectively, in our analysis. The probabilities of treatment outcomes were also extracted from the on-going cohort study, where it was possible to distinguish outcomes from those with TB only and those with TB-diabetes comorbidity. The national TB treatment success rate in the Philippines reported to WHO was 80% for new and relapse cases and 79% for multidrug-resistant and rifampicin-resistant TB cases in 2021 (https://worldhealthorg.shinyapps.io/tb_profiles/), which was not markedly different from the results of the main study.

For those who survived, age specific population life expectancies were used based on life expectancy in the general population in the Philippines and published data related to life expectancy of people with TB or diabetes in other countries [25-29]. DALY weights for health states of TB and diabetes were extracted from the latest Global Burden of Disease study [35]. Since DALYs for TB comorbid with diabetes were not available in the Global Burden of Disease study, it was calculated as a sum of DALYs for TB and for diabetes, given that the impact of not adjusting disability weights for comorbidities was minimal to small [36-38]. A DALY weight of 0.053 was used for post-TB after TB treatment success and applied for lifetime [37]. A discount rate of 3% per year was applied to estimate lifetime costs and DALYs. Disaggregated DALY weights by drug susceptibility (by DS-TB and DR-TB) were not available, and therefore, a DALY weight for TB was applied to any target populations including DR-TB population.

Costs were estimated from the provider perspective and also from the societal perspective, using provider costs of TB and diabetes services and costs incurred by people with TB and diabetes and their households in the Philippines. The provider perspective assessed costs of providing TB and diabetes services (provider costs), while the societal perspective included costs incurred by people with TB and diabetes and their households (patient costs) on top of provider costs included in the provider perspective. Costs of TB services in the Philippines were extracted from the VALUE-TB study that

assessed health system costs of TB interventions using a nationally representative sample of health facilities in the Philippines [39,40]. Incremental costs of providing diabetes screening with RPG, diagnosis with FBS and diabetes management were extracted from a study that assessed health system costs of providing diabetes outpatient services for people with TB in the Philippines [22]. We assumed that diabetes medicines, consultations with clinicians and the monitoring of blood sugar level by RPG using a glucometer were required monthly for those who initiated diabetes management (monthly diabetes management costs), which ranged from USD 8.95 (diabetes medicines and prescriptions only) to USD 12.26 (diabetes medicines, prescriptions, monitoring of blood sugar level and consultation visits) per month in our analysis [22]. Since the study did not include overhead costs in the cost assessments, a mark-up was applied separately to the medications (0%), diabetes testing (37%) and consultations with clinicians (40%), based on the proportion of above service level costs estimated in the VALUE-TB study in the Philippines [39]. Costs incurred by people with TB and diabetes were extracted from a study that assessed the difference in costs incurred by people with TB comorbid with diabetes and by those with TB-only in the Philippines. In addition, for DR-TB, we considered a higher costs both from the provider and patient perspectives were considered, and in the cost estimates from the patient perspectives, received social protection mechanisms were included [33]. Furthermore, the incidence of diabetes-related complications and the provider costs for diabetes-related complications were included in the lifetime model for the population with managed and unmanaged diabetes [41-45] (**Table 23**). Considering the cost differences between using RPG and HbA1c, a supplementary sensitivity analysis was conducted using costs of HbA1c for routine diabetes monitoring, instead of RPG (**Additional information**).

Cost effectiveness analysis, uncertainty and sensitivity analysis

The primary outcome of this analysis was the incremental cost-effectiveness ratio (ICER), which is reported as the incremental cost per DALY averted per person. The cost-effectiveness was assessed for five target populations i.e. people aged ≥18 years, aged >45 years, with BMI >18.5 kg/m^2 with drug-resistant TB and males aged ≥18 years. ICER as a primary outcome of the analysis was compared to a willingness to pay threshold (WTP) of 50% and 7.3% (which corresponds to the lower end of the country specific WTP) [46] of the gross domestic products (GDP) per capita to establish cost-effectiveness. One way sensitivity analysis was performed on the model parameters. We also performed a probabilistic sensitivity analysis for all parameters over 1000 simulations. Parameter uncertainty was tested in a cost-effectiveness plane. To assess the proportion of simulations that would be cost-effective, cost-effectiveness acceptability curves were used with willingness to pay per

DALY averted. All the model development, data processing, deterministic and probabilistic sensitivity analyses, and data visualizations were performed using R4.4.1 [47].

Ethical considerations

The Asian Eye Institute Ethics Review Committee (Makati City, The Philippines) reviewed and provided the Philippines national ethics approval: 2018-008 for a study that conducted diabetes testing and assessed the costs incurred by people with TB and diabetes, and 2021-010 for a study that collected provider costs of diabetes outpatient costs. Approvals were also obtained from the London School of Hygiene & Tropical Medicine, London, UK (#14894 and #25149) and Nagasaki University, Nagasaki, Japan [22,33,34]. All participants provided written informed consent before the commencement of the interview. The informed consent explicitly stated that only the principal investigators could access the study dataset, which was anonymised.

Ethics clearance was not required for the TB provider cost data as the secondary dataset from the VALUE-TB project is publicly available, and the data were already anonymised, and no personal identifying information was accessed during the analysis.

Role of the funding source

The funder of this study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author has full access to all the data in the study and had final responsibility for the decision to submit for publication.

Table 23. Parameter values used in the model for providing diabetes screening and diagnosis for people with TB

Parameters	Distribution	Best estimates					SE, Range	Ref
		people aged ≥18 years	people aged >45 years	BMI >18.5	Drug-resistant	Male aged ≥18 years		
DALYs								
Post TB	Beta	0.053	0.053	0.053	0.053	0.053	0.010	[37]
Active TB	Beta	0.333	0.333	0.333	0.333	0.333	0.020	[35]
Post TB with managed diabetes	Beta	0.062	0.062	0.062	0.062	0.062	0.010	Assumption based on [35,37]
Active TB with managed diabetes	Beta	0.342	0.342	0.342	0.342	0.342	0.020	Assumption based on [35,37]
Post TB with unmanaged diabetes	Beta	0.239	0.239	0.239	0.239	0.239	0.020	Assumption based on [35,37]
Active TB with unmanaged diabetes	Beta	0.519	0.519	0.519	0.519	0.519	0.030	Assumption based on [35,37]
Costs								
Provider perspective								
Costs for TB treatment	Gamma	135.50	135.50	135.50	1325.50	135.50	12.38	[22,33,39]
Costs for TB treatment with diabetes management	Gamma	296.20	296.20	296.20	1486.20	296.20	14.04	[22,33,39]
Costs for diabetes management	Gamma	160.70	160.70	160.70	160.70	160.70	7.56	[22,33,39]
Costs for diabetes screening with RPG	Gamma	1.85	1.85	1.85	1.85	1.85	1.17	[22]
Costs for diabetes diagnosis with FBS	Gamma	4.19	4.19	4.19	4.19	4.19	1.50	[22]
Societal perspective								
Costs for TB treatment	Gamma	1052.80	1052.80	1052.80	2242.80	1052.80	31.99	[22,33,39]
Costs for TB treatment with diabetes management (no integration)	Gamma	1659.40	1659.40	1659.40	2664.10	1659.40	40.56	[22,33,39]
Costs for TB treatment with diabetes management (with integration)	Gamma	1213.50	1213.50	1213.50	2403.50	1213.50	34.52	[22,33,39]
Costs for diabetes management	Gamma	217.50	217.50	217.50	217.50	217.50	14.90	[22,33,39]
Costs for diabetes screening with RPG	Gamma	1.85	1.85	1.85	1.85	1.85	1.17	[22]
Costs for diabetes diagnosis with FBS	Gamma	4.19	4.19	4.19	4.19	4.19	1.50	[22]
Diabetes complication-related parameters								
Costs of diabetes related complications in managed diabetes	Norm	395.20	395.20	395.20	395.20	395.20	152.61	[41,45]
Costs of diabetes related complications in unmanaged diabetes	Norm	1908.70	1908.70	1908.70	1908.70	1908.70	262.33	[41,45]
Incidence of complications in managed diabetes	Norm	0.165	0.251	0.165	0.165	0.165	0.139-0.192, 0.241-0.261	[42,44]
Incidence of complications in unmanaged diabetes	Norm	0.380	0.578	0.380	0.380	0.380	0.319-0.441, 0.555-0.601	[42,44]
Time (year) to incidence of complications	Norm	4.62	3.85	4.62	4.62	4.62	3.6-6.2, 3.0-5.2	Assumption based on [43]
TB treatment outcomes*								
Success (non diabetes)	Norm	0.788	0.796	0.809	0.724	0.788	0.050	Main study
loss-to-follow-up (non diabetes)	Norm	0.160	0.127	0.167	0.103	0.162	0.020	Main study
Failure (non diabetes)	Norm	0.010	0.012	-	0.086	0.009	0.005	Main study
Success (managed diabetes)	Norm	0.839	0.829	0.826	0.750	0.831	0.050	Main study
loss-to-follow-up (managed diabetes)	Norm	0.149	0.158	0.174	0.250	0.169	0.020	Main study
Failure (managed diabetes)	Norm	-	-	-	-	-	-	Main study
Success (unmanaged diabetes)	Norm	0.787	0.803	0.745	0.600	0.762	0.050	Main study
loss-to-follow-up (unmanaged diabetes)	Norm	0.135	0.121	0.164	0.133	0.159	0.020	Main study

Failure (unmanaged diabetes)	Norm	0.034	0.030	0.036	0.133	0.032	0.010	Main study
Transitions								Main study
% with known diabetes at TB diagnosis	Norm	0.106	0.127	0.156	0.182	0.103	0.010	Main study
% with managed diabetes among known diabetes	Norm	0.849	0.825	0.852	0.850	0.833	0.050	Main study
% diabetes not suspected with RPG	Norm	0.451	0.459	0.526	0.455	0.518	0.020	Main study
% no diabetes confirmed with FBS	Norm	0.610	0.377	0.571	0.600	0.600	0.030	Main study
% initiating diabetes management after FBS	Norm	0.877	0.833	0.878	0.600	0.860	0.050	Main study
Life expectancy (years)								
Post TB	Norm	26.8	21.4	26.8	26.8	26.8	24.2-29.4	Assumption using [25-29]
Active TB	Norm	10.1	8.1	10.1	5.9	10.1	8.1-12.1	Assumption using [25-29]
Post TB with managed diabetes	Norm	16.8	13.4	16.8	24.8	16.8	13.5-20.1	Assumption using [25-29]
Active TB with managed diabetes	Norm	6.8	5.4	6.8	3.9	6.8	5.5-8.1	Assumption using [25-29]
Post TB with unmanaged diabetes	Norm	21.8	17.4	21.8	19.8	21.8	17.5-26.1	Assumption using [25-29]
Active TB with unmanaged diabetes	Norm	7.6	6.1	7.6	2.9	7.6	6.1-9.1	Assumption using [25-29]

*probability of death as a TB treatment outcome = 1-(success + Loss-to-follow-up + failure)

BMI: body mass index, DALY: disability adjusted life years, FBS: fasting blood glucose, RPG: random plasma glucose, USD: US dollars

5.6 Results

Deterministic model results

In the baseline scenario (providing TB treatment without diabetes screening and diagnosis), the total lifetime cost of an episode of TB and diabetes per person was USD 928 from the provider perspective and USD 1885 from the societal perspective, with cumulative DALYs per person of 9.63. In the intervention scenario, where diabetes testing was provided for 90% of people with diabetes status unknown at TB diagnosis, the total lifetime cost per person was USD 781 from the provider perspective and USD 1698 from the societal perspective, with cumulative DALYs per person of 9.10 (**Table 24**), resulting in savings of USD 147 per person from the provider perspective and USD 187 per person from the societal perspective, showing that the intervention is cost saving from both perspectives. The estimated incremental number of TB treatment success and newly diagnosed diabetes cases were 786 and 14,927 per 100,000 respectively in the intervention scenario.

Table 24. Expected costs, days of life gained, and incremental cost effectiveness providing diabetes care for people with TB

Scenario	Incremental number of TB treatment success per 100 000	Incremental number of TB-diabetes with diabetes management per 100 000	Average costs per person (2022 USD)	Lifetime DALY per person (2022 USD)	DALY averted per person	Incremental cost effective ratio	Cost saving per person (2022 USD)
Provider perspective							
Baseline scenario (TB treatment without diabetes screening/diagnosis)			928	9.63			
Provide diabetes care for 90% of people with TB (diabetes status unknown)	786	14,927	781	9.10	0.53	Cost saving	147
Societal perspective							
Baseline scenario (TB treatment without diabetes screening/diagnosis)			1,885	9.63			
Provide diabetes care for 90% of people with TB (diabetes status unknown)	786	14,927	1,698	9.10	0.53	Cost saving	187

DALY: disability adjusted life years, ICER: incremental cost effectiveness ratio, USD: US dollars

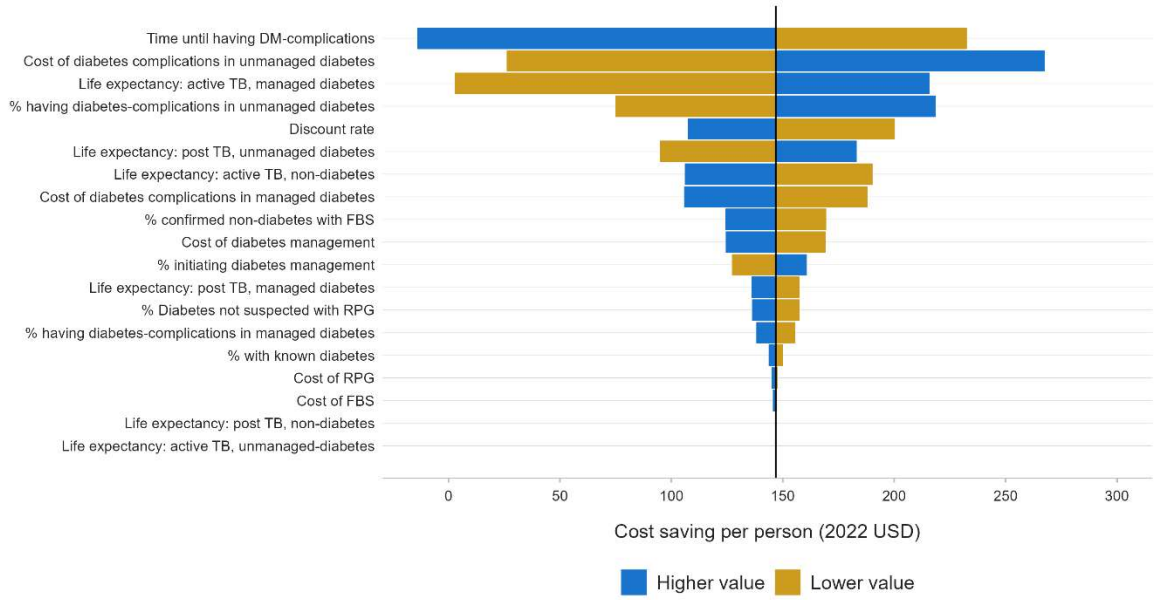
One-way sensitivity analysis

Variables that influenced the cost-effectiveness results using a one-way sensitivity analysis were the life expectancy of the population without diabetes, the cost of routine diabetes management, and discount rate for costs (**Figure 17a**). The extent of saving was highly sensitive to the cost of diabetes

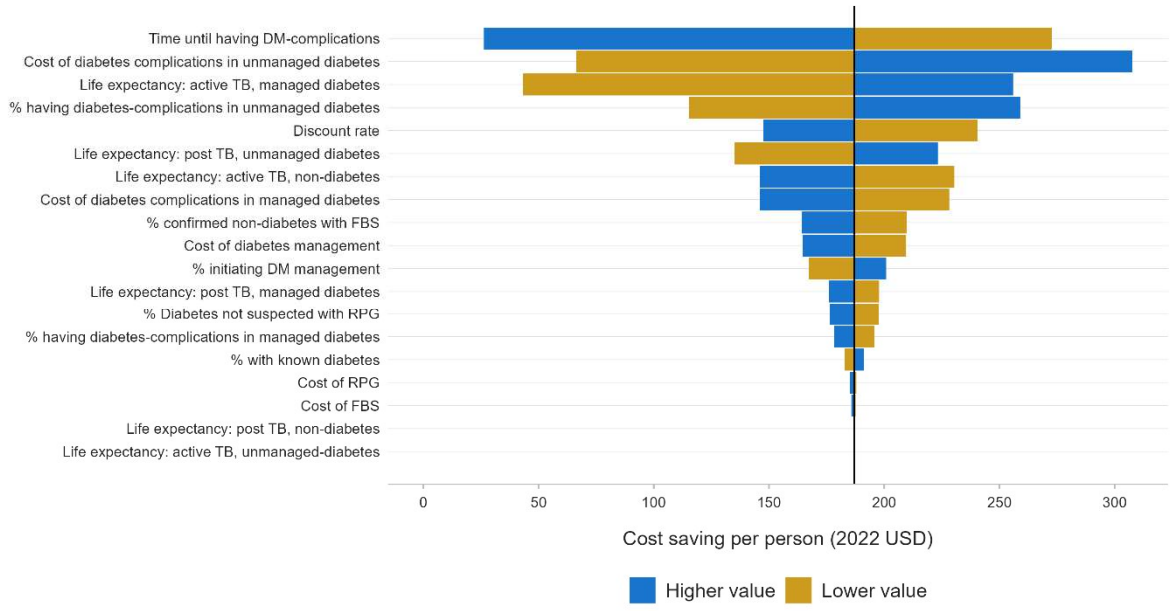
complications in the population with unmanaged diabetes (saving from USD 26 to USD 267 per person), time (in years) to develop diabetes-related complications (saving USD -USD 13 to USD 232 per person), and the proportion with diabetes-related complications in the population with unmanaged diabetes (saving from USD 75 to USD 219 per person). The results were also sensitive to life expectancy of the population with active TB treatment with managed diabetes (saving USD 43 to USD 256 per person) (**Figure 17a**). Consistent and more cost saving results were obtained from the societal perspective (**Figure 17b**).

Figure 17. One-way sensitivity analysis on cost-effectiveness of providing diabetes services for people with TB

(a) Provider perspective



(b) Societal perspective



DALY: disability adjusted life years, FBS: fasting blood glucose, ICER: incremental cost effectiveness ratio, RG: random plasma glucose, USD: US dollars

Scenario analysis

We conducted scenario analysis to assess the difference in the cost-effectiveness of the intervention in various target populations with TB. DALYs averted per person ranged from 0.413 (drug-resistant TB) to 0.679 (aged >45 years) (**Table 25**). Results of incremental costs per person showed the intervention being cost saving in any target population: saving USD 79 (drug-resistant TB) to USD 317 (aged >45 years) per person from the provider perspective, and saving USD 119 (drug-resistant TB) to USD 364 (aged >45 years) per person from the societal perspective. The most cost-effective approach was to provide the intervention to people aged >45 years, saving USD 317 per DALY averted from the provider perspective and USD 364 per DALY averted from the societal perspective, followed by people with BMI >18.5 kg/m^2 (**Table 25**).

Table 25. Incremental costs and DALYs averted per person and incremental cost effectiveness ratio

Target population with TB	Incremental number of TB treatment success per 100 000	Incremental number of TB-diabetes with diabetes management per 100 000	DALYs averted per person	Incremental cost-effective ratio	Cost saving per person (2022 USD)
Provider perspective					
Aged ≥18 years	786	14,927	0.532	Cost saving	147
Aged >45 years	573	21,760	0.679	Cost saving	317
BMI >18.5	1,099	13,562	0.485	Cost saving	153
Drug-resistant TB	1,444	9,629	0.413	Cost saving	79
Male aged ≥18 years	924	13,386	0.478	Cost saving	145
Societal perspective					
Aged ≥18 years	786	14,927	0.532	Cost saving	187
Aged >45 years	573	21,760	0.679	Cost saving	364
BMI >18.5	1,099	13,562	0.485	Cost saving	212
Drug-resistant TB	1,444	9,629	0.413	Cost saving	119
Male aged ≥18 years	924	13,386	0.478	Cost saving	183

DALY: disability adjusted life years

Probabilistic sensitivity analysis

The probabilistic sensitivity analysis showed less uncertainty in the outcome of the cost-effectiveness in target populations from the provider perspective (**Figure 18a**). The intervention was cost saving in all target populations, and the probability of being cost saving was 78.6% in the target population of people aged ≥18 years. The probability was the similar from the societal perspective: 84.2% in people aged ≥18 years(**Figure 18b**).

At a willingness-to-pay per DALY averted of 50% of GDP per capita (2022 GDP per capita was USD 3498), 99.7% of the simulations of the ICER for the target population of people aged ≥18 years were

cost-effective (**Figure 19a**). Even with a lower WTP per DALY averted (7.3% of GDP per capita which reflects the country-specific threshold), the probability of intervention being cost saving remained at 97.5% in the target populations of people aged ≥18 years. The probability was highest in people with BMI >18.5 kg/m^2 and people aged >45 years. The results were consistent from the societal perspective (**Figure 19b**).

Figure 18. Results of probabilistic sensitivity analysis

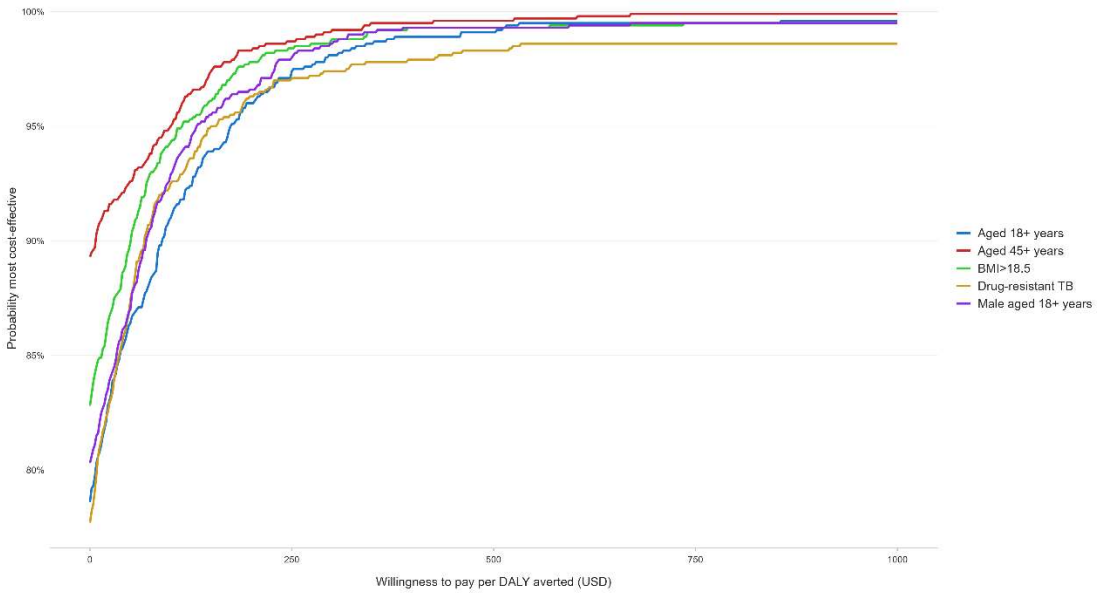
(a) Provider perspective

(b) Societal perspective

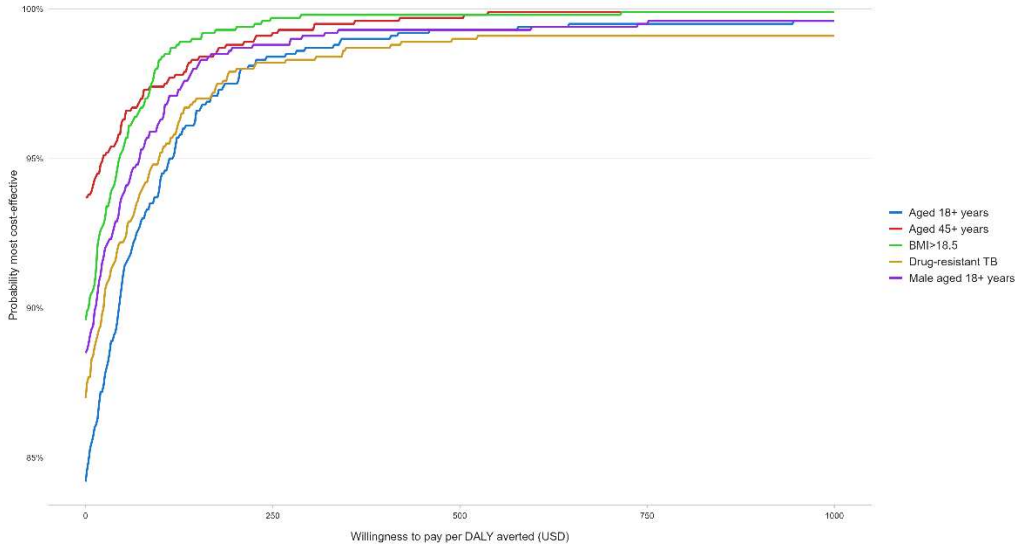
BMI: body mass index, DALY: disability adjusted life years

Figure 19. Cost-effectiveness acceptability curves for providing diabetes services for people with TB

(a) Provider perspective



(b) Societal perspective



BMI: body mass index, DALY: disability adjusted life years, USD: US dollars

5.7 Discussion

Key findings

We estimated the incremental cost-effectiveness of implementing diabetes screening and diagnosis for people with TB at their TB diagnosis and subsequent diabetes management in the Philippines, in five different target populations that were assessed in this study. Our study found that the intervention was highly likely to be cost-saving in all target populations. Targeting the population of people aged >45 years, the intervention saved USD 147 per person from the provider perspective and USD 187 per person from the societal perspective.

Interpretation of the findings and generalizing results to other settings

While our study showed that the intervention was cost-saving with considerations of various variables in the one-way sensitivity analysis, the results were highly sensitive to the cost of routine diabetes management and diabetes-related complications. In our analysis, when the cost of diabetes-related complications in managed and unmanaged diabetes varied; in the target population of people aged ≥18 years, savings ranged from USD 105 to USD 188 per person and from USD 26 to USD 268 per person, respectively, from the provider perspective. The costs of diabetes-related complications were extracted from a study that assessed diabetes medical costs in two central hospitals in Metro Manila, the area of the capital city, in the Philippines [41]. The cost estimates of the complications in two hospitals varied considerably, that is USD 1909 vs USD 3272 for those with hospitalizations and USD 395 vs USD 351 for those without hospitalizations. Although we used the lower estimate for diabetes-related complications (USD 1909 was used for complications in unmanaged diabetes and USD 351 in managed diabetes), the cost estimates could look different depending on study settings. Since the costs of diabetes complications had a significant impact on cost saving and are uncertain, a further assessment would be required to estimate national budgetary implications.

The cost saving results were affected also by the cost of routine diabetes management, saving from USD 124 to USD 169 from the provider perspective. The cost of diabetes management used in our analysis was USD 10.28 per month (diabetes medicines and prescriptions, monitoring of blood sugar level) which was extracted from a recent study that assessed health system costs of providing diabetes outpatient care for people with TB in the Philippines [22]. In that recent costing study, the estimated mean monthly costs of diabetes management ranged from USD 8.95 (diabetes medicines and prescriptions only) to USD 12.26 (diabetes medicines, prescriptions, monitoring of blood sugar level and consultation visits) per month [22]. Therefore, the cost-effectiveness of the intervention would be affected by the design of the diabetes interventions integrated with TB services. Furthermore, in

our analysis, the extracted costs for diabetes management were marked up since the recent cost study did not include the overhead and start-up costs for providing diabetes outpatient services for people with TB [22]. The study was not able to collect overhead and start-up costs due to COVID-19 disruptions. Since diabetes outpatient services are already being implemented in public health facilities in which TB and diabetes services are provided separately, only costs for training TB staff to provide diabetes outpatient services might have been missed in the cost estimates. The uncertainty of the overhead costs of diabetes services may also affect the cost-effectiveness of the intervention. Similarly, in other country settings, the cost-effectiveness of the intervention could be affected by the prevalence of diabetes in people with TB, costs of diabetes complications and monthly costs of diabetes management.

Strengths and limitation of this study

One of the strengths of this study is that this is the first study to assess the cost-effectiveness of providing diabetes care for people with TB in a LMIC. A previously published study assessed the cost-effectiveness of diabetes screening in household contacts of people with TB in Myanmar, and showed that providing diabetes screening for TB household contacts was cost-effective [48]. Our findings add new evidence to the cost-effectiveness of integrating diabetes services into TB services.

This analysis was conducted both from the provider perspective and from the societal perspective, and our results showed that the intervention would be cost saving from both perspectives. To analyse the cost effectiveness of the intervention from the societal perspective, in addition to the latest evidence of health system costs of providing diabetes outpatient services [22], the difference in patient costs between people with TB-diabetes comorbidity and TB-only was taken into account in our analysis [33]. The study revealed that people with TB-diabetes comorbidity incurred higher costs due to more frequent visits to health facilities. Therefore, providing integrated diabetes services for people with TB may reduce the costs incurred from the patient or household perspective and save the households from falling further into poverty caused by the dual financial burden of TB and diabetes.

This study also has several limitations. A lack of access to diabetes diagnosis, treatment and health facilities can result in the development of earlier and more severe complications (e.g. blindness due to retinopathy or cataracts, kidney disease, coronary heart disease, cerebrovascular disease or stroke) and those complications can lead to premature disability and death [49]. Also, diabetes increases the risk of developing active TB by 2.3 to 4.3 times [3,5] and increases the risk of TB relapse with a relative risk of 3.9 [4,50,51]. However, given that the data were not available for the Philippines, the long-term

health outcomes and bidirectional relationship between TB and diabetes were not considered in our analysis. While there are several suggestions and discussions around disease models that incorporate health transitions for TB and diabetes, they are not fully understood or developed [30,31,51]. Therefore, our analysis only included a decision tree to provide diabetes screening and confirmatory testing for people with TB at TB diagnosis. A conceptual framework and model that incorporates TB-diabetes interactions were recently developed [31]. With the model and data of long-term health outcomes and interactions of TB and diabetes (e.g. reduction in incidence of recurrent TB and/or in occurrence of diabetes-related severe complications), the probability of providing diabetes services for people with TB being cost-effective would be further improved. Second, our study assumed the use of RPG for routine diabetes monitoring and applied the UK-population based incidence of diabetes complications [22,44]. However, these assumptions may have a significant impact on the probability of the intervention being cost-effective or cost-saving. For further improvement of these assumptions, a population-based long-term study in the Philippines is required. Third, our analysis found that the intervention could be cost saving in all the target populations in this study including people with drug-resistant TB since the benefit of integrated service exceeded the incremental costs of providing diabetes screening, diagnosis and management for people with TB. Despite all evidence generated around integrated care, the operational feasibility and financial affordability of the intervention in the target populations needs to be assessed in the context of the Philippines. Fourth, a DALY weight for TB comorbid with diabetes was not available in the Global Burden of Disease study. Therefore this study used a simple sum of DALYs for TB and for diabetes, which may have resulted in overestimating DALYs averted for TB comorbid with diabetes, while the impact of not adjusting disability weights for comorbidities were expected to be minimal [38].

Policy implications in the Philippines

In the Philippines, the national guideline to integrate the screening and management of TB and diabetes was published in 2022 [52]. This was followed by the national strategic plans on TB control for 2020-2023 that was published in 2020 and included a target to achieve screening for diabetes in 90% of TB cases by 2022 [16]. Even though the integration of TB and diabetes management was introduced in the policies at the national level, the policies have not yet been implemented at the community or primary care levels [22]. A recent WHO policy brief identified a wide range of country specific challenges, which served as barriers for implementing the policies, including poor coordination between the two disease programmes, lack of involvement of local stakeholders in policy development, and lack of sufficient training for healthcare workers to provide health care services to detect people with TB-diabetes comorbidity [16,53]. Our analysis found that the intervention was cost

saving, and a high probability of being cost-effective was observed in various target populations, when a range of values for the willingness-to-pay threshold was applied, even at a low willingness-to-pay threshold (7.3% of GDP per capita). The probability of being cost saving was highest in the target population of people with BMI >18.5kg/m^2 and in people aged >45 years. This was consistent with previous findings of cost-effectiveness of early screening and diagnosis of diabetes in populations with a high prevalence of diabetes and high-risk populations for diabetes, which contribute to the reduction of lifetime costs and improvement of health outcomes [10-12,54]. Therefore, our study findings support extending the high-risk population-based approach to TB, and providing the intervention to people with BMI >18.5 kg/m^2 or those aged >45 years could be an entry point to starting implementation of the national policy of integrating TB and diabetes management at the local level in countries with a large number of the estimated TB incidence attributable to TB, including the Philippines, depending on the willingness-to-pay of the intervention.

5.8 Conclusion

Our findings indicated that providing diabetes care for people with TB at their TB diagnosis is likely to be cost-saving. The Philippines national TB programme should consider the implementation and scale-up of the intervention. Further studies assessing the nationally representative cost estimates of diabetes complications will be required as these costs had a significant impact on the cost-effectiveness of the intervention. Additionally, the operational feasibility of implementing and expanding the intervention needs to be assessed in the context of the Philippines.

5.9 Additional information

Figure 20. Results of probabilistic sensitivity analysis using costs of HbA1c instead of RPG for routine diabetes monitoring

(a) Provider perspective

(b) Societal perspective

5.10 Reference

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CHAPTER 6. DISCUSSION

6.1 Main findings and remaining research gaps

6.1.1 Summary findings

This PhD thesis contributes to the evidence around the limitations of surveys of costs incurred by people with TB and their households using the WHO recommended cross-sectional design, making suggestions for the optimal approaches for sampling and interpolating cross-sectional data to estimate these costs and the proportion of TB-affected households facing catastrophic costs due to TB. This PhD also presented evidence on the financial burden incurred by people with TB and diabetes, the costs of providing diabetes outpatient services to people with TB from the health system perspective and the cost-effectiveness of an intervention to identify and manage comorbid diabetes from the societal perspective (**Table 26**).

This chapter recaps the four research gaps that were addressed by this PhD project and summarizes how the research activities were conducted to contribute to the research areas. Also, this final chapter discusses the policy implications from the results of this PhD project and areas for future research.

Table 26. Research gaps addressed by this PhD project, linked to objectives, methods and key findings

#	Research gaps	Objectives	Methods	Key findings
1	Lack of evidence on financial burden incurred by TB and diabetes.	To estimate direct costs and income loss associated with TB and diabetes care seeking, diagnosis, and treatment using longitudinal data collection.	Longitudinal study assessing TB and diabetes patient costs, with four data collection timepoints over the TB episode (at TB diagnosis, the end of TB intensive phase, the mid- and end-points of TB continuation phase) in the Philippines	People with TB and diabetes had more frequent visits for TB treatment (120 vs 87 visits, p=0.054) as well as more total visits for TB and diabetes treatment (129 vs 88 visits, p=0.010) compared to those with TB-only. There was no significant difference in the proportion of TB-affected households facing catastrophic costs between those with TB and diabetes (76.3%) and those with TB-only (68.7%, p=0.691).
2	Lack of evidence on the degree of effect of assumptions used in the WHO recommended methods on estimating TB patient costs and	To identify the potential biases of the WHO recommended cross-sectional study design for TB catastrophic cost estimates and to	Using data from the longitudinal study assessing TB and diabetes patient costs: 1) compare the results of total TB patient costs and the catastrophic costs between the	With the longitudinal study design, the catastrophic cost estimate for TB-affected households was 69%. The catastrophic cost estimates with the simulated cross-sectional design were affected by the

#	Research gaps	Objectives	Methods	Key findings
	the catastrophic cost estimates.	explore optimal approaches for sampling and analysing cross-sectional cost data for the catastrophic cost estimates.	longitudinal study design and the simulated cross-sectional study designs with different sampling proportions from TB intensive and continuation phases 2) reassessing the impact of indirect costs before TB diagnosis on the total TB patient costs and the catastrophic cost estimates	reduction and recovery in household income during the episode of TB care and ranged from 40-55%. The mean total costs incurred by TB-affected households was USD 932, and of these costs 24% (USD 219) was indirect costs borne during care seeking before TB diagnosis.
3	Limited evidence on costs of providing diabetes services for people with TB.	To assess the provider costs of diagnosing and managing diabetes for people with TB within TB services.	Cross-sectional micro-costing study assessing diabetes outpatient services provided for people with TB at their TB diagnosis	From the provider perspective, the cost per diabetes case detected using different algorithms varied from USD 17.43 to USD 80.81. The monthly cost per people with diabetes was estimated between USD 8.95 and USD 12.36.
4	Lack of evidence on the cost-effectiveness of providing diabetes screening and diagnosis for people newly diagnosed with TB.	To assess the cost-effectiveness of integrating diabetes services within the TB programme in the Philippines.	Using data on patient costs for TB and diabetes, provider costs for diabetes outpatient services within the TB programme, assessing the cost-effectiveness of providing diabetes screening and diagnosis from the provider and societal perspectives.	Providing diabetes diagnosis and management for people diagnosed with TB would be cost saving from the societal perspective, saving USD 147 per DALY averted per person from the provider perspective and USD 187 per DALY averted per person from the societal perspective in the target population of people aged ≥18 years. At a willingness-to-pay threshold per DALY of 50% of GDP per capita, the probability of the intervention being cost-effective was 99% in the target populations of people aged ≥18 years, from the provider perspective and the societal perspective respectively.

6.1.2 Costs incurred by people with co-morbid tuberculosis and diabetes and their households in the Philippines

Chapter 2 addressed research gap #1 and PhD objective #1.

This research was the first to adapt the WHO recommended method for surveys of costs incurred by people with TB and their households to a longitudinal study design and assess patient costs of multiple diseases i.e. concurrent TB and diabetes. The research provided a longitudinal assessment of costs incurred by people with concurrent TB and diabetes and their households, by comparing health service utilization, detailing changes in costs and household income over the TB episode and estimating catastrophic cost between people with concurrent TB and diabetes vs those with TB-only.

This research found that people with concurrent TB and diabetes, compared to people with TB-only, had more frequent visits for TB treatment (TB-diabetes: 120.0, TB-only: 86.9, p=0.054). For TB services, while people with TB and diabetes incurred higher costs, there was no significant difference in TB costs between people with TB and diabetes and TB only (TB-diabetes: USD 1,053, TB only: USD 914, p=0.464). Unsurprisingly, the proportion of TB-affected households spending more than 20% of their annual household income on TB-related services was 69.0% (95%CI: 64.7-73.3%), and there was no statistically significant difference between people with TB-diabetes (68.7%, 95%CI: 64.0-73.3%) and TB-only (71.2%, 95%CI: 59.3-83.1%), with a p-value of 0.691. We also assessed the difference in the costs between people with TB and managed diabetes and those with TB and unmanaged diabetes. Our study was not powered enough to detect the difference in the total TB and diabetes costs (TB and managed-diabetes: USD 1363, TB and unmanaged-diabetes: USD 841, p=0.078).

This research also found the changes in household income over the TB episode. Overall, the mean reported monthly household income before having TB was USD 183 (95%CI: 155-210), and it declined during care seeking until TB diagnosis (USD 80, 95%CI: 68-92) and at the end of the intensive phase of TB treatment (USD 9, 95%CI: 6-11). Then, it increased towards the middle of the continuation phase (USD 195, 95%CI: 164-227) and was sustained to the end of that phase (USD 197, 95%CI: 165-228).

Our study was not able to detect a significant difference in patient costs between people with TB and diabetes vs those with TB-only. However, this study found that people with TB and diabetes had on average 40 extra visits to health facilities and/or treatment partners for DOT compared with those with TB only. Therefore, this finding suggested that the integrated care for TB and diabetes may result in the reduction in visits to healthcare providers and related costs (e.g. travel and food costs in direct

non-medical costs). More importantly, the study highlighted the importance of further assessment of TB and diabetes patient costs in people with diabetes to capture the financial burden of diabetes related complications. This study also highlighted the necessity to conduct a study assessing costs due to TB-related sequelae and/or prolonged social consequences after TB treatment.

6.1.3 Comparing disease specific catastrophic cost estimates using longitudinal and cross-sectional designs: the example of tuberculosis

Chapter 3 addressed research gap #2 and PhD objective #2.

This study was conducted using the longitudinal patient cost data incurred by people with TB and their households that were collected in the study conducted for PhD objective 1. The study highlighted the potential bias of estimating disease-specific catastrophic costs using the WHO recommended cross-sectional study design. It also provided the impact of indirect costs in pre-TB diagnosis on the total cost and catastrophic cost estimates.

The catastrophic cost estimates of TB were underestimated with the WHO recommended cross-sectional study design compared to the longitudinal design used in this PhD project. Furthermore, strikingly the catastrophic cost estimates were considerably affected by the sampling proportion of patients in the TB intensive and continuation phases, and the catastrophic cost estimates ranged from 40% with the sampling proportion of 20% from TB intensive phase and 80% of TB continuation phase to 55% with the proportion of 50% from TB intensive phase and continuation phase. This issue was caused by an inherit failure in the study design of the WHO recommended method that is not able to capture changes in household income over the course of the TB episode. In order to resolve this issue, this PhD project suggested that WHO guidelines for surveys of costs incurred by people with TB and their households should explore a more feasible option for a longitudinal design, e.g. having two data collection timepoints, once in each of the TB intensive and continuation phases. Even with the cross-sectional designs, WHO guidelines should have an official recommendation about the sampling proportions of patients in TB intensive and continuation phases since the absence of such a recommendation allowed countries to use a wide range of the sampling proportions i.e. 19%:81% in the Philippines up to 53%:47% in Solomon Islands, which might result in under- or over-estimation of TB catastrophic costs.

This study also highlighted an inconsistency between WHO recommendations and the implementation of surveys of costs incurred by people with TB and their households. This study found

that the indirect costs before TB diagnosis accounted for 24% of total costs incurred by TB affected households. This finding was consistent with a previous systematic review of TB patient cost studies showing that indirect costs before TB diagnosis accounted for 26% of total costs [1]. Although the WHO guidelines for surveys of costs incurred by people with TB and their households stated that indirect costs before TB diagnosis need to be included in the cost assessments, the majority of surveys of costs incurred by people with TB and their households so far conducted with the output approach for estimating indirect costs did not include the income loss before TB diagnosis.

The current WHO recommended method for surveys of costs incurred by people with TB and their households were designed with the consideration of operational feasibility and affordability to facilitate implementation. However, given the potential limitations and implications of estimating indirect costs using a cross-sectional design and the output approach in the catastrophic cost estimates shown in this study, the WHO Task Force for conducting surveys of costs incurred by people with TB and their households may need to revise and improve the survey recommendations and guidelines.

6.1.4 Health system cost of outpatient care for diabetes in people with tuberculosis; estimates from the Philippines

Chapter 4 addressed research gap #3 and PhD objective #3.

Given that patient costs for TB and diabetes were assessed in chapter 3 and a nationally representative study for assessing provider costs of TB (VALUE-TB) was conducted in the Philippines, this study provided the latest evidence on provider costs of diabetes outpatient services, which is the minimum required data to conduct a cost-effectiveness analysis for integrated diabetes services within TB services.

This study estimated the provider costs of diabetes outpatient services that can be integrated within TB services for people newly diagnosed with TB. With data collected from 60 health professionals providing diabetes services in 11 health care facilities, this study provided the unit cost of risk assessment, screening and confirmatory testing with FBS, RPG, HbA1c and OGTT, consultation and diabetes medications. Also, based on the results of the unit costs, this study calculated the cost per diabetes case detected in people with TB and the monthly costs of routine diabetes management per patient.

While there are many studies that assessed diabetes outpatient and inpatient provider costs, this study was the first to estimate the cost per diabetes case detected in people with TB in a LMIC, the Philippines. Therefore, the results of this study filled the evidence gap on costs of integrated diabetes services within TB services and will contribute to planning, budgeting and assessing its cost-effectiveness.

6.1.5 Cost-effectiveness of diabetes screening and diagnosis services for people with TB in the Philippines

Chapter 5 addressed research gap #4 and PhD objective #4.

Given that TB is a disease that is affected by socioeconomic status and related risk factors such as smoking, undernutrition, HIV infection and diabetes, there is a growing interest in managing TB and its comorbidities. WHO has been recently publishing the operational handbook on TB and comorbidities, and the handbook for managing concurrent TB and diabetes is under development. In the technical consultation, the cost-effectiveness of early detection and management of diabetes in people with TB was highlighted as an area with evidence gap.

This study assessed the cost-effectiveness of providing diabetes screening and confirmatory testing for 90% of people diagnosed with TB, based on a target included in the Philippines national strategic plan for TB control. This study showed that the intervention in the adult population was highly likely to be cost-effective, especially when provided for people with BMI >18.5 kg/m^2 and people aged >45 years. Also, this found that the results of the cost-effectiveness analysis were highly sensitive to the cost of diabetes routine management and diabetes-related complications.

Although a target to achieve screening diabetes in 90% of TB cases by 2022 was included in the Philippines TB national strategic plan, the policy has not been implemented at community nor at primary care level in the Philippines. The findings of this study will inform policy makers and can accelerate the implementation of the policy to provide diabetes screening for people with TB, and also fill the evidence gap highlighted in the technical consultation meeting of WHO handbook for managing TB and comorbidities.

6.1.6 Remaining research gaps

While this PhD project addressed several evidence gaps, the studies of this PhD project had a number of limitations due to practical and budget restrictions.

Chapter 2 presented the results of the first assessment of the costs incurred by people with TB and diabetes and their households. However, the study was unable to capture the financial burden of diabetes related complications because of its sample size and also due to the scope of the cost assessment which was designed to capture costs incurred during an episode of TB. Therefore, future studies assessing costs of TB and diabetes incurred by people with diabetes should capture the cost estimation of diabetes related complications among people with TB and diabetes. Also, due to the scope of the cost assessment, any financial consequences of TB were not included, and therefore it highlighted the necessity to conduct a study assessing costs due to TB-related sequelae and/or prolonged social consequences after TB treatment.

Chapter 3 showed the cross-sectional study design may in general underestimate the catastrophic cost estimates compared to the longitudinal study design, and the sampling proportions of the TB intensive and continuation phases may have influenced the results of catastrophic cost estimates. However, it is not entirely clear if this finding can be applied to other country settings, and therefore, further assessment would be required to compare the results of catastrophic cost estimates between the cross-sectional and longitudinal study designs. Also, in this PhD project, the underestimation of the catastrophic cost estimates was caused by the use of cost extrapolations. Therefore, in addition to the current method, WHO may need to explore implementing an alternative option e.g. enrolling survey participants only from those in the TB continuation phase and collect cost and income data at all three time points (pre-diagnosis, in the TB intensive phase and in the TB continuation phase) so that the surveys do not rely on arbitral cost extrapolation methods. Since this suggestion may cause issues of recall bias (for people in the TB continuation phase, they need to recall their costs and income at least 3-4 months ago) and also of a longer interview time due to additional data collection items (which could be a burden for survey participants), operational feasibility and effect of recall bias needs to be carefully investigated by e.g. comparing the interview time and results of cost estimates between the currently recommended method with cost extrapolations and a suggest method without cost extrapolations.

Chapter 4 presented the results of provider costs of diabetes outpatient services for people with TB. To have a nationally representative value of the provider costs, nationally representative study sites across several regions in the Philippines (as was done for of the VALUE-TB project) is required. The cost assessment should also have included overhead costs e.g. start-up, training costs and also other recurrent overhead costs. This was not possible in this PhD project due to the budget constraint and

the restrictions of data collection during the COVID-19 pandemic. A further assessment of the provider costs with a larger and nationally representative sample size will be necessary to fill these evidence gaps.

Chapter 5 showed the cost saving results of the intervention providing diabetes screening and diagnosis for people diagnosed with TB, from the societal perspective. Due to poor data availability and a lack of models for comorbid TB and diabetes, the long-term health outcomes and bidirectional relationship between TB and diabetes over a lifetime were not considered in this analysis. Also, while there are several suggestions and discussions, disease models that incorporate health transitions for TB and diabetes are not fully understood and developed [2-4]. This PhD project only included a decision tree to provide diabetes screening and confirmatory testing for people with TB at TB diagnosis. With the model and data of long-term health outcomes and lifetime interactions of TB and diabetes (e.g. reduction in incidence of recurrent TB and/or in occurrence of diabetes-related severe complications), the probability of providing diabetes services for people with TB being cost-effective or saving could be further improved.

6.2 Methods recommendations

6.2.1 Measurement of costs incurred by people with TB and their households

The implementation of the surveys of costs incurred by people with TB and their households started in 2015 to capture the situation of TB-associated household costs and monitor the progress toward achieving a target "to ensure that no family is burdened with catastrophic expenses due to TB by 2020" in the End TB Strategy [5,6]. The surveys have been implemented with the WHO recommended cross-sectional design.

Before starting this PhD project, there was limited evidence on the results of catastrophic costs due to TB with the longitudinal design and the comparison between the WHO cross-sectional design and the longitudinal design. At the time of writing this PhD thesis, several studies assessing TB patient costs and catastrophic costs due to TB have been implemented in India, Nepal and Viet Nam as in the Philippines [7-12]. These studies provided various suggestions to improve the WHO recommended methods such as methods to capture diagnostic journey to estimate pre-diagnosis costs, to capture changes in costs and social consequences during TB treatment and to apply multiple approaches to estimate indirect costs [7,11,13].

The first WHO handbook for surveys of costs incurred by people with TB and their households was published in 2017 [5,6]. Since the WHO guidance for other TB surveys periodically implemented in countries such as TB prevalence surveys and drug resistance surveys has been updated every 5-10 years, the time of writing this PhD thesis (2024) is the ideal timing to release the second edition of the survey handbook, and it is in development [14].

The study of longitudinal TB (and diabetes) patient costs in this PhD project suggested:

1. Redesigning surveys of costs incurred by people with TB and their households for more robust estimates of indirect costs.

   This project found that with the WHO recommended cross-sectional design, the changes in household income cannot be captured, and therefore suggested considering a feasible longitudinal data collection in surveys of costs incurred by people with TB and their households, such as two data collection timepoints: once in each of the intensive and continuation phases. However, given that the current WHO recommendations of cross-sectional study design and the use of cost extrapolation methods were developed based on operational feasibility, pilot testing must be conducted to assess the operational feasibility e.g. additional duration of data collection period and additional funding required. In 2023, preparations for a repeat national survey have

been started in several countries, and therefore, the pilot testing with a revised data collection tool that can incorporate both extrapolation methods and multiple data collection methods may need to be conducted.

2. Providing a recommendation for the sampling proportion of survey participants from the TB intensive and continuation phases

   The absence of the WHO recommendation for the sampling proportion from each treatment phase meant that countries adopted arbitrary sampling proportions from the intensive and continuation phases, which may have resulted in over- or under-estimation of catastrophic costs due to TB. Therefore, in the second edition of the WHO guidance for the surveys, the recommendation for applying an ideal sampling balance at survey design stage would need to be added. Also at the analysis stage, when over/under sampling from each phase happened in the data collection, weight adjustment should be applied as is recommended for adjusting for the effect of cluster size in the analysis.

3. Ensuring the inclusion of pre-diagnosis indirect costs in total cost estimates

   This project found that indirect costs before TB diagnosis were not included in the total cost estimates in surveys of costs incurred by people with TB and their households that used the output approach for indirect costs. This means that the majority of the national surveys did not follow the WHO recommended methods and underestimated the pre-diagnosis costs. Therefore, the WHO guideline should ensure and re-highlight the necessity to include the indirect costs before TB diagnosis. One of reasons for the inconsistency was that the generic questionnaire and Stata/R scripts do not have a variable to estimate the pre-diagnosis indirect costs. As a part of the development of the second edition of the WHO guidance for the surveys, the generic questionnaire and analysis scripts must be revised accordingly.

While this PhD project was conducted in the Philippines, key findings and policy implications from the project can be applied to the global contexts and contribute to the formulation of revised WHO guidance for national surveys of costs incurred by people with TB and their households.

6.2.2 Measurement of provider costs

In this PhD project, the costs of providing diabetes outpatient services for people with TB were assessed within the setting of the main cohort study which provided diabetes point-of-care HbA1c testing as a part of the observational study. Since there was no integrated care of TB and diabetes implemented in the study sites, it was not possible to assess the provider costs in the actual setting of

the intervention. In March 2024, the U.S. Agency for International Development (USAID) and the Philippines' Department of Health announced a new initiative named "the Support Wide-scale Interventions to Find TB (SWIF-TB)" which will support the expansion of ongoing interventions by local NGOs and private sector partners; this includes integrated TB screening with the testing of other lung diseases, HIV, and diabetes. For a better understanding and measurement of the provider costs of diabetes services "provided for people with TB", a further cost assessment within the actual intervention across different settings of integrating a range of diabetes related interventions with TB services would be required. This will also allow the reflection of overhead costs e.g. costs of start-up and training of diabetes services within TB services, which was listed as one of limitations of this PhD project.

For the cost assessment of TB interventions, *"Costing Guidelines for Tuberculosis Interventions"* was published in 2019 by WHO, and the standardised data collection and analytical methods were used in the VALUE-TB project which allowed the comparison of the TB provider costs across five countries [15,16]. In this PhD project, the WHO's *"Costing Guidelines for Tuberculosis Interventions"* was adapted for data collection, analysis and reporting to assess the cost of outpatient diabetes services. The standardization of data collection items e.g. diabetes medications, testing, consumables and equipment would be useful for future studies that assess the diabetes intervention costs within TB services across multiple countries.

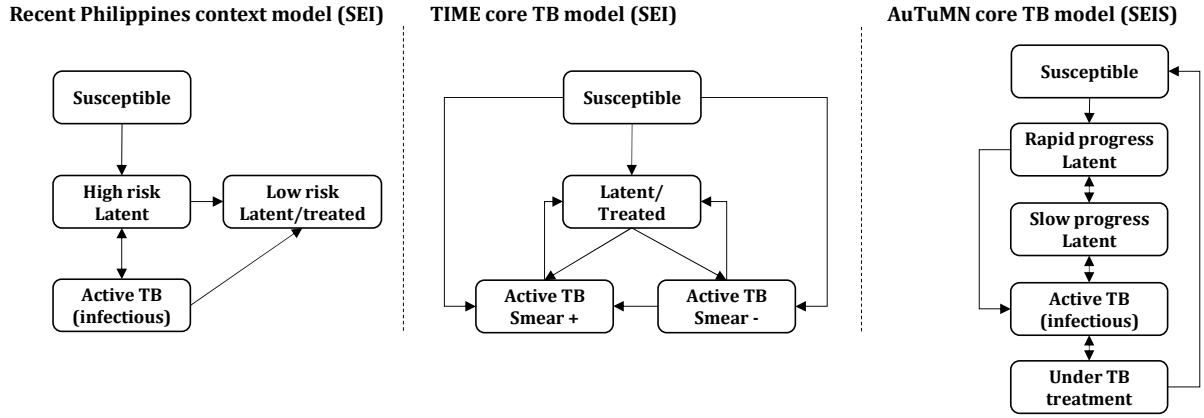
6.2.3 Measurement and data gaps to estimate TB and diabetes

As discussed in **section 6.1.6**, one of the limitations of the cost-effectiveness analysis in this PhD was that the analysis was not able to include the effect of lifetime interaction of TB and diabetes due to a lack of established models and associated data. A specific limitation is that my model only estimates the direct impact of TB, and to project and estimate budgets and population impact over time, indirect impact needs to be considered

For TB control, the importance of country-level TB modelling to support TB policy making is increasing, especially for the NSP development [17,18]. TIME Impact model and AuTuMN model capture indirect effects and have been used by NTPs to justify their resource mobilization for planned activities to achieve the End TB strategy [19,20]. The models allow users to estimate TB epidemiological impact of NTP activities (e.g. prevalence, incidence, notification, mortality) by population strata such as age groups, DS/DR-TB, TB history, HIV status, and CD4 cell count [19-21]. Various model structures have been used for TB modelling, and most structures consist of disease compartments of Susceptible (S),

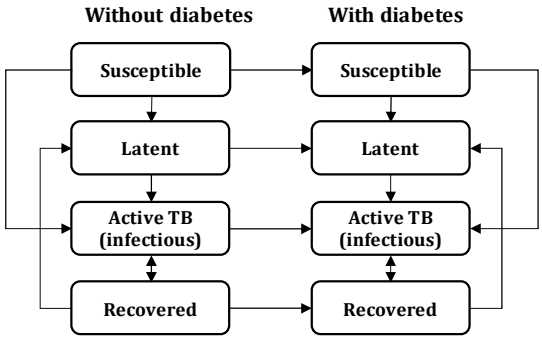
Latent/Pre-disease (E), Active TB/Infectious (I). A recent TB modelling study adapted to the Philippines context was published in 2018, and the study used a simple SEI model (**Figure 21**) to assess impact of different TB interventions on the disease burden [22].

Figure 21. Simplified structures of TB core model in previous modelling studies



For TB and diabetes interactions, four publications have been identified so far that have included TB transmission models with diabetes effects. All of them incorporated a transition from without diabetes to with diabetes within a simple SEIR (SEI + Recovered stage: R) structure for TB (**Figure 22**), whereas Awad et al used a more complex model of SEIR with two pre-infectious stages (rapid or slow disease progress) and treatment stage within infectious stage [4,23-25].

Figure 22. Simplified structure of TB model with diabetes effect in recent modelling studies

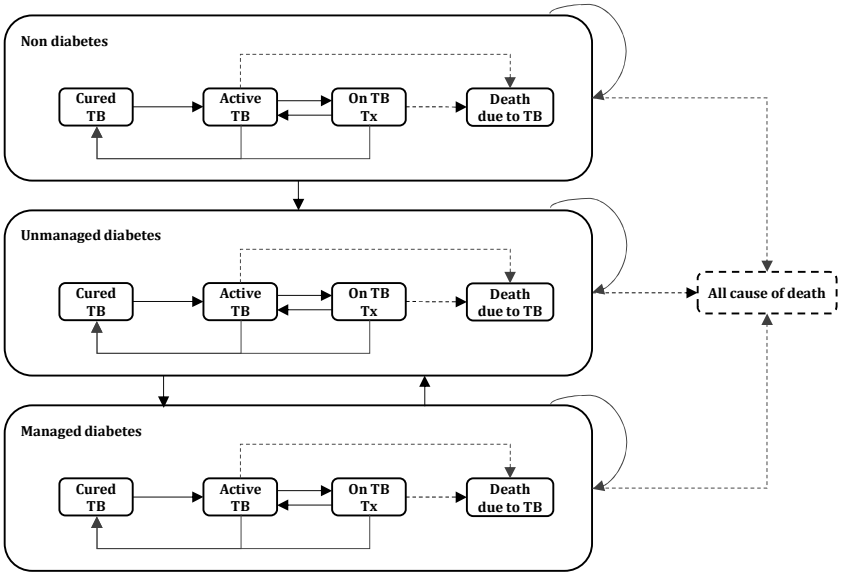


As section 2 of this PhD project presented, there was a difference in costs incurred by people with managed diabetes and those with unmanaged diabetes, and also, in a longer time horizon, the incidence of diabetes-related complications and its lifetime financial burden could be different [26-28]. Therefore, from the results and lessons learnt from this PhD, there should be at least three

categories of diabetes status in future joint models of TB and diabetes: non-diabetes, unmanaged diabetes and managed diabetes.

Further studies with a simple model such as **Figure 23**, with parameters of e.g. annual transitions from non-diabetes to unmanaged diabetes, between unmanaged and managed diabetes, and recurrence of TB, should be used to help fill the remaining evidence gaps for assessing the cost-effectiveness of providing diabetes services for people with TB (**Figure 23**). In addition, a population-based longitudinal study in the Philippines that assesses the incidence of diabetes, along with complications, initiation and dropout of diabetes treatment etc. may help provide the country-specific parameters of diabetes-related events over a lifetime, although it will require a huge amount of research funding. Alternatively, the parameters can be taken from population-based studies in other countries (mostly high-income countries) such as the UK Prospective Diabetes Study (UKPDS) [29,30].

Figure 23. Proposed simple structure of TB model with diabetes effect



6.3 Policy recommendations

6.3.1 Implementation of integrated management of TB and diabetes

The collaborative framework for TB and diabetes was first developed in 2011 by WHO, and the framework consisted of three pillars including bi-directional screening of TB in people with diabetes and that of diabetes in TB patients; plus monitoring and evaluation of collaborative diabetes and TB activities [31]. Even more than 10 years after the publication of the WHO framework, the policies for the collaborative management of TB and diabetes have not been implemented widescale [32,33].

The studies in this PhD project addressed three research gaps identified in the WHO guidance development group for management of TB and diabetes: financial burden incurred by people with TB and diabetes and their households, provider costs of providing diabetes outpatient services for people with TB, and cost-effectiveness of providing integrated diabetes outpatient services for people diagnosed with TB.

Before conducting this PhD project, there was no data available on patient costs incurred by people with TB and diabetes. The longitudinal study of TB and diabetes patient cost found that people with TB and diabetes had more visits to health facilities compared to those with TB. While the study was not able to present substantial differences in the incidence of catastrophic cost, it provided the evidence that people with TB and diabetes, particularly with managed diabetes, incurred higher household costs. At the time of writing this thesis, there was no evidence on health system costs of diabetes services for people with TB or its cost-effectiveness in a LMIC setting. The study in this PhD was the first that assessed costs of providing outpatient services for people with TB and showed the cost-effectiveness of integrating diabetes outpatient services for people diagnosed with TB.

Although future studies will be required to answer further questions such as feasibility and cost-effectiveness of different forms/levels of integration in different health system settings, the findings of this PhD project can contribute to the formulation of policy recommendations on the integration of TB and diabetes at the global level.

Also, in 2022, the Regional Committee for the WHO Western Pacific Region approved and endorsed the regional framework supporting integrated surveillance, analysis and strategic planning for both communicable and noncommunicable diseases [34]. Hence, the new evidence provided by this PhD project draw a particular interest in advancing integrated disease control, specifically TB and diabetes in the Western Pacific Region and in the Philippines.

6.3.2 Financial protection for people with TB and diabetes in the Philippines

In the Philippines, a national health insurance has been implemented since 1995 by the Philippines Health Insurance Corporation (PhilHealth). Health service coverage is different by the type of insurance membership. The national health insurance covers both TB and diabetes services; TB services such as the diagnosis, treatment, drugs, and consultations are covered by PhilHealth TB DOTS package, while diabetes services such as screening and diagnostic testing, and diabetes medications are covered by the primary care benefit package, but it is available only for indigent and sponsored members [28,35]. For diabetes-related complications such as coronary artery bypass or kidney transplants, another package called Z-package is required. This situation, with a lack of comprehensive coverage of diabetes services, could force people with diabetes to face a lifetime of heavy financial burden. This project found that people with TB and diabetes incurred USD 125 for diabetes during an episode of TB, without even having diabetes complications. Therefore, an expansion of the service coverage of Philhealth is required to reduce the cost incurred by people with diabetes.

In the Philippines, a TB specific social protection scheme, a TB enabler package, has been provided by NTP, but only for people with DR-TB. The national survey of cost incurred by people with TB and their households conducted in the Philippines concluded that the TB enabler package for DR-TB had a minimal impact on the TB catastrophic cost estimates, lowering the percentage in people with DR-TB from 89.7% to 76.6%, but for the overall percentage, only by 0.4 percentage points from 42.4% to 42.0%, due to the target population of the scheme being limited to people with DR-TB [35]. In this PhD project, the TB specific social support was received by approximately 13-15% of study participants during TB treatment, which corresponds to the proportion of participants with DR-TB.

In addition to a TB specific scheme, there is also a TB sensitive (non-TB specific) social protection scheme in the Philippines, which is a conditional cash transfer programme for households living under poverty, called "Pantawid Pamilyang Pilipino Program (4Ps)". The cash transfer programme has been implemented since 2007 by the Department of Social Welfare and Development (DSWD). In the national survey of cost incurred by people with TB and their households conducted in 2016-2017 in the Philippines, the proportion of survey participants who received the cash transfer was only 1.3% despite that 47% of TB-affected households were under the poverty line of USD 1.90 PPP according to the reported household income during TB treatment [35,36]. Based on the national survey results, in 2019, DSWD committed to strengthen and expand the cash transfer programme to people diagnosed with TB as a part of national “Comprehensive Tuberculosis Elimination Plan Act” [37]. An improvement

in the proportion of those who received the cash transfer programme was seen in this PhD project (conducted in 2018-2020) but remained low around 15-16%. This finding suggests that a policy change has been made at the national level in the Philippines to improve the social protection for people with TB, but implementation is still underway. The progress and impact of the enhanced social protection policy for TB must be assessed in the second national survey of costs incurred by people with TB in the Philippines.

6.4 Areas for future research

This PhD project provided the added value of longitudinal data collection of patient costs, and the results revealed potential biases in the estimation of catastrophic cost for TB. Also, this PhD project filled evidence gaps on concurrent TB and diabetes patient costs, diabetes provider costs for people diagnosed with TB and the cost-effectiveness of integrating diabetes outpatient services within TB programmes. However, not all of research gaps were addressed by this PhD project due to the methodological limitations.

6.4.1 TB and diabetes patient costs in people with diabetes

Delay in diabetes diagnosis and treatment may result in having diabetes-related complications such as blindness, kidney disease, coronary heart disease, cerebrovascular disease or stroke, and such complications can be a cause of having heavier financial burden in affected households [38,39]. Median time to have diabetes related complications varies from three years for chronic kidney disease to six years for lower extremity amputation with a wide range of 10 years cumulative incidence from 1.3% for lower extremity amputation to 33.3% for peripheral neuropathy [26,40]. In this PhD project, TB and diabetes patient costs were assessed in people diagnosed with TB, and the study was designed to assess the patient costs during a TB episode (~1 year). Therefore, due to the limited number of the study samples with diabetes (N=144), the study was not able to capture the costs for diabetes complications and hospitalizations during the course of TB treatment.

This limitation resulted in having a relatively low diabetes-related patient cost (USD 210 in those with managed diabetes), compared to previous patient cost studies that assessed diabetes related complications and inpatient costs e.g. USD 673 in Kenya or USD 1401 in China [41,42]. Hence, to understand patient costs, incidence of catastrophic costs, and impoverishment due to TB and diabetes, a study assessing patient costs of TB and diabetes incurred by people with diabetes over a longer time horizon is required.

Identification of undiagnosed TB among people living with diabetes was highlighted as a research area with evidence gap in the technical consultation meeting for WHO handbook for managing TB and diabetes, especially for cost-effectiveness of strategies to identify TB in people with diabetes and risk factors associated with prevalence of undiagnosed TB in people with diabetes. Therefore, conducting a study for screening and diagnosing TB in people with diabetes and assessing patient costs of TB and diabetes in people with diabetes will fill another evidence gap. This may provide cost assessment of diabetes-related complications in people with TB.

6.4.2 Post treatment economic impact of TB

In this PhD project, the post treatment costs were omitted from the scope of the study, nor did any of the surveys of costs incurred by people with TB and their households that followed WHO recommended methods include that component. Hence a study is required to develop a methodology to assess the costs incurred by TB-affected households and its impoverishment e.g. 12 months after the completion of TB treatment. The results will provide evidence on the financial impact of TB after the treatment and whether the post treatment costs should be included as part of TB patient costs [43].

One potential way to assess the long-term economic impact in TB-affected households is measuring costs incurred and social/financial consequences in households of people with TB before, during and after TB care. TB Sequel is an on-going study assessing the pathophysiologic and long-term economic impact of TB in four African countries, and the study assesses patient costs, household income, coping mechanism, and social consequences at baseline and months 2, 6, 12, and 24 during and after TB treatment both for DS- and DR-TB [43]. However, no studies assessing the long-term economic shock in TB-affected households have been conducted yet in Asian countries, and therefore more evidence on the association between during TB care and consequences after the treatment are required.

Total post treatment patient costs can be estimated and compared with total patient costs until the end of TB treatment to assess if TB patients incur substantial costs even after TB treatment. Total patient costs and catastrophic costs during TB treatment using the 20% threshold need to be first estimated using the data collected during the TB episode. Then it requires an assessment of the association between indicators during TB treatment (total patient costs and proportion of catastrophic costs) and consequences after TB treatment (income loss after treatment, employment status, social impacts such as continuous job loss and social exclusion). This approach would help to understand if the current globally recommended approach for patient and catastrophic costs for people with TB is predictive for non-recoverable long-term socio-economic shock in TB-affected households.

Table 27. Suggestion for data collection items for post treatment costs and household economic impact

Data category	Detail
Index patient costs	visit(s) for any follow-up for TB
	visit(s) for TB symptom recurrence and/or TB-related sequelae (COPD, Bronchiectasis etc)
	costs for nutritional supplement/additional food for TB symptom recurrence
Lost time	time lost for visits for any follow-up for TB
	time lost for visits for TB symptom recurrence
Employment status	at end of TB treatment
	at the time of interview (12 months after TB treatment)
Household income	monthly income at end of TB treatment
	monthly income at the time of interview (12 months after TB treatment)
Changes of household expenditure	Changes in household expenditure compared with that during TB treatment
Social impact after TB treatment	Experiences of social exclusion, continuous job loss, divorce/separation etc

Since this component will need additional data collection (**Table 27**) and the extension of the data collection period, additional funding will be required to implement this component as a cross-sectional study within national surveys of costs incurred by people with TB and their households. Therefore, before adding this component as a part of the survey, WHO may need to take several steps, e.g.:

1. Conduct a systematic review for available evidence on costs and financial/social consequences incurred after the completion of TB treatment, to assess the impact of post treatment financial hardship and its necessity to be included in the national surveys.
2. Conduct a pilot study for data collection and analysis as a part of ongoing national surveys of costs incurred by people with TB and their households, to investigate the operational feasibility of the data collection and the amount of survey budget required for implementing this component.

6.4.3 Economic evaluations incorporating health equity

Although in this PhD study, the cost-effectiveness of providing diabetes screening and confirmatory testing for people diagnosed with TB was assessed from the societal perspective (chapter 5) using the data of TB and diabetes patient and provider costs (chapter 3 and 4), the outcomes relied on health consequences, and health equity and non-health benefit of the intervention were not included in the analysis.

WHO describes equity in health as a fair opportunity to have full potential health without being disadvantaged from achieving the potential and regardless of socio-economic determinant of health [44]. In a recent publication, health equity was explained as everyone has a fair and just opportunity to be healthier. This requires removing obstacles to health such as poverty, discrimination, and their consequences, including powerlessness and lack of access to jobs with fair pay, quality education and housing, safe environments, and health care" [45,46].

Traditional cost-effectiveness analysis (CEA) assesses economic efficiency with a range of healthcare interventions that maximize health benefits at population level, and therefore the analysis is usually based on aggregated costs and health consequences regardless of who suffers costs and gains health [46,47]. In this sense, the traditional economic evaluation methods fail to promote health equity as distribution of resources, beneficiaries, healthcare access or health outcomes were not considered in the analytical approaches [47,48].

A review identified three new approaches to consider health equity into economic evaluation including Multi-Criteria Decision Analysis (MCDA) and two frameworks incorporating health equity into CEA: Distributional Cost-Effectiveness Analysis (DCEA) and Extended Cost-Effectiveness Analysis (ECEA) [49,50].

MCDA is a method to compare various potential interventions across several criteria such as number of beneficiaries, severity of disease, and poverty reduction, to determine which interventions should be prioritized, and it enables CEA to be weighed with health equity to target specific subpopulations defined by age, sex and severity of diseases [51,52]. Though this approach was applied to healthcare interventions in a few LICs such as Ghana and India, HICs more commonly apply this approach due to practical challenges such as difficulty adapting expert opinions and ensuring MCDA reflects local cultural and social contexts in LMICs [46,53,54]. DCEA is an approach to model the distribution of health gains and opportunity costs of different healthcare interventions and adjust those for social value judgements about equity [46,50,55]. This method can also evaluate trade-off issues between improving total health and reducing inequity [55,56].

ECEA is a method to compare distribution of protection against disease-related impoverishment in various interventions as well as health outcomes [46,57]. Though DCEA can take health-related opportunity costs into consideration, ECEA is indicated as a relevant approach in LMICs as patients usually require drastic coping mechanisms to pay healthcare-related costs such as borrowing money

or selling household assets that may threaten their life permanently [46,55,58,59]. ECEA assesses health policies in terms of four domains in addition to total costs and aggregated health benefits that can be assessed in conventional CEA: 1) health consequences, 2) financial benefits, 3) total costs for implementing policies, and 4) distributional consequences across sub-groups [57,60,61]. The financial benefits can be measured by cases of catastrophic costs averted, poverty cases averted, or value of insurance [60]. The sub-grouping for the distributional consequences includes by socio-economic status, by sub-national unit, and/or by demographic status (e.g. sex or age group) [60]. Considering the proportion of catastrophic costs was much higher in low-income groups or DR-TB patients, and drastic coping mechanisms were commonly required to pay TB-related costs, ECEA would be an appropriate approach to assess cost-effectiveness of health policies to avert economic impacts due to TB.

Using ECEA, assessing health gains (deaths averted or DALYs averted) and non-health benefits (catastrophic costs averted) for most commonly suggested recommendations from TB patient costs surveys/studies will provide estimated costs of various interventions vs health benefit and financial risk protection [57,60]. Therefore, the results of model based ECEA can help policy makers to select interventions to achieve epidemiological and economical goals in End TB strategy from perspectives of health and non-health benefits based on results of TB patient cost surveys and studies in the Philippines and other countries.

A study in Ethiopia assessed the number of deaths averted (health benefit) and individual poverty cases averted (non-health benefit) for nine health interventions including improvement of the coverage of TB DOTS [57]. The study showed that the extent of health and non-health benefits varied widely across the interventions, and TB treatment averts a small number of deaths and a large number of poverty cases [57]. The analysis showed that a 10% increase in TB treatment and malaria treatment provides a similar health benefit, but TB provides considerably more financial benefits. Therefore, results of ECEA allow policy makers to take both benefits into account especially when developing health-care benefit packages [60]. A modelling study using ECEA methods in South Africa and India showed that the number of TB patients with catastrophic costs can be reduced by improving quality of care and by expanding access to care especially among those who were in the bottom 40% of income groups [21].

For the End TB Strategy, all countries need to enhance financial and social protection policies to avert the catastrophic costs due to TB [5]. A recent modelling study revealed that none of the LMICs have achieved the target yet [62]. However, as it is discussed in this section, the traditional CEA is not able

to assess the cost-effectiveness of such policies to avert the catastrophic costs due to TB, as the analysis can only incorporate health benefits as an outcome of an intervention. The use of ECEA will allow the assessment of the cost-effectiveness of new and/or enhanced financial and social protection policies to mitigate the financial hardship faced by people with TB, as a non-health outcome, and it will further provide evidence on whether the policies are efficiently delivered across, for example different income groups from an equity perspective.

6.5 Conclusion remarks

New evidence from this PhD project, namely concurrent TB and diabetes patient costs, diabetes provider costs for people with TB and the cost-effectiveness of integrating diabetes services within TB services, have filled an evidence gap for providing diabetes services integrated within TB programmes. The evidence will contribute to advancing global discussion on the implementation and expansion of TB and diabetes service integrations. This PhD project also showed the limitations of the WHO recommended cross-sectional design for surveys of costs incurred by people with TB and their households and an inconsistency between the recommendation and implementation of the surveys. The suggestions from this PhD project will help to improve and revise the WHO guidance on surveys of costs incurred by people with TB and their households.

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SUPPLEMENTARY MATERIALS

Supplementary material 1. Ethics approvals

Ethics Approvals for study assessing costs incurred by people with TB and diabetes

LSHTM ethics review committee

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Doctor Sharon Cox
Associate Professor
Department of Population Health (DPH)
Epidemiology and Population Health (EPH)
LSHTM

10 May 2018

Dear Sharon

Study Title: Effects of malnutrition and diabetes on treatment outcome and total patient costs in Filipino drug resistant and non-resistant patients starting anti-TB treatment: A cohort study.

LSHTM Ethics Ref: 14094

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Information Sheet	St-ATT ENGLISH_ICsheet_HIV_D1	24/01/2018	D1
Investigator CV	Cox_CV_full_Jan2018_short	31/01/2018	Jan2018_short
Investigator CV	Edwards_CV_2017_MRC-Newton_2pages	01/02/2018	MRC
Investigator CV	juansoloncv_2017_Nov 2017	01/02/2018	LSHTM
Protocol / Proposal	St-ATT_Protocol_NEC_D6.2_7Feb2018	07/02/2018	D6.2
Information Sheet	St-ATT ENGLISH_ICsheet_HHCs_D3_LSHTM_clean	11/02/2018	D3
Information Sheet	St-ATT ENGLISH_IC sheet_D5_LSHTM_clean	11/02/2018	D5
Local Approval	St-ATT TMGH Ethical approval_1stMarch2018	01/03/2018	1
Information Sheet	St-ATT ENGLISH_IC sheet_D5.1_AEI_re-submit_18April2018 (1)	17/04/2018	5.1
Information Sheet	St-ATT ENGLISH_ICsheet_HHCs_D3.1_AEI_re-submit_18April2018 (1)	17/04/2018	3.1
Information Sheet	St-ATT ENGLISH_ICsheet_HIV_D1.1_AEI_re-submit_18April2018 (1)	17/04/2018	1.1
Covering Letter	Cover_letter_LSHTM_responses_23Apr2018_submitted	23/04/2018	1.0

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

Page 1 of 2

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

[redacted]

Professor John DH Porter
Chair

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

Improving health worldwide

Nagasaki university, TMGH ethics review committee

Ethical Committee
Graduate School of Tropical Medicine and Global Health
Nagasaki University

APPROVAL FORM

March 1, 2018

Project Title:	Effects of malnutrition and diabetes on treatment outcome and total patient costs in Filipino drug resistant and non-resistant patients starting anti-TB treatment: A cohort study.
Principle Investigator:	Sharon Cox
Date Submitted:	February 2, 2018
Protocol version	NEC_6.0_31stJan2018

Dear Sir / Madam,

We are pleased to inform you that the above project has been approved.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the Ethical Committee.

Sincerely,

[redacted]

Kiyoshi Kita
Dean, School of Tropical Medicine and Global Health
Nagasaki University, Japan

Asian Eye Institute ethics review committee

ST. CABRINI MEDICAL CENTER
ASIAN EYE INSTITUTE

14 May 2018

Sharon Cox, PhD
Primary Investigator
Nagasaki School of Tropical Medicine and Global Health

ERC # 2018-008

RE: Protocol No. St-ATT[1]; Protocol Title: Effects of Malnutrition and Diabetes on Treatment Outcome and Total Patient Costs in Filipino Drug Resistant and Drug Sensitive Patients Starting Anti-TB Treatment: A Cohort Study

Dear Dr. Cox,

In response to the documents submitted dated 24 April 2018 regarding the above-mentioned study, the SCMC-AEI ERC approves the following documents:

1. *Protocol (D6.4, 20th April 2018)*

2. *Informed Consent Forms–*
   - *2.1 St-ATT FILIPINO_ICsheet_HIV_D1_AEI_20April2018*
   - *2.2 St-ATT ENGLISH_ICsheet_HIV_D1.1_AEI_re-submit_18Apil2018*
   - *2.3 St-ATT FILIPINO_ICsheet_HHCs_D3_20April2018*
   - *2.4 St-ATT ENGLISH_ICsheet_HHCs_D3.1_AEI_re-submit_18April2018*
   - *2.5 St-ATT FILIPINO_IC sheet_D5_AEI_20April2018*
   - *2.6 St-ATT ENGLISH_IC sheet_D5.1_AEI_re-submit_18April2018*

It is hereby confirmed that neither you nor any member of the study team has participated in the review, decision making and voting procedures of the above study protocol/document.

This approval shall be valid for **1 year** from the date above. The investigator is required to submit progress report 1 month prior to the expiration date. During the duration of the study, the investigator is required to submit the following reports at a schedule set in the SCMC-AEI ERC SOP: SAE/SUSAR, protocol deviations, close-out report, early study termination, final report and any modifications or amendments in the study.

This SCMC-AEI ERC is organized and operates in compliance with ICH-GCP, 21 CFR Parts 50&56, NEGHR 2011 and according to the applicable laws and regulations.

Yours sincerely,

[redacted]

Emerson M. Cruz, MD
SCMC-AEI ERC Chairperson

WHO/WPRO ethics

WPRO - MEMORANDUM

From WPRO-ERC

To Fukushi Morishita
Technical Officer, STB

Date 3 May 2019

Our ref. 2019.18.PHL.4.STB

Attention

Your ref.

Originator

Subject WPRO-ERC DECISION ON RESEARCH PROPOSAL
ID: 2019.18.PHL.4.STB

This refers to your research proposal titled "**Assessing TB patient costs and treatment adherence in the Philippines by longitudinal data collection",** submitted to the Ethics Review Committee of Western Pacific Regional office of WHO on 17 April 2019. I am pleased to notify that proposal has been considered exempt from review by WPRO-ERC:

Principal Investigator (PI):
Mary Christine Castro, MD, Executive Director, Nutrition Center of the Philippines.

Responsible Technical Officer:
Fukushi Morishita, Technical Officer, End TB and Leprosy Unit, Division of Communicable Diseases, WPRO.

WPRO role in research: Main funder for the proposed research (US$ 14,990), technical assistance/collaboration

Protocol Title: Assessing TB patient costs and treatment adherence in the Philippines by longitudinal data collection

Unique ID Number: 2019.18.PHL.4.STB

Type of review: Initial screening by WPRO-ERC Secretariat

Decision: Exempt from review

Reasons for exemption from review:
The study will assess total costs incurred by DS-TB patients enrolled in the ongoing cohort study with longitudinal data collection, while also assessing TB treatment adherence and the associated risk factors. It has no more than minimal risk, and results will support WHO and the National TB Programme by assessing the limits of the globally recommended cross-sectional approach. The results will be disseminated through national/international conference and international peer-review journals. Appropriate safety measures are in place and consent forms will be sought. However, the study shall only proceed once local ethics approval has been sought and a copy shall be sent to this committee.

Dr Jun Gao
WPRO-ERC Secretary

Starting anti-TB Treatment Study (St-ATT): Participant Informed Consent Form for TB patients

Introduction

Tuberculosis (TB) disease can cause poor appetite and increases the risk of poor nutritional states, or "malnutrition". There is scientific evidence to suggest that malnutrition plays a role in the risk of becoming infected with TB, the risk of progressing to active TB disease, and an increased risk of TB treatment failure.

Diabetes is a condition where a person's blood sugar becomes too high. Around 5% or more of Filipinos have diabetes and probably more TB patients may have diabetes, as we now know that having diabetes can increase a person's risk of developing active TB disease. Many people with diabetes may not know that they have diabetes until symptoms become severe, which can include kidney problems, nerve damage and poor blood flow, particularly in the feet. TB may worsen control of blood sugars among diabetics and diabetes may increase the risk of TB treatment failure.

As of 2018, there continues to be a high rate of TB infections in the Philippines while diabetes prevalence is increasing.

Purpose

"The purpose of this study is to find out if malnutrition and diabetes in TB patients will affect TB treatment success and if total TB patient costs are increased by malnutrition and diabetes. This information will help scientists plan what kind of interventions and services are helpful and practical for TB patients to address malnutrition and diabetes.

This study is voluntary and is external to the health center. Participating or refusing to take part in this study will not alter the TB treatment you receive in any way.

I am _____ and I work for Nagasaki University and Nutrition Center of the Philippines as a Research Nurse. You are invited to participate in the study entitled "**Effects of malnutrition and diabetes on treatment outcome and total patient costs in Filipino patients starting anti-TB treatment**" under the supervision of Professor Sharon Cox (Nagasaki University and London School of Hygiene and Tropical Medicine), Dr. Celina Garfin (National TB Programme) and Dr. Juan Antonio Solon (Nutrition Center of the Philippines).

We would like to explain to you the following before you sign the informed consent:

Duration of participation:

The duration of your participation in the study is expected to be for 6-12 months, depending on the duration of the planned TB treatment period.

Procedures

If you agree to take part in the research, we will request the following from you:

(A) At the **baseline visit**, after TB diagnosis and before or within 5 days of starting anti-TB treatment and after signing the consent form we will request the following from you:

a. information about your general health, age and background and to provide a contact number and area of residence.

b. We will measure your **height and weight; handgrip strength**; and your **mid-upper arm circumference** to assess wasting (malnutrition) and your **blood pressure**. If you are attending TB-DOTS in San Lazaro Hospital (SLH), we will also measure your body fat and muscle using a simple electronic device (2-3 minutes, painless process requiring you to stand on a special weighing scale and hold the handgrips while it calculates your body fat and muscle.

c. We will collect **a 0.2ml (spot of blood) from a finger prick sample and provide results in 20 minutes.** We will use this for the following:

   i. **Screen for diabetes** by measuring a random blood sugar from a finger-prick sample. If it is high we will also measure HbA1C. If you are already known to have diabetes, HbA1C only will be measured and this is used to assess your disease severity and, if applicable, how well your treatment is controlling it.

   ii. Measure your blood level to test for **anemia** (low level of blood) from a finger-prick sample.

d. We may request a chest x-ray if you don't have one already.

e. **If you give additional consent** we will collect **a 5ml (1 teaspoon) venous blood sample**. We will use this to measure your **immune responses to TB** antigens as we want to know if this is affected by malnutrition or diabetes. In this case, a finger prick sample (c.) for screen for diabetes and anaemia will not be collected.

f. **If you give additional consent**, we will test for **HIV**, in case you have not already been tested at the start of your TB-DOTS treatment. In many areas of the Philippines and in the rest of the world this is standard practice as HIV increases the risk of TB treatment failure, and effective HIV treatment is available sponsored through the government and Philhealth. You will be provided with the standard pre- and post-test counselling by a DOH registered counsellor and the results will be treated as confidential, but will be included in your medical records.

g. We will collect a **study-specific sputum sample** from you. This will be stored for future additional testing to try to learn more about the nature of TB infections.

h. We will ask that you **encourage all your household members to come for free, voluntary TB-testing at your local health centre**. We would also like to enroll 1 adult member of your household, who has been screened and not found to have TB for assessment. **If the member of your household gives additional consent**, we will measure and follow up of their nutrition and anemia status at 3 monthly visits (using finger-prick blood samples).

(B) **At monthly follow-up visits when you attend either your TB-DOTS health centre or Barangay health post**, we will:

a. **conduct a short interview** and ask about your medication history and if you have experienced any side effects.

b. Measure your **weight, handgrip, mid-upper arm circumference** and **blood pressure**, plus body fat and muscle (if at SLH).

c. If you have diabetes or pre-diabetes (possible early stage diabetes), every 3 months, we will also measure your HbA1C (finger prick sample).

(C) **At the end of your intensive treatment phase and mid and end of continuation treatment phase, as well as at baseline,** we will ask you **questions** designed to assess the impact of TB and diabetes (if

applicable) on your **quality of life** and asses your **household food security**. These interviews will be combined with the normal monthly interview so will not require an additional study visit.

(D) If you provide **additional consent**, we will conduct **detailed TB patient-cost assessment interviews during a home visit** organized at your convenience at the following intervals: start of treatment, end of intensive treatment phase, in the middle of the continuation phase and at the end of treatment. These interviews will comprise:

a. Questions about costs you incurred relating to your TB and diabetes diagnosis/treatments (as applicable) in the previous month, including direct medical cost (e.g. consultation fees, laboratory tests, drugs), direct non-medical costs (e.g. transportation and special foods/drinks you buy for TB/diabetes) and indirect costs (e.g. loss of income).

b. Questions about what kinds of financial sources you utilized to pay for these costs (e.g. using cash/mobilizing savings, sales of assets, taking loans or support from relatives or community).

Collection of Samples:

If you are selected and agree, a 5 mL of venous blood (equivalent to 1 teaspoon) will be collected by the study research nurse for testing immune responses to TB. This blood sample will also be used to test if you might have diabetes and to test for anemia. Otherwise a finger-prick blood spot (0.2ml) will be collected by the study research nurse for diabetes and anaemia testing.

The results of the diabetes screening and anemia testing will be shared with you immediately. The HIV screening will be done at an approved laboratory and will take time until the result is available. It will be shared with you by the appropriate health facility staff in charge at each health center. The results of the immune responses test will not be shared with you since it is measured only for the research purpose.

Sputum samples and any remaining blood (for those that participate in the immune sub-study) will be stored in a study freezer archive at -80°C and used for further TB-related tests during this study or by other researchers for ethically approved research – please see confidentiality section below.

All clinical and experimental data will be carefully handled as confidential information.

Benefits

We will conduct an assessment of your nutritional status. The results (weight and body mass index (BMI)) will be shared with you. The BMI will help you know whether your weight is appropriate for your height. The blood sample will be used to screen you for possible diabetes, anemia and HIV if additional consent is given. If the sugar in your blood is high, you will be referred for further confirmatory tests for diabetes. A certain degree of anemia is expected in TB patients but if it is severe you will be referred for further follow-up. There will be no other benefit from you taking part in the study but you will also not incur any costs. This research will help to improve the delivery of TB treatment programmes for future patients.

Risks and discomfort

The risks involved in this study are minimal and include: the discomfort when drawing blood, and very rarely infection at the site of the needle stick. The procedure will be done using a clean technique and will be performed by a trained staff, so the risk of infection is minimized. A new sterile needle will be used for each patient so there is no risk for transmitting diseases.

Compensation

You will receive some small compensation in the form of phone credit compensation for your time at each study visit. At the baseline visit you will receive the equivalent of PHP 150 and then PHP 50 at each monthly follow-up visit completed. If you agree to participate in the TB patient cost study you will receive an additional PHP 250 for each home visit (4 in total) as phone credit or cash. This larger amount is to reflect the increased time required for these interviews. You will not incur any cost for taking part in this study.

Confidentiality

All information that you provide will be considered confidential. Information will be digitally collected using a tablet, but all the information will be sent to and kept in a password protected database after each participant is interviewed. Only members of the research team will have access to the information you provide until the data is anonymized. Anonymized data (with your name, address, phone number removed) will be stored in a database and then kept in a university research data repository for 10 years after completion of the project. Any sputum or blood remaining after this project is finished will be stored in the Philippines for up to 10 years and linked only to your anonymized data. This anonymized data and any remaining sputum/blood samples will be available for use by other health researchers for ethically approved projects related to TB after the end of this project to maximize benefit from your contribution to research on the health and wellbeing of Filipinos. After the 10-year period, unless data/samples are still being used, they will be deleted/destroyed.

Right to Refuse or Withdraw

You may choose not to participate in this study and you may refuse to participate or withdraw from the study at any time without penalty or loss of benefits to which you would otherwise be entitled. You do not have to explain why you do not wish to participate or why you want to withdraw. Refusing to take part in this study will not alter the treatment you are receiving in any way. This study is external to the health center and the staff conducting the research are not hired by where you are receiving care. This study is completely voluntary.

Contact information:

If you have any questions, clarification or if any problems arise, you may contact the following:

1. _____, Project Manager, Nagasaki Office-San Lazaro Hospital, Manila . Tel No:_____
2. _____ - Project Research Nurse, Malnutrition and Tuberculosis in the Philippines: prevalence of under-nutrition and diabetes in TB control programmes Tel,No.: _____
3. Dr. Mary Christine R. Castro, Executive Director of Nutrition Center of the Philippines
Tel No: +632-807-4982 or Mobile: +63-922-801-39-56

St-ATT CERTIFICATE OF CONSENT – TB Patients

I have been invited to participate in a research project of "**Effects of malnutrition and diabetes on treatment outcome and total patient costs in Filipino patients starting anti-TB treatment**". I agree to participate in this research study where I will be asked to answer some questions about my health and recent treatments. I have read the foregoing information, (or it has been read and explained to me). I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to participate in this study.

☐ I agree to participate in this study, including TB patient cost study - OR

☐ I agree to participate in this study, but NOT the TB patient cost study

☐ I understand that the data, sputum samples and any remaining blood collected from me may be used to support other future research and may be shared anonymously with other researchers, for their ethically-approved projects.

For immune assessment

☐ I agree to provide a 5ml venous blood sample ☐ NOT applicable

Print Full Name of Participant _____

Signature of Participant _____

Date (DD/MMM/YY) _____

If illiterate (Statement of witness): I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely and voluntarily.

AND Thumb print of participant

Print name of witness_____

Signature of witness _____

Date (DD/MMM/YY) _____

Statement by the researcher/person taking consent

I have accurately read and explained to the best of my ability, the informed consent sheet to the potential participant. I ensured that he/she understands what is involved in participation and their right to withdraw at any time without giving a reason and that this would not affect their treatment.

I confirm that the potential participant was given an opportunity to ask questions about the study, and all questions asked have been answered correctly to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.

Print Name of Researcher/person taking the consent _____

Signature of Researcher /person taking the consent _____

Date (DD/MMM/YY) _____

Ethics Approval for the diabetes provider costs study

LSHTM ethics review committee

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Observational / Interventions Research Ethics Committee

Mr Takuya Yamanaka
LSHTM

5 July 2021

Dear Mr Takuya Yamanaka

Study Title: Assessing the provider costs of diagnosing and managing diabetes for TB patients across 2 different models of integration of diabetes screening within TB services - resubmission

LSHTM Ethics Ref: 25149

Thank you for responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Investigator CV	TYamanaka_CV_Jan2021	01/02/2021	Jan2021
Other	Taku_GCP1	01/02/2021	1
Other	Taku_GCP2	01/02/2021	2
Other	Taku_GCP3	01/02/2021	3
Other	Taku_GCP4	01/02/2021	4
Local Approval	20210201_153_Takuya Yamanaka	02/02/2021	0201
Investigator CV	ANNA VASSALL CV 2020	31/03/2021	2020
Investigator CV	CV_YL	31/03/2021	2020
Investigator CV	TA_Sharon new CV_2 page_MRC	31/03/2021	2018
Investigator CV	PI_MCC CV Mar2018	31/03/2021	2018
Local Approval	2021-010_Form II-E_ Protocol Decision Form_Approved_22April2021 (1)	22/04/2021	NA
Protocol / Proposal	c.PHL_DM_provider_tool_v1.1	16/06/2021	1_1
Protocol / Proposal	d.PHL_DM_provider_budget_v3_1	16/06/2021	3_1
Protocol / Proposal	g.PHL_dm_prov_operation_v4_1	19/06/2021	4_1
Information Sheet	f. ICF_english_v4_1	29/06/2021	4_1
Information Sheet	e.PHL_DM_provider_study info_v4_1	29/06/2021	4_1
Protocol / Proposal	b.PHL_DM_provider_protocol_v4_1	29/06/2021	4_1
Covering Letter	a.Response to Reviewers_v3_LSHTMtemplate	30/06/2021	3

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

[redacted]

Professor Jimmy Whitworth
Chair

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

Improving health worldwide

Nagasaki university, TMGH ethics review committee

Ethical Committee
Graduate School of Tropical Medicine and Global Health
Nagasaki University

APPROVAL FORM

February. 1, 2021

Project Title:	Assessing the provider costs of diagnosing and managing diabetes for TB patients across 2 different models of integration of diabetes screening within TB services	
Principle Investigator:	Takuya Yamanaka	
Date Submitted:	January 4th, 2021	Ref.No.153
Approval Number:	NU_TMGH_2021_153_1	
Protocol version:	PHL_DMprov_V2.0	

Dear Sir / Madam,

We are pleased to inform you that the above project has been approved.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the Ethical Committee.

Sincerely,

[redacted]

Kiyoshi Kita
Dean, School of Tropical Medicine and Global Health
Nagasaki University, Japan

Asian Eye Institute ethics review committee

SCMC-AEI Ethics Review Committee

FORM II-E

PR-RSH-000-03/09/09152020

PROTOCOL DECISION FORM

22 April 2021

RE: ERC No.: 2021-010; Title: Assessing the provider costs of diagnosing and managing diabetes for TB patients across 2 different models of integration of diabetes screening within TB services

Takuya Yamanaka
Principal Investigator

Dear Ms. Yamanaka:

Peace and all good!

The SCMC-AEI ERC had an expedited review on the above-mentioned protocol and has approved the same.

For your guidance, the necessary *Certificate of Approval* is attached in this communication with the necessary details of the said approval.

This SCMC-AEI ERC is organized and operates in accordance with the requirements set by the Philippine Health Research Ethics Board (PHREB); and in compliance with the WHO Standards and Operational Guidance for Ethics Review of Health-related Research with Human Participants (2011), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (2016), and the National Ethical Guidelines for Health and Health-related Research (2017).

Yours sincerely,

[redacted]

Emerson M. Cruz, M.D.
Chairperson
St. Cabrini Medical Center – Asian Eye Institute Ethics Review Committee

CERTIFICATION OF APPROVAL

This certifies that the *St. Cabrini Medical Center – Asian Eye Institute Ethics Review Committee* (SCMC-AEI ERC) which is constituted and established, and functions in accordance with the requirements set by the Philippine Health Research Ethics Board (PHREB); and in compliance with the WHO Standards and Operational Guidance for Ethics Review of Health-related Research with Human Participants (2011), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (2016), and the National Ethical Guidelines for Health and Health-related Research (2017), has approved the following study protocol and related documents:

<table>
<tr><td colspan="2">Type of Submission: Re-submssion</td></tr>
<tr><td colspan="2">SCMC-AEI ERC Protocol Reference No.: 2021-010</td></tr>
<tr><td colspan="2">Protocol No. and Title:
Assessing the provider costs of diagnosing and managing diabetes for TB patients across 2 different models of integration of diabetes screening within TB services</td></tr>
<tr><td colspan="2">Principal Investigator: Takuya Yamanaka</td></tr>
<tr><td colspan="2">Address: Nagasaki University, School of Tropical Medicine & Global Health, Nagasaki, Japan
& London School of Hygiene & Tropical Medicine, London UK</td></tr>
<tr><td>Contract Research Organization:
Nagasaki University, LSHTM, Nutrition center of the Philippines</td><td>Sponsor:
Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan</td></tr>
<tr><td colspan="2">Co-Investigator/s: (please use additional page for a complete list of co-investigators if necessary)
Dr Anna Vassall: Primary supervisor, and is a health economist with over twenty five years of experience in economic analysis and research in low and middle income countries. She is a founding member of the TB-MAC modelling consortium and sits on the Strategic and Technical Advisory Group for the WHO's Global TB Programme (STAG-TB) and Task Force on Catastrophic Cost Measurement for TB, and recently sat on the Lancet Commission for TB. <Task description>: oversight of the study as primary supervisor of PI and providing technical supports in health economics
Dr Yoko Laurence: Secondary supervisor, and completed her PhD at LSHTM in 2017. Se has been working at LSHTM as a Research Fellow in Health Economics since then. Her work includes a multi-country costing study for all tuberculosis services (Value TB) as well as a cost-effectiveness analysis of integrated management of depressive disorders for people in HIV care in Uganda (HIV+D). <Task description>: oversight of the study as secondary supervisor of PI and providing technical supports in health economics
Dr. Sharon Cox: She is a nutrition scientist and epidemiologist with a long-standing interest in the interaction between nutrition and infection. She oversees the study as third supervisor of PI
Dr.MARY CHRISTINE R. CASTRO: she is a medical doctor with a Master of Science in Epidemiology London School of Hygiene and Tropical Medicine and a Doctor of Medicine University of the Philippines College of Medicine. <Task description>: oversight of local implementation by Nutrition Centre Philippines partner</td></tr>
<tr><td colspan="2">Type of Review: Expedited Review</td></tr>
<tr><td>Approval Date: 22 April 2021</td><td>Expiry of Ethical Clearance: 22 April 2022
Study protocols are reclassified as Inactive after expiry of ethical clearance.</td></tr>
</table>

Due Date of Application for Renewal of Ethical Clearance (30 days before expiry): 22 March 2022 Submit application using the Continuing Review Application/Progress Report Form (SCMC-AEI ERC FORM II-N).	**Frequency of Continuing Review: Yearly**
Approved site/s: Cebu and Negros Occidental, Philippines	
Date of ERC Meeting: N/A	
Quorum: N/A	
Conflict of interest: None	
Members in Attendance: N/A	

Documents Approved by SCMC-AEI ERC:

1. *PHL_DM_provider_protocol_v3_1*
2. *Appendix 2. Study information and consent form PHL_DMprov_V3.1, 31/03/2021*
3. *PHL_DM_provider_consent form_study info_v3_1*
4. *Data Collection Items*

Documents as reference:

1. *PHL_DM_provider_summary of changes_v3_1*
2. *PHL_DM_provider_tool_v1.1*
3. *PHL_DM_provider_budget_v3_1*
4. *Form II-B_Editable Template_Request Letter for Review_09102020_PHL_DMprov_V3.1*
5. *JRA_Form II-D_Editable Template_Study Protocol and Informed Consent Assessment Form_09092020*
6. *JRA_Form II-F_ Editable Template_Protocol Amendment Submission Form_09112020*
7. *1-f. budget&funding*
8. *PI_MCC CV Mar2018*
9. *TA_Laurence_CV_2 page 2018*
10. *TA_Sharon new CV_2 page_MRC*
11. *TA Vassall CV+LoP ESRC*
12. *TYamanaka_CV_Jan2021*
13. *Taku_GCP1*
14. *Taku_GCP2*
15. *Taku_GCP3*
16. *Taku_GCP4*

Responsibilities of Principal Investigator while Study is in Progress:

1. Register research study in the Philippine Health Research Registry upon approval (http://registry.healthresearch.ph)
2. Progress report using the attached *Continuing Review Application/Progress Report Form* (SCMC-AEI ERC FORM II-N), as indicated above, which includes the following: (NOTE: In view of active ethical clearance, this report is mandatory even if the study has not started or is still awaiting release of funds.)
   - ✓ Date covered by the report
   - ✓ Protocol summary and status report on the progress of the research
   - ✓ Philippine Health Research Registry ID
   - ✓ Number of participants accrued
   - ✓ Withdrawal or termination of participants
   - ✓ Complaints on the research since the last SCMC-AEI ERC review
   - ✓ Summary of relevant recent research literature, interim findings and amendments since the last SCMC-AEI ERC review
   - ✓ Any relevant multi-center research reports
   - ✓ Any relevant information especially about risks associated with the research
   - ✓ A copy of the informed consent document
3. Any amendment/s in the protocol, especially those that may adversely affect the safety of the participants during the conduct of the trial including changes in personnel, and revisions in the informed consent, must be submitted or reported using *Protocol Amendment Submission Form* (SCMC-AEI ERC FORM II-F).
4. Report of non-compliance (deviation/violation), whether minor or major, at the soonest possible time up to six (6) months after the event, using *Study Protocol Deviation Report Form* (SCMC-AEI ERC FORM II-O).
5. Reports of adverse events including from other study sites (national, international) using the *Serious Adverse Event/s (SAE) / Suspected Unexpected Serious Adverse Reaction/s (SUSAR) Report Form* (SCMC-AEI ERC FORM II-N), with timelines for submission guided by the GL 02 Version 2.0: Guideline on Reporting Serious Adverse Events; or list of reportable negative events.
6. Notice of early termination of the study and reasons for such, or notice of time of completion of the study using *Final Report Form* (SCMC-AEI ERC FORM II-M)
7. Any event which may have ethical significance, and/or any information which is needed by the SCMC-AEI ERC to do ongoing review.

SCMC-AEI ERC Chairperson	Signature:	[redacted]	Date: (dd/mm/yyyy)
	Printed Name:	Emerson M. Cruz, MD	22 April 2021

Supplementary material 2. Data collection tools

Tool used for collecting costs incurred by people with TB and diabetes and their households – Questionnaire for enrolment

St-ATT Form 7-1 TB and DM patient cost: Enrollment V3_2

FOLLOWING QUESTIONS SHOULD BE FILLED BEFORE STARTING INTERVIEW.
PLEASE FILL BASED ON PATIENT COST LOG IN GOOGLE SHEET.

PLEASE ENTER THE INTERVIEWER'S THREE-LETTERS INITIALS. *

Please enter the patient's ID

PLEASE SCAN THE PATIENT QR CODE	INPUT UNIQUE STUDY NUMBER
Use your smartphone with the suggested app to create the QR code. *If you can't scan the QR code repeatedly, please enter the ID manually in the text box on the bottom of the page.*	*Please enter participants unique study number using format 100-XXX-000-TB-000* *Please only use **uppercase** letters.*

ATTENTION: THIS PATIENT HAS NO ID INPUT. PLEASE CORRECT THIS BEFORE PROCEEDING TO THE REST OF THE QUESTIONNAIRE.

◯ OK

THIS PATIENT'S ID IS

Please check that the ID is what you intended.
If you notice an error, please go back to correct it.

INPUT THE DATE YOU ARE FILLING THIS FORM *

yyyy-mm-dd

INPUT INITIALS OF PATIENTS *

Use the full name

WHAT IS THE PATIENT'S DATE OF BIRTH? *

Use "15th July" if you don't know day or month

yyyy-mm-dd

WHAT IS THE PATIENT'S SEX? *

◯ Female

◯ Male

Part 0. patient information.

PART 0.
FOLLOWING QUESTIONS ARE RELATED TO THE PATIENT INFORMATION. PLEASE FILL PATIENT TREATMENT CARD AND RESERVATION INFO TO VISIT PATIENT'S HOME IN ADVANCE

PLEASE INDICATE IN WHICH REGION ARE THE PARTICIPANT REGISTERED *

- ◯ Manila, NCR
- ◯ Negros Occidental, Western Visayas
- ◯ Cebu, Central Visayas

PROVIDE THE NAME OF THE TB DOTS FACILITY PATIENT IS REGISTERED UNDER:

- ◯ San Lazaro Hospital
- ◯ San Nicolas Health Center

PROVIDE THE NAME OF THE TB DOTS FACILITY PATIENT IS REGISTERED UNDER:

- ◯ Villadolid Health Center
- ◯ Bago City Health Center
- ◯ Bacolod Health Center
- ◯ La Carlota Health Center

PROVIDE THE NAME OF THE TB DOTS FACILITY PATIENT IS REGISTERED UNDER:

- ◯ Compostela Health Center
- ◯ Carmen Health Center
- ◯ Consolacion Health Center
- ◯ Lapu lapu Health Center
- ◯ Eversley Childs Sanitarium & General Hospital

WHEN WAS THE PATIENT REGISTERED? *

yyyy-mm-dd

TYPE OF TB *

- ◯ Drug-susceptible
- ◯ Drug-resistant

TB DISEASE TREATMENT REGIMEN

- ◯ **I. 2HRZE/4HR** PTB, New-bacteriologically confirmed
- ◯ **I. 2HRZE/4HR** PTB, New - clinically diagnosed
- ◯ **II. 2HRZES/1HRZE/5HRE** Relapse
- ◯ **II. 2HRZES/1HRZE/5HRE** Treatment After Failure
- ◯ **II. 2HRZES/1HRZE/5HRE** TALF
- ◯ **II. 2HRZES/1HRZE/5HRE** PTOU
- ◯ **II. 2HRZES/1HRZE/5HRE** Other
- ◯ Other

IS THE PATIENT ENROLLED ON MDR-TB WHO SHORTER REGIMEN?

- ◯ No
- ◯ Yes

BACTERIOLOGICAL STATUS AT START OF TREATMENT / REASON FOR STARTING TREATMENT

- ◯ Bacteriologically-confirmed RR-TB/ MDR-TB
- ◯ Bacteriologically-confirmed XDR-TB
- ◯ Presumptive RR-TB/ MDR-TB
- ◯ Clinically-diagnosed RR-TB/MDR-TB
- ◯ Other DR-TB

PLEASE EXPLAIN 'OTHER'

» Start date of current TB treatment

START DATE OF CURRENT TB TREATMENT *

yyyy-mm-dd

START DATE UNKNOWN?

- ◯ No
- ◯ Yes

START MONTH OF CURRENT TB TREATMENT

yyyy-mm

END OF PART 0.
THIS IS THE END OF PREPARATION. FOLLOWING QUESTION MUST BE FILLED IN THE INTERVIEW WITH PATIENT

Part1. Patient contact information and previous TB history

PART I
NOW IS THE BEGINNING OF THE PATIENT INTERVIEW.

RESIDENCE ADDRESS OF THE PATIENT
« Where do you sleep? »

PLACE OF INTERVIEW WITH THE PATIENT
If you select « Other », please specify on the next screen.

- ◯ TB DOTS Clinic
- ◯ Barangay Health Station
- ◯ Participants House
- ◯ Other

PLEASE EXPLAIN 'OTHER'

» Summary information on previous TB

FOLLOWING QUESTIONS ARE RELATED TO PREVIOUS TB

HAS THE PATIENT EVER BEEN PREVIOUSLY TREATED? *

- ◯ No
- ◯ Yes

HOW MANY TIMES HAS THE PATIENT BEEN PREVIOUSLY TREATED (**EXCLUDING THIS TIME**)?

» Summary information on the current TB

FOLLOWING QUESTIONS ARE RELATED TO THE CURRENT TB

FOR THIS EPISODE OF THE CURRENT TB, WHEN DID YOU FIRST EXPERIENCE SYMPTOMS? *

Symptoms may refer to the following: cough, weight loss, chest and back pains, night sweats, fever, bloody sputum, easy fatigueability, and difficulty of breathing.
First construct a timeline of events in relation with TB symptoms.

yyyy-mm-dd

TREATMENT DURATION OF THE CURRENT DS-TB

TREATMENT FOR THE CURRENT TB IS SUPPOSED TO LAST 2 MONTHS FOR INTENSIVE PHASE AND 4 MONTHS FOR CONTINUATION PHASE.

	No	Yes
DOES THE PATIENT AGREE WITH THIS INFORMATION?	◯	◯

WHAT DOES THE PATIENT THINK IS CORRECT?

WHAT DOES THE PATIENT THINK IS CORRECT FOR THE INTENSIVE PHASE? *In months.*	WHAT DOES THE PATIENT THINK IS CORRECT FOR THE CONTINUATION PHASE? *In months.*

TREATMENT DURATION OF THE CURRENT DR-TB

TREATMENT FOR THE CURRENT TB IS SUPPOSED TO LAST 4 MONTHS FOR INTENSIVE PHASE AND <5 MONTHS FOR CONTINUATION PHASE.

	No	Yes
DOES THE PATIENT AGREE WITH THIS INFORMATION?	◯	◯

WHAT DOES THE PATIENT THINK IS CORRECT?

WHAT DOES THE PATIENT THINK IS CORRECT FOR THE INTENSIVE PHASE? *In months.*	WHAT DOES THE PATIENT THINK IS CORRECT FOR THE CONTINUATION PHASE? *In months.*

DOES THE PATIENT FOLLOW A REGULAR SCHEDULE IN VISITING THE TREATMENT FACILITY FOR TB TREATMENT?

- ◯ No
- ◯ Yes

WHAT IS THE PATIENT'S TB TREATMENT SCHEDULE?

- ◯ Every day
- ◯ Six times a week
- ◯ Five times a week
- ◯ Four times a week
- ◯ Three times a week
- ◯ Twice a week
- ◯ Every week
- ◯ Every two weeks
- ◯ Every three weeks
- ◯ Every month
- ◯ Every five weeks
- ◯ Every six weeks
- ◯ Other

PLEASE EXPLAIN 'OTHER'

Part 2. Overview of previous TB history before current treatment (for re-treatment cases only)

PART II.
OVERVIEW OF TB TREATMENTS BEFORE THE CURRENT TREATMENT (FOR RE-TREATMENT CASES ONLY)

PAST TREATMENTS WITHIN THE PAST TWO YEARS

HOW MANY TIMES HAVE YOU BEEN TREATED FOR TB BEFORE THE CURRENT TREATMENT, INCLUDING COMPLETED AS WELL AS NON-COMPLETED TREATMENTS IN THE **PAST TWO YEARS**?
ACCORDING TO THE DATA ENTERED PREVIOUSLY, THE PATIENT HAS TIME(S) PREVIOUS TB TREATMENT(S).

	No	Yes
DO YOU AGREE WITH THIS INFORMATION?	◯	◯

HOW MANY TIMES HAVE YOU BEEN TREATED FOR TB BEFORE THE CURRENT TREATMENT, INCLUDING COMPLETED AS WELL AS NON-COMPLETED TREATMENTS IN THE **PAST TWO YEARS**?

» First TB treatment within the past two years

IN THE PAST TWO YEARS, WHAT YEAR WERE YOU TREATED FOR THE FIRST TIME FOR TB?

yyyy

WHERE WERE YOU TREATED?

Please enter the name of the facility

» » Facility Type

IN WHICH TYPE OF FACILITY WERE YOU TREATED?

- ◯ **Public sector:** Hospital
- ◯ **Public sector:** PMDT facility
- ◯ **Public sector:** RHU/Urban Health Center
- ◯ **Public sector:** Barangay Health Center
- ◯ **Public sector:** Other (specify)
- ◯ **Private sector:** Private Hospital
- ◯ **Private sector:** Private Clinic
- ◯ **Private sector:** PPM DOTS
- ◯ **Private sector:** Private Pharmacy
- ◯ **Private sector:** NGO Clinic
- ◯ **Private sector:** Other (specify)

PLEASE SPECIFY:

PLEASE SPECIFY:

HOW MANY MONTHS WERE YOU TOLD THAT YOU NEED TO TAKE THE TB MEDICINE?

HOW MANY MONTHS OF TREATMENT DID YOU COMPLETE FOR THIS TREATMENT?

WERE YOU CONFINED IN A HOSPITAL DURING THIS TREATMENT?

- ◯ No
- ◯ Yes

FOR HOW LONG?

In days.

» Second treatment

IN THE PAST TWO YEARS, WHAT YEAR WERE YOU TREATED FOR THE SECOND TIME FOR TB?

yyyy

WHERE WERE YOU TREATED?

» » Facility Type

IN WHICH TYPE OF FACILITY WERE YOU TREATED?

- ◯ **Public sector:** Hospital
- ◯ **Public sector:** PMDT facility
- ◯ **Public sector:** RHU/Urban Health Center
- ◯ **Public sector:** Barangay Health Center
- ◯ **Public sector:** Other (specify)
- ◯ **Private sector:** Private Hospital
- ◯ **Private sector:** Private Clinic
- ◯ **Private sector:** PPM DOTS
- ◯ **Private sector:** Private Pharmacy
- ◯ **Private sector:** NGO Clinic
- ◯ **Private sector:** Other (specify)

PLEASE SPECIFY:

PLEASE SPECIFY:

HOW MANY MONTHS WERE YOU TOLD THAT YOU NEED TO TAKE THE TB MEDICINE?

HOW MANY MONTHS OF TREATMENT DID YOU COMPLETE FOR THIS TREATMENT?

WERE YOU CONFINED IN A HOSPITAL DURING THIS TREATMENT?

- ◯ No
- ◯ Yes

FOR HOW LONG?

In days.

» Third treatment

IN THE PAST TWO YEARS, WHAT YEAR WERE YOU TREATED FOR THE THIRD TIME FOR TB?

yyyy

WHERE WERE YOU TREATED?

» » Facility Type

IN WHICH TYPE OF FACILITY WERE YOU TREATED?

- ◯ **Public sector:** Hospital
- ◯ **Public sector:** PMDT facility
- ◯ **Public sector:** RHU/Urban Health Center
- ◯ **Public sector:** Barangay Health Center
- ◯ **Public sector:** Other (specify)
- ◯ **Private sector:** Private Hospital
- ◯ **Private sector:** Private Clinic
- ◯ **Private sector:** PPM DOTS
- ◯ **Private sector:** Private Pharmacy
- ◯ **Private sector:** NGO Clinic
- ◯ **Private sector:** Other (specify)

PLEASE SPECIFY:

PLEASE SPECIFY:

HOW MANY MONTHS WERE YOU TOLD THAT YOU NEED TO TAKE THE TB MEDICINE?

HOW MANY MONTHS OF TREATMENT DID YOU COMPLETE FOR THIS TREATMENT?

WERE YOU CONFINED IN A HOSPITAL DURING THIS TREATMENT?

- ◯ No
- ◯ Yes

FOR HOW LONG?

In days.

END OF PART II.
WE HAVE NOW FINISHED THE OVERVIEW OF PREVIOUS TB TREATMENTS.
The next part of this questionnaire is about costs during current treatment.

Part 3. Costs before the current TB treatment/diagnosis

PART 3.
FOLLOWING QUESTIONS ARE RELATED TO COSTS BEFORE THE CURRENT TB DIAGNOSIS

ACCORDING TO PREVIOUS INFORMATION, THIS PATIENT STARTED EXPERIENCING TB SYMPTOMS ON .
PLEASE USE THIS DATE AS A REFERENCE FOR THE NEXT QUESTIONS.

HOW MANY TIMES DID YOU SEEK CARE OR ADVICE FOR YOUR SYMPTOMS ? (INCLUDING CARE FOR TB SYMPTOMS, SPUTUM COLLECTION, TB DIAGNOSIS)

From start having TB symptoms, until TB treatment started.
***Public Sector** (Hospital, PMDT, RHU/Urban Health Center, Barangay Health Center)*
***Private Sector** (Private Hospital, Private or NGO Clinic, PPM DOTS, Private Pharmacy)*
If one provider refered you to another one, it registers as two different visits.

» Enter in the visits in CHRONOLOGICAL ORDER.

HEALTH INSURANCE REIMBURSEMENT FOR TB

*Amount reimbursed **After having SYMPTOM of the current TB** through medical insurance for **TB** so far, does not include expected future reimbursement.*
from symptoms started () and before the start of the current TB treatment (

).

» Costs for nutritional/food supplements

FOLLOWING QUESTIONS ARE RELATED TO EXPENSES TO NUTRITIONAL SUPPLEMENT AND SPECIAL FOOD/DRINK DUE TO TB ILLNESS OUTSIDE OF REGULAR DIET

DO YOU BUY ANY NUTRITIONAL SUPPLEMENTS OR SPECIAL FOOD/DRINKS OUTSIDE YOUR REGULAR DIET BECAUSE OF THE TB ILLNESS, FOR EXAMPLE VITAMINS, MEAT, ENERGY DRINKS, OR FRUITS AS RECOMMENDED BY HEALTH CARE STAFF?

- ◯ No
- ◯ Yes

COSTS FOR NUTRITIONAL SUPPLEMENTS AND SPECIAL FOOD/DRINKS FOR TB ILLNESS OUTSIDE YOUR REGULAR DIET BECAUSE OF THE TB ILLNESS

PAST ONE MONTH (30 DAYS PRIOR TO INTERVIEW)

EXPENSES ON NUTRITIONAL SUPPLEMENTS APART FROM PAYMENT TO PRESCRIBED SUPPLEMENT AT HEALTH FACILITIES	SPECIAL EXPENSES ON MEAT (AND ALSO EGG)
SPECIAL EXPENSES ON FISH	SPECIAL EXPENSES ON DRINKS WITH VITAMIN/CARNITINE OR MILK ETC

SPECIAL EXPENSES ON FRUITS/VEGETABLES

END OF PART III.

WE HAVE NOW GATHERED INFORMATION ABOUT COSTS BEFORE CURRENT TB DIAGNOSIS.

The next part of this questionnaire is about patient household information.

Part 4. Household information

FOLLOWING QUESTIONS ARE RELATED TO PATIENT'S HOUSEHOLD INFORMATION SUCH AS EDUCATION, INCOME, ASSET, SOCIAL PROTECTION

» Social protection and insurance

WHICH HEALTH INSURANCE DO YOU BELONG TO NOW? *

- ☐ Not covered by health insurance
- ☐ Philhealth paying
- ☐ Philhealth dependent of paying member
- ☐ Philhealth indigent member
- ☐ Philhealth dependent of indigent member
- ☐ Philhealth senior citizen
- ☐ GSIS
- ☐ SSS
- ☐ Private health insurance/HMO/Pre-need insurance plan
- ☐ Other

PLEASE EXPLAIN 'OTHER'

AT THE TIME OF THE INTERVIEW DO YOU OR ANY MEMBER OF YOUR FAMILY RECEIVE ANY GIFT/SUPPORT/ASSISTANCE/RELIEF IN CASE FROM CONDITIONAL CASH TRANSFER (CCT/4PS)? *

- ◯ No
- ◯ Yes

MONTHLY AMOUNT IN PHP.

» Social position

THESE NEXT QUESTIONS ARE ABOUT THE PATIENT'S SOCIAL POSITION. *

- ◯ OK

WHAT EDUCATION LEVEL DID YOU COMPLETE? *

- ◯ Not attended school
- ◯ No grade completed
- ◯ Don't know
- ◯ Preschool
- ◯ **Elementary**: Grade 1
- ◯ **Elementary**: Grade 2
- ◯ **Elementary**: Grade 3
- ◯ **Elementary**: Grade 4
- ◯ **Elementary**: Grade 5
- ◯ **Elementary**: Grade 6
- ◯ **Elementary**: Elementary graduate
- ◯ **High school**: Year 1/Grade 7
- ◯ **High school**: Year 2/Grade 8
- ◯ **High school**: Year 3/Grade 9
- ◯ **High school**: Year 4/Grade 10
- ◯ **High school**: Grade 11
- ◯ **High school**: Grade 12
- ◯ **High school**: High school graduate
- ◯ **Higher**: Post secondary year 1
- ◯ **Higher**: Post secondary year 2
- ◯ **Higher**: College year 1
- ◯ **Higher**: College year 2
- ◯ **Higher**: College year 3
- ◯ **Higher**: College year 4
- ◯ **Higher**: College year 5
- ◯ **Higher**: College year 6 or more
- ◯ **Higher**: College graduate
- ◯ **Post baccalaureate**
- ◯ **Vocational**

TOTAL YEAR OF SCHOOLING OF YOURS

WAS THE PATIENT THE PRIMARY INCOME EARNER (HIGHEST INCOME IN THE HOUSEHOLD)?
BEFORE

- ◯ No
- ◯ Yes

WHAT EDUCATION LEVEL DID THE PRIMARY INCOME EARNER IN THE HOUSEHOLD COMPLETE?

- ◯ Not attended school
- ◯ No grade completed
- ◯ Don't know
- ◯ Preschool
- ◯ **Elementary**: Grade 1
- ◯ **Elementary**: Grade 2
- ◯ **Elementary**: Grade 3
- ◯ **Elementary**: Grade 4
- ◯ **Elementary**: Grade 5
- ◯ **Elementary**: Grade 6
- ◯ **Elementary**: Elementary graduate
- ◯ **High school**: Year 1/Grade 7
- ◯ **High school**: Year 2/Grade 8
- ◯ **High school**: Year 3/Grade 9
- ◯ **High school**: Year 4/Grade 10
- ◯ **High school**: Grade 11
- ◯ **High school**: Grade 12
- ◯ **High school**: High school graduate
- ◯ **Higher**: Post secondary year 1
- ◯ **Higher**: Post secondary year 2
- ◯ **Higher**: College year 1
- ◯ **Higher**: College year 2
- ◯ **Higher**: College year 3
- ◯ **Higher**: College year 4
- ◯ **Higher**: College year 5
- ◯ **Higher**: College year 6 or more
- ◯ **Higher**: College graduate
- ◯ **Post baccalaureate**
- ◯ **Vocational**

TOTAL YEAR OF SCHOOLING OF THE PRIMARY INCOME EARNER?

» Constructing a socio-economic status index with household asset questions.

WHAT IS YOUR USUAL MAIN SOURCE OF DRINKING WATER? *

- ◯ **Piped water**: Piped into dwelling
- ◯ **Piped water**: Piped to yard/plot
- ◯ **Piped water**: Public tap/standpipe
- ◯ Tube well or borehole
- ◯ Dug well
- ◯ Water from spring
- ◯ Rainwater
- ◯ Tanker truck
- ◯ Cart with small tank
- ◯ Surface water (river/dam/ lake/pond/stream/canal/ irrigation channel)
- ◯ Bottled water/refilling station
- ◯ Other

PLEASE EXPLAIN 'OTHER'

WHAT KIND OF TOILET FACILITIES DO YOU HAVE? *

- ◯ **Flush or pour flush toilet**: Flush to piped sewer system
- ◯ **Flush or pour flush toilet**: Flush to septic tank
- ◯ **Flush or pour flush toilet**: Flush to pit latrine
- ◯ **Flush or pour flush toilet**: Flush to somewhere else
- ◯ **Flush or pour flush toilet**: Flush, don't know where
- ◯ Pit latrine
- ◯ No facility/bush/field
- ◯ Public toilet
- ◯ Other

PLEASE EXPLAIN 'OTHER'

DOES YOUR HOUSEHOLD HAVE? *

-

- [ ] Electricity
- [ ] Television
- [ ] Motorcycle/Tricycle
- [ ] Wardrobe
- [ ] CD/VCD/DVD player
- [ ] Car/Jeep/Van
- [ ] Motorized boat/banca
- [ ] Aircon
- [ ] Fan
- [ ] Washing machine
- [ ] Stove with oven/Gas range
- [ ] Refrigerator/Freezer
- [ ] Personal computer (desktop/laptop/netbook/ipad/ipod/tablet)
- [ ] Cellular phone
- [ ] Landline/Wireless telephone
- [ ] Audio component/Stereo set
- [ ] Karaoke/Videoke/Magic sing
- [ ] Radio/Radio Cassette player
- [ ] Gold/jewelry

» Income (reported) before contracting TB

FOLLOWING QUESTIONS ARE RELATED TO INCOME PRIOR TO HAVING SYMPTOMS OF TB
PLEASE USE A REFERENCE MONTH
BEFORE THE DATE OF TB SYMPTOMS: *

- ◯ OK

WERE YOU THE PERSON WHO EARNED THE HIGHEST INCOME IN YOUR HOUSEHOLD BEFORE YOU SHOWED SYMPTOMS OF TB? *

BEFORE

- ◯ No
- ◯ Yes

HOW WERE YOU USUALLY PAID BEFORE YOU SHOWED SYMPTOMS OF TB?

BEFORE

- ◯ Bank/ATM transferred salary
- ◯ Cash
- ◯ In kind
- ◯ Cash and in kind
- ◯ Not paid
- ◯ Unemployed
- ◯ Other

PLEASE EXPLAIN 'OTHER'

HOW MANY HOURS A WEEK WERE YOU WORKING BEFORE YOU SHOWED SYMPTOMS OF TB?

BEFORE

BEFORE YOU SHOWED SYMPTOMS OF TB, DID YOU OR ANY HOUSEHOLD MEMBER RECEIVE REGULARLY SALARIES AND WAGES FROM EMPLOYMENT IN CASH (INCLUDING ALLOWANCES, HONORARIA, TIPS, BONUS, COMMISSIONS) *OR* IN KIND (INCLUDING HOUSING, FOOD, GROCERY, CLOTHING, AND MEDICAL BENEFITS)? *

BEFORE

Please try to estimate income per month

- ◯ No
- ◯ Yes

HOW MANY HOUSEHOLD MEMBERS WERE RECEIVING REGULAR SALARIES IN CASH OR IN KIND BEFORE HAVING TB SYMPTOMS?

Excluding yourself (the patient). BEFORE

» » MONTHLY Earnings before TB symptom

PLEASE GIVE AN ESTIMATE OF THE LAST FULL ONE MONTH CASH EARNINGS AND EARNINGS IN KIND **BEFORE YOU START HAVING TB SYMPTOMS** *

.

PLEASE ESTIMATE AS WELL THE CASH EARNINGS OF HOUSEHOLD MEMBERS WHO RECEIVE SALARY AND WAGES FROM EMPLOYMENT DURING THIS PERIOD.

BEFORE the date of TB symptoms:

- ◯ OK

PATIENT HIM/HERSELF

WHAT WAS THE YOUR OCCUPATION **BEFORE YOU SHOWED SYMPTOMS OF TB**.	LAST FULL ONE MONTH EARNINGS **BEFORE YOU SHOWED SYMPTOMS OF TB**. *
BEFORE	*including pension*

» Income changes and social consequences

FOLLOWING QUESTIONS ARE RELATED TO INCOME CHANGES AND SOCIAL CONSEQUENCES **AFTER HAVING SYMPTOMS OF TB** BUT **BEFORE THE DIAGNOSIS** *

.

PERIOD <SPAN STYLE="COLOR:RED">BETWEEN () AND (

)</SPAN>.

◯ OK

DO YOU THINK YOUR INCOME AND/OR YOUR HOUSEHOLD MEMBERS' INCOMES CHANGED AFTER HAVING TB SYMPTOMS COMPARED TO THE PERIOD BEFORE () *

Do you/family member stop working or lose jobs or some working days/opportunity after ()?

◯ No

◯ Yes

DID YOU OR ANY MEMBER OF YOUR HOUSEHOLD RECEIVE SALARY AND WAGES FROM EMPLOYMENT IN CASH (INCLUDING ALLOWANCES, TIPS) OR IN KIND (INCLUDING HOUSING, CLOTHING FOOD)? **AFTER HAVING SYMPTOMS OF TB** BUT **BEFORE THE DIAGNOSIS** *

.

Period between () and (

).

◯ No

◯ Yes

» » MONTHLY Earnings after having symptoms of TB but before the diagnosis

HOW MANY HOUSEHOLD MEMBERS RECEIVED REGULAR SALARIES IN CASH OR IN KIND? **AFTER HAVING SYMPTOMS OF TB** BUT **BEFORE THE DIAGNOSIS**. *

Excluding the patient.
Period between () and (

).

PLEASE GIVE AN ESTIMATE OF THE LAST FULL ONE MONTH CASH EARNINGS AND EARNINGS IN KIND, **AFTER HAVING SYMPTOMS OF TB** BUT **BEFORE THE DIAGNOSIS**.

PLEASE ESTIMATE AS WELL THE CASH EARNINGS OF HOUSEHOLD MEMBERS 10 YEARS OLD AND OLDER WHO RECEIVE SALARY AND WAGES FROM EMPLOYMENT DURING THIS PERIOD.

PATIENT HIM/HERSELF

WHAT WAS THE PATIENT'S OCCUPATION **AFTER HAVING SYMPTOMS OF TB** BUT **BEFORE THE DIAGNOSIS**.	LAST FULL ONE MONTH EARNINGS *__AFTER HAVING SYMPTOMS OF TB__ BUT __BEFORE THE DIAGNOSIS__.
Period between () and (*).*	*including pension*

ARE YOU STILL UNEMPLOYED ?

◯ No

◯ Yes

HOW MANY HOURS PER WEEK WERE YOU WORKING **AFTER HAVING SYMPTOMS OF TB** BUT **BEFORE THE DIAGNOSIS**?

Period between () and (

).

APPROXIMATELY HOW MANY WORKING DAYS OF INCOME HAVE YOU LOST FROM THE TIME THAT YOU STARTED TO EXPERIENCE TB SYMPTOMS () UNTIL YOU WERE DIAGNOSED TO HAVE TB (

)?

Report for total TB episode, incl. all days before and after job loss.

DID YOU OR YOUR HOUSEHOLD RECEIVE ANY SOCIAL WELFARE PAYMENT AFTER HAVING SYMPTOMS OF TB UNTIL THE TB DIAGNOSIS? IF YES, WHAT TYPE AND AMOUNT (AFTER TAX) DURING THE LAST MONTH? *

Period between () and (

).

- ☐ Not received
- ☐ Paid sick leave
- ☐ Disability grant
- ☐ Cash grant for poor/SSS
- ☐ Others cash transfers

PAID SICK LEAVE AMOUNT IN PHP

DISABILITY GRANT AMOUNT IN PHP

CASH GRANT FOR POOR AMOUNT IN PHP

OTHERS CASH TRANSFERS AMOUNT IN PHP

HAVE YOU OR A FAMILY MEMBER RECEIVED ASSISTANCE FROM A RELATIVE OR FRIEND NOT LIVING WITH YOU AFTER HAVING SYMPTOMS OF TB UNTIL THE TB DIAGNOSIS? *

Period between () and (

).

- ◯ No
- ◯ Yes

HOW MUCH DID YOU GET?

in Php.

DO YOU CURRENTLY RECEIVE VOUCHERS, ENABLERS, HALFWAY HOUSE ACCOMMODATION, OR GOODS IN KIND TO COPE WITH TB SYMPTOMS BEFORE HAVING THE TB DIAGNOSIS? *

Period between () and (

).

- ◯ No
- ◯ Yes

WHAT ESTIMATED AMOUNT PER MONTH?

TRAVEL VOUCHER/TREATMENT ALLOWANCE	FOOD SUPPORT PACKAGE

OTHER, ENABLERS ETC.

FROM WHOM DO YOU RECEIVE THE VOUCHER/ GOODS?

- ☐ Government
- ☐ NGO
- ☐ Employer
- ☐ Private donation
- ☐ Other

PLEASE EXPLAIN 'OTHER'

HOW MANY ADULT AND CHILDREN REGULARLY SLEEP IN YOUR HOUSE? (INCLUDING PATIENT, IF VARIABLE, AT TIME OF DIAGNOSIS)

NUMBER OF ADULTS (AGED 15 AND UP)	NUMBER OF CHILDREN (YOUNGER THAN 15)

HOW MANY ROOMS ARE THERE IN THE HOUSE EXCLUDING THE BATHROOM?

*Total number of rooms **including kitchen**.*

HAS THE TB ILLNESS AFFECTED YOUR SOCIAL OR PRIVATE LIFE IN ANY WAY? IF YES, IN WHAT WAY? *

from symptoms started () and before the start of the current TB treatment(

)

- ☐ Not affected in any way
- ☐ Lack of access to food
- ☐ Divorce or separated from spouse/partner
- ☐ Loss of job and/or loss of working days
- ☐ Interrupted schooling
- ☐ Social exclusion
- ☐ Other

PLEASE EXPLAIN 'OTHER'

» Coping

DID YOU OR YOUR HOUSEHOLD USE ANY SAVINGS (CASH OR BANK DEPOSITS) TO COVER COSTS DUE TO THE SYMPTOMS OF TB UNTIL THE TB DIAGNOSIS? *

AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS

.

from symptoms started () and before the start of the current TB treatment(

)

- ◯ No
- ◯ Yes

HOW MUCH DID YOU USE...?

AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS.

from symptoms started () and before the start of the current TB treatment(

)

DID YOU BORROW ANY MONEY OR PAWN YOUR ASSETS TO COVER COSTS DUE TO THE TB SYMPTOMS? *

AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS

.

from symptoms started () and before the start of the current TB treatment(

)

- ◯ No
- ◯ Yes

HOW MUCH DID YOU BORROW OR GET FROM PAWNING...?

AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS.

FROM WHOM DID YOU BORROW OR PAWN?

- ☐ GSIS
- ☐ SSS
- ☐ Pag-ibig
- ☐ Microfinance institution
- ☐ Relative/Friend
- ☐ Credit union
- ☐ Bank
- ☐ Informal lender
- ☐ Pawnshop
- ☐ Other

ARE YOU EXPECTED TO PAY THE LOAN(S) OR PAWN BACK?

- ◯ No
- ◯ Yes

HAVE YOU STARTED PAYING BACK THE LOAN? IF NO, WHEN WILL YOU START?

- ◯ Yes, before treatment started
- ◯ No, it will start during the intensive treatment phase
- ◯ No, it will start during the continuation phase
- ◯ No, timing to start repayment is not decided yet

AMOUNT OF PAYBACK

WHAT IS THE REPAYMENT ON THE LOAN, EXCLUDING INTEREST?

Get TOTAL if multiple loans.

WHAT IS THE REPAYMENT ON THE INTEREST?

INTEREST ONLY

Get TOTAL if multiple loans.

HAVE YOU SOLD ANY OF YOUR PROPERTY TO FINANCE THE COST DUE TO THE SYMPTOMS OF TB?

AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS

.

from symptoms started () and before the start of the current TB treatment(

)

- ◯ No
- ◯ Yes

WHAT DID YOU SELL?

- ☐ Land
- ☐ Livestock
- ☐ Transport/vehicle
- ☐ Household item
- ☐ Farm produce
- ☐ Gold/jewelry
- ☐ Other

HOW MUCH MONEY DID YOU RECEIVE FROM THE SALE OF ALL ITEMS OF YOUR PROPERTY...?

AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS.

THE ASSETS THAT YOU SOLD WERE THEY PREVIOUSLY SUPPORTING THE FAMILY INCOME (OR EXPENDITURE)?

- ◯ No
- ◯ Yes

INDICATE MONTHLY INCOME PREVIOUSLY GENERATED BY THE ASSETS.

WHAT IS THE ESTIMATED MARKET VALUE OF ALL THE PROPERTY YOU SOLD?

DID ANYONE IN YOUR HOUSEHOLD DROP OUT OF SCHOOL OR INTERRUPT SCHOOLING TO ASSIST THE HOUSEHOLD AS A CONSEQUENCE OF THE SYMPTOMS OF TB?
AFTER HAVING SYMPTOMS OF TB BUT BEFORE THE DIAGNOSIS

Period between () and (

).

- ◯ No
- ◯ Yes

HOW MANY HOUSEHOLD MEMBERS DID DROP OUT FROM SCHOOLING?

TO WHAT EXTENT HAS THE CURRENT TB ILLNESS AFFECTED THE HOUSEHOLD FINANCIALLY?

So far after having TB symptoms
from symptoms started () and before the start of the current TB treatment(

)

- ◯ No impact
- ◯ Little impact
- ◯ Moderate impact
- ◯ Serious impact
- ◯ Very serious impact

» Other members of the household on treatment

ARE THERE ANY MEMBERS OF YOUR HOUSEHOLD CURRENTLY ON TB TREATMENT?

- ◯ No
- ◯ Yes

HOW MANY OF THEM?

» » TB Treatment facility for other household members

IF THIS PATIENT IS SCREENED AS "DIABETIC" OR "PRE-DIABETIC", WE WILL HAVE A SET OF QUESTIONS TO ASK COSTS RELATED TO DIABETES COSTS

- ◯ OK

DOES THE PATIENT HAVE "KNOWN-DIABETES", OR SCEENED AS "DIABETIC" OR "PRE-DIABETIC" IN ST-ATT?

- ◯ No
- ◯ Yes

Part 5. Diabetes treatment information

DO YOU USUALLY TAKE ANY MEDICATION AND TREATMENT FOR YOUR DIABETES? *

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD ANY DIABETES-RELATED COMPLICATIONS? *

- ◯ No
- ◯ Yes

WHAT KINDS OF COMPLICATIONS HAVE YOU EVER HAD?

- ☐ None
- ☐ Myocardial Infarction (heart attack)
- ☐ Ischaemic heart disease (heart failure)
- ☐ Other coronary events
- ☐ Stroke
- ☐ Leg problem (Ulcer, amputation etc)
- ☐ Kidney failure
- ☐ Eye problem (Cataract, Glaucoma, Blindness etc)
- ☐ Other

PLEASE SPECIFY "OTHER":

HAVE YOU EVER HAD MYOCARDIAL INFARCTION (HEART ATTACK)?

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD ISCHAEMIC HEART DISEASE (HEART FAILURE)?

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD OTHER CORONARY EVENTS?

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD STROKE?

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD LEG PROBLEM (ULCER, AMPUTATION ETC)?

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD KIDNEY FAILURE?

- ◯ No
- ◯ Yes

HAVE YOU EVER HAD EYE PROBLEM (CATARACT, GLAUCOMA, BLINDNESS ETC)?

- ◯ No
- ◯ Yes

FOLLOWING QUESTION(S) ARE RELATED TO REGULAR DRUG PICK-UP/FOLLOW-UP FOR DIABETES

*Please refer to the **USUAL COSTS at one visit** of regular follow-up/monitoring/treatment for diabetes.*

» information on health facility for diabetes drugs/treatment

WHERE DO YOU USUALLY GET THE DRUGS/MEDICATIONS FOR DIABETES?

If the patient has visited different places, tick the most recent one.

- ◯ Dispensary
- ◯ **Health facility**: Baranguay health station
- ◯ **Health facility**: Health center/Rural health unit
- ◯ Public hospital
- ◯ Pharmacy/Drugstore
- ◯ Herbalist/Traditional practitioners
- ◯ Private clinic
- ◯ Private hospital
- ◯ Community Health Worker
- ◯ Other

PLEASE SPECIFY "OTHER":

WHAT TESTS ARE USUALLY PERFORMED DURING DIABETES MANAGEMENT VISITS?

- ☐ Glucose
- ☐ liver function tests (LFTs)
- ☐ thyroid-stimulating hormone(TSH)
- ☐ Other
- ☐ None

PLEASE SPECIFY "OTHER":

» Costs of Diagnosis/Drug pick-up/Follow-up for DIABETES

USUAL COSTS OF DIAGNOSIS/DRUG PICK-UP/FOLLOW-UP FOR DIABETES

*Please refer to the **USUAL COSTS at one visit** for diabetes*

DO YOU OR A HOUSEHOLD MEMBER PICK UP DIABETES DRUGS TO BE TAKEN AWAY FROM HEALTH FACILITY?
including pharmacy/drug-store/clinic/hospital

- ◯ No
- ◯ Yes

HOW OFTEN DO YOU OR A HOUSEHOLD MEMBER USUALLY PICK UP DIABETES DRUGS?

- ◯ Every day
- ◯ Six times a week
- ◯ Five times a week
- ◯ Four times a week
- ◯ Three times a week
- ◯ Twice a week
- ◯ Every week
- ◯ Every two weeks
- ◯ Every three weeks
- ◯ Every month
- ◯ Every five weeks
- ◯ Every six weeks
- ◯ Other

PLEASE SPECIFY:

» » Travel time

TRAVEL TIME TO THE FACILITY (ROUND-TRIP)
(Minutes/hours/days spent to travel to and from facility)

DAYS	HOURS

MINUTES

» » Time spent in the facility

TIME SPENT IN THE FACILITY
(Fill in hours/minutes for outpatient visits for follow-up/monitoring for diabetes)

HOURS	MINUTES

PART A : MEDICAL CHARGES/PAYMENTS (PAYMENT AT THE FACILITY!)

MEDICAL CHARGES/PAYMENTS FOR REGULAR VISIT FOR DIABETES

*Please refer to the **USUAL COSTS at one visit** for diabetes.*

PAYMENTS FOR LABORATORY TESTS *such as glucose, Liver function tests (LFTs), Thyroid-Stimulating Hormone(TSH)*	OTHER PROCEDURES *Out-of-pocket payments for any other tests related to diabetes*
PAYMENTS FOR MEDICINE/DRUGS *Any medicine prescribed for diabetes*	CONSULTATION FEE *Other charges, not covered under day charge, including direct payment to health care staff*
SUPPLEMENTS/VITAMINS PRESCRIBED AT THE FACILITY *such as nutritional supplements*	OTHER *Any other expenses for medical payments*

TOTAL MEDICAL PAYMENTS (IF THE PATIENT CAN'T DISAGGREGATE MEDICAL COSTS)

Please only fill this if the patient was not able to give you the full details of the expenses. For a calculated total of the expenses, wait for next screen.

PART B : NON-MEDICAL CHARGES/PAYMENTS

NON-MEDICAL CHARGES/PAYMENTS FOR REGULAR VISIT FOR DIABETES

*Please refer to the **USUAL COSTS at one visit** for diabetes.*

TRAVEL/TRANSPORTATION COSTS (ROUND-TRIP) *Out-of-pocket payments for travel to the facility (does not include income loss), for both patient and any household member.*	EXPENSE FOR FOOD AND DRINK DURING HEALTH CARE VISIT *Out-of-pocket payments for additional food bought in relation to travelling the health care visit, and during visit for both patient and any household member.*
ACCOMMODATION COSTS *Includes out-of-pocket payments related to renting a room/bed during health care visits, and any other non-medical payments related to health care visit, for both patient and any household member.*	OTHER *Any other expenses for non-medical expenses (photo copy, mobile load, mask etc)*

TOTAL NON-MEDICAL PAYMENTS (IF THE PATIENT CAN'T DISAGGREGATE NON-MEDICAL COSTS)

» » Part C: Caring for dependents

DO YOU USUALLY HAVE TO MAKE ALTERNATIVE ARRANGEMENTS FOR CHILDCARE OR CARING FOR OTHER DEPENDANTS IN ORDER TO VISIT HEALTH FACILITY FOR DIABETES?

- ◯ No
- ◯ Yes

WHO IS USUALLY TAKING CARE OF YOUR DEPENDANTS/CHILD(REN) WHILE YOU ARE TRAVELLING TO OR AT THE HEALTH FACILITY FOR DIABETES CARE?

- ◯ Other family member
- ◯ Friend
- ◯ Paid childcare

HOW MUCH DID YOU PAY FOR THAT CARE?

FOLLOWING QUESTIONS ARE RELATED TO IRREGULAR VISIT(S) COMPLICATIONS DUE TO DIABETES APART FROM REGULAR DRUG PICK-UP/FOLLOW-UP

from symptoms started () and before the start of the current TB treatment(

).

» information on expenses on diabetes complications

AFTER HAVING SYMPTOMS OF THE CURRENT TB

, HAVE YOU HAD IRREGULAR FACILITY VISITS DUE TO ANY DIABETES COMPLICATIONS?

Period between () and (

).

- ◯ No
- ◯ Yes

HOW MANY TIMES DID YOU HAVE IRREGULAR FACILITY VISITS DUE TO ANY DIABETES COMPLICATIONS?

Period between () and (

).

WHAT WERE THE REASONS FOR THE IRREGULAR VISITS

- ☐ None
- ☐ Myocardial Infarction (heart attack)
- ☐ Ischaemic heart disease (heart failure)
- ☐ Other coronary events
- ☐ Stroke
- ☐ Leg problem (Ulcer, amputation etc)
- ☐ Kidney failure
- ☐ Eye problem (Cataract, Glaucoma, Blindness etc)
- ☐ Other

PLEASE SPECIFY "OTHER":

WAS THE FACILITY THE SAME FACILITY YOU USULALLY VISIT FOR DRUG PICK-UP?

- ◯ No
- ◯ Yes

» » Travel time for irregular visits

TRAVEL TIME TO THE FACILITY (ROUND-TRIP) *(Minutes/hours/days spent to travel to and from facility)*	
DAYS	HOURS
MINUTES	

» » Time spent in the facility for irregular visits

TIME SPENT IN THE FACILITY *(Fill in hours/minutes for outpatient visits for follow-up/monitoring for diabetes)*	
HOURS	MINUTES
PART A : MEDICAL CHARGES/PAYMENTS (AT THE FACILITY!)	
MEDICAL CHARGES/PAYMENTS FOR IRREGULAR VISITS FOR DIABETES *Please refer to the **COSTS at the last irregular visit** for diabetes.*	
PAYMENTS FOR LABORATORY TESTS *such as glucose, Liver function tests (LFTs), Thyroid-Stimulating Hormone(TSH)*	OTHER PROCEDURES *Out-of-pocket payments for any other tests related to diabetes*
PAYMENTS FOR MEDICINE/DRUGS *Any medicine prescribed for diabetes*	CONSULTATION FEE *Other charges, not covered under day charge, including direct payment to health care staff*
SUPPLEMENTS/VITAMINS PRESCRIBED AT THE FACILITY *such as nutritional supplements*	OTHER *Any other expenses for medical payments*
TOTAL MEDICAL PAYMENTS (IF THE PATIENT CAN'T DISAGGREGATE MEDICAL COSTS) *Please only fill this if the patient was not able to give you the full details of the expenses. For a calculated total of the expenses, wait for next screen.*	
PART B : NON-MEDICAL CHARGES/PAYMENTS	
NON-MEDICAL CHARGES/PAYMENTS FOR IRREGULAR VISIT FOR DIABETES *Please refer to the **COSTS at the last irregular visit** for diabetes.*	
TRAVEL/TRANSPORTATION COSTS (ROUND-TRIP) *Out-of-pocket payments for travel to the facility (does not include income loss), for both patient and any household member.*	EXPENSE FOR FOOD AND DRINK DURING HEALTH CARE VISIT *Out-of-pocket payments for additional food bought in relation to travelling the health care visit, and during visit for both patient and any household member.*

ACCOMMODATION COSTS	OTHER
Includes out-of-pocket payments related to renting a room/bed during health care visits, and any other non-medical payments related to health care visit, for both patient and any household member.	*Any other expenses for non-medical expenses (photo copy, mobile load, mask etc)*

TOTAL NON-MEDICAL PAYMENTS (IF THE PATIENT CAN'T DISAGGREGATE NON-MEDICAL COSTS)

» » Part C: Caring for dependents

DID YOU HAVE TO MAKE ALTERNATIVE ARRANGEMENTS FOR CHILDCARE OR CARING FOR OTHER DEPENDANTS FOR THE IRREGULAR FACILITY VISITS?

*Please refer to the **the last irregular visit** for diabetes.*

- ◯ No
- ◯ Yes

WHO WAS TAKING CARE OF YOUR DEPENDANTS/CHILD(REN) WHILE YOU ARE IN HEALTH FACILITY FOR UNSCHEDULED VISITS FOR DIABETES?

*Please refer to the **the last irregular visit** for diabetes.*

- ◯ Other family member
- ◯ Friend
- ◯ Paid childcare

HOW MUCH DID YOU PAY FOR THAT CARE?

*Please refer to the **COSTS at the last irregular visit** for diabetes.*

FOLLOWING QUESTIONS ARE RELATED TO HOSPITALIZATION DUE TO DIABETES **AFTER HAVING SYMPTOM OF CURRENT TB**

from symptoms started () and before the start of the current TB treatment(

).

HAVE YOU BEEN HOSPITALIZED DUE TO DIABETES? **AFTER HAVING SYMPTOM OF CURRENT TB**

Period between () and (

).

- ◯ No
- ◯ Yes

HOW MANY TIMES HAVE YOU BEEN HOSPITALIZED DUE TO DIABETES? **AFTER HAVING SYMPTOM OF CURRENT TB**

Period between () and (

).

WHAT WERE THE REASONS FOR THE HOSPITALIZATION(S)

- [ ] None
- [ ] Myocardial Infarction (heart attack)
- [ ] Ischaemic heart disease (heart failure)
- [ ] Other coronary events
- [ ] Stroke
- [ ] Leg problem (Ulcer, amputation etc)
- [ ] Kidney failure
- [ ] Eye problem (Cataract, Glaucoma, Blindness etc)
- [ ] Other

PLEASE SPECIFY "OTHER":

WAS THE FACILITY FOR HOSPITALIZATION(S) THE SAME FACILITY YOU USULALLY VISIT FOR DRUG PICK-UP?

- ◯ No
- ◯ Yes

» information on expenses on diabetes hospitalization

» » Travel time

TRAVEL TIME TO THE FACILITY FOR HOSPITALIZATION(S) (ROUND-TRIP)

round-trip for the LAST hospitalization due to diabetes

DAYS	HOURS

MINUTES

DURATION OF HOSPITALIZATION

In days. for the LAST hospitalization due to diabetes

PART A: MEDICAL CHARGES/PAYMENTS AT HEALTH FACILITY
PAYMENTS FOR HOSPITALIZATION DUE TO DIABETES

for the LAST hospitalization due to diabetes

PAYMENTS FOR LABORATORY TESTS DURING HOSPITALIZATION(S) *such as glucose, Liver function tests (LFTs), Thyroid-Stimulating Hormone(TSH)*	OTHER PROCEDURES DURING HOSPITALIZATION(S) *Out-of-pocket payments for any other tests related to diabetes*

PAYMENTS FOR MEDICINE/DRUGS DURING HOSPITALIZATION(S) *Any medicine prescribed for diabetes*	CONSULTATION FEE DURING HOSPITALIZATION(S) *Other charges, not covered under day charge, including direct payment to health care staff*
SUPPLEMENTS/VITAMINS DURING HOSPITALIZATION(S) *such as nutritional supplements*	ROOM AND BOARD / DAY CHARGES (FOR HOSPITALIZATION ONLY) IN TOTAL *Fees for hospital days. Only for hospitalizations.*
OTHER *Any other expenses incurred during hospitalizations*	TOTAL MEDICAL PAYMENTS (IF THE PATIENT CAN'T DISAGGREGATE MEDICAL COSTS)

PART B : NON-MEDICAL CHARGES/PAYMENTS FOR DIABETES HOSPITALIZATION

for the LAST hospitalization due to diabetes

TRAVEL/TRANSPORTATION COSTS (ROUND-TRIP) *Out-of-pocket payments for travel to and from the facility (does not include income loss), for both patient and any household member.*	EXPENSE FOR FOOD AND DRINK DURING HOSPITALIZATION *Out-of-pocket payments for additional food bought in relation to travelling the health care visit, and during HOSPITALIZATION for both patient and any household member.*
ACCOMMODATION COSTS *Includes out-of-pocket payments related to renting a room/bed during HOSPITALIZATION for both patient and any household member.*	OTHER *Any other expenses for non-medical expenses (photo copy, mobile load, mask etc) related to HOSPITALIZATION due to diabetes*

TOTAL NON-MEDICAL PAYMENTS (IF THE PATIENT CAN'T DISAGGREGATE NON-MEDICAL COSTS)

HEALTH INSURANCE REIMBURSEMENT FOR DIABETES

*Amount reimbursed **After having SYMPTOM of the current TB** through medical insurance for **DIABETES** so far, does not include expected future reimbursement.*
Period between () and (

).

» Costs for nutritional/food supplements

FOLLOWING QUESTIONS ARE RELATED TO EXPENSES TO NUTRITIONAL SUPPLEMENT AND SPECIAL FOOD/DRINK DUE TO DIABETES OUTSIDE OF REGULAR DIET

DO YOU BUY ANY NUTRITIONAL SUPPLEMENTS/SPECIAL FOODS/DRINKS OUTSIDE YOUR REGULAR DIET BECAUSE OF DIABETES, FOR EXAMPLE VITAMINS, MEAT, ENERGY DRINKS, OR FRUITS AS RECOMMENDED BY HEALTH CARE STAFF? *

- ◯ No
- ◯ Yes

COSTS FOR NUTRITIONAL SUPPLEMENTS AND SPECIAL FOOD/DRINKS FOR DIABETES OUTSIDE YOUR REGULAR DIET

past one month (30 days prior to interview)

EXPENSES ON NUTRITIONAL SUPPLEMENTS/VITAMINS APART FROM PAYMENT TO PRESCRIBED SUPPLEMENT AT HEALTH FACILITIES	SPECIAL EXPENSES ON MEAT (AND ALSO EGG)
SPECIAL EXPENSES ON FISH	SPECIAL EXPENSES ON DRINKS WITH VITAMIN/CARNITINE OR MILK ETC
SPECIAL EXPENSES ON FRUITS/VEGETABLES	

PLEASE INFORM THE PATIENT THAT WE WILL HAVE THE NEXT INTERVIEW FOR COSTING AT THE END OF INTENSIVE PHASE: *

EXPECTED DATE IS AROUND INVALID DATE

.

◯ OK

Interview guide for diabetes provider costs

The questions below are a guide for the topic areas that need to be covered in the data collection. They will be adapted as the study progresses and further understanding is obtained of the study setting and activities being costed.

Note to interviewers: In advance, make sure you are fully familiar with the interview questions. Questions should be added where a participant mentions something of interest or touches on something that needs further clarification. Questions can be skipped where a participant answers the question in a previous response. It may not be necessary to go through all questions.

Ideally, the interview(s) should be conducted after the data collection of staff timesheet to understand the routine tasks involved in providing diabetes testing, drug-prescribing, consultation, etc. During the interview(s), please focus on the information especially for diabetes services related to testing and drug-prescribing.

A. Introduction

Thank you for agreeing to take part in this interview. My name is ..... and I am part of a team conducting research on provider costs for diabetes services in the Philippines.

I am now going to ask you some questions regarding your daily work or tasks related to diabetes services. As explained in the consent form, you are free to stop the interview at any time.

If you feel uncomfortable answering any questions, please feel free to tell me that you don't want to answer the question(s).

This interview will be audio-recorded and will take approximately 45 minutes. Thank you for your time.

B. Interview information

- Location of the interview
- People present during the interview
- Name of the interviewer
- Date of the interview
- Start time
- End time

C. General information

- What is the title of your job? (doctor, nurse, healthcare volunteer, etc.)
- How long have you been working in that capacity? (capture 3 values: total, in this facility, and/or in TB services)
- How many days are you currently working per week in this facility?

- What is your working hour in a day? (from xx AM to xx PM)
- Describe the typical working schedule from start of a day until the end of a day
- Describe routine tasks in a week you usually work (including TB-diabetes services and other services)

D. Diabetes screening and diagnostic tests for TB patients

- What kind of diabetes screening and/or diagnostic tests do you usually provide in daily work (for TB patients)?
- What is detail of the procedure/workflow of each type of screening/diagnostic tests (e.g. risk score assessment, HbA1c, RPG, FBS, OGTT etc)? (from the preparation until the completion)
- What is the average number of each type of screening/diagnostic tests you perform per week/month (e.g. risk score assessment, HbA1c, RPG, FBS for TB patients etc)?
- How many minutes (hours) does each type of screening/diagnostic test take? (total and also by step, e.g. preparation, consultation, testing itself, waiting time etc)
- What kind of equipment is used for each type of screening/diagnostic tests you provide?
- How many minutes (hours) does it take to use the equipment for each screening/diagnostic test?
- What kind of supplies is usually used for each type of screening/diagnostic tests you provide?
- What is the usual amount used for each type screening/diagnostic tests?
- Do you have any works/tasks for follow-up after each type of screening/diagnostic tests? (e.g. making follow-up phone call for other tests, documentation for referral etc).
- If you have any follow-up works/tasks, how many minutes (hours) does each type of follow-up works take?

E. Diabetes drug prescription (if you provide diabetes drugs to TB patients)

- How frequently patients with TB and diabetes visit your facility to pick their diabetes drugs? (e.g. once a week, every two weeks etc)
- What types and doses of diabetes drugs are usually prescribed?
- Approximately how many % of patients with diabetes treatment are taking each type of drugs?
  (e.g. Metformin xx %, Gliclazide xx %, Insulin xx %).
- What is the average amount of drug prescribed to a patient per month? (by type of diabetes drugs)
- What is detail of the procedure/workflow of drug-prescription (e.g. preparation, consultation, documentation, actual prescription etc)
- How many minutes (hours) does each drug prescription take? (total)
- What kind of supplies/consumables is usually used for each drug prescription?
- What is the usual amount used for each drug prescription?

F. Any other diabetes management for TB patients (if applicable)

- Please describe workflow of diabetes counselling for TB patients, and time consumed for each counselling/consultation

- Please describe workflow of diabetes consultation for drug initiation, and time consumed for each consultation for drug initiation
- Please describe workflow of diabetes consultation for regular monitoring, and time consumed for each consultation for regular monitoring for TB patients
- Please describe workflow of diabetes consultation for adverse events/complications, and time consumed for each consultation for adverse events/complications for TB patients

G. Impact of COVID-19 on diabetes services

- Does (did) COVID-19 outbreak affect your daily work for providing diabetes services? If so, how?
- Does (did) COVID-19 outbreak affect patterns of patients visits?
  e.g. reduction in:
  - frequency of facility visits
  - number of patients newly diagnosed as being diabetic
  - adherence/compliance of taking diabetes medications

  etc

Supplementary material 3. Additional analysis for costs incurred by people with TB

With the human capital approach, productivity losses as indirect costs were estimated by multiplying an estimated hourly wage, reported lost time per one visit by purpose of visits and frequency of each visit type in each treatment phase. If lost time was reported in days, one day was converted into 8 hours assuming 8 working hours per day. An hourly wage was estimated for each patient using reported working hours per week and monthly income before having TB. With the human capital approach, we were able to compare the full TB illness episode. Using the longitudinal method, the mean total cost was estimated at USD 307 (95%CI: USD 257-357). Using the cross-sectional design, the mean total cost was at USD 264 (95%CI: USD 225-304) with 20%:80% for the proportion of patients in the TB intensive and continuation phases respectively. The result was consistent regardless of the proportion of patients by the TB treatment phase: USD 272 (95%CI: USD 233-312) with 35%:65%, and USD 271 (95%CI: USD 232-310) with 50%:50% (**Table 28**).

Table 28. Detail of costs incurred per TB-affected households, by design, mean (95%CI), human capital approach

TB patient costs, US$			Longitudinal			Cross-sectional								
						Proportion of samples in intensive and continuation phases								
						20:80			35:65			50:50		
			Mean	(95% CI)	%	Mean	(95% CI)	%	Mean	(95% CI)	%	Mean	(95% CI)	%
Pre-TB diagnosis	Direct medical costs		28.7	(20.1-37.3)	9.3%	13.9	(14.9-18.5)	5.3%	16.2	(14.4-18.1)	6.0%	16.7	(14.9-18.5)	6.2%
	Direct non-medical costs		29.1	(24.3-33.9)	9.5%	18.4	(19.7-27.3)	7.0%	19.6	(17.2-22.1)	7.2%	23.5	(19.7-27.3)	8.7%
	Indirect costs		40.1	(31.1-49.1)	13.1%	37.1	(31.6-42.6)	0.0%	34.7	(29.4-40.0)	0.0%	35.2	(30.5-39.9)	0.0%
Post-TB diagnosis	Direct medical costs	Drug pickup	0.05	(0-0.1)	0.0%	0.002	(0.001-0.02)	0.0%	0.004	(0-0.009)	0.0%	0.01	(0.001-0.02)	0.0%
		Directly observed therapy	0.0	(0.0-0.0)	0.0%	0.0	(0.0-0.0)	0.0%	0.0	(0.0-0.0)	0.0%	0.0	(0.0-0.0)	0.0%
		Follow-up	1.8	(0.9-2.6)	0.6%	1.5	(0.2-2.2)	0.6%	1.9	(0.8-3.1)	0.7%	1.2	(0.2-2.2)	0.4%
		Hospitalization	1.8	(0-4.3)	0.6%	2.7	(0-4.8)	1.0%	2.2	(0-5.8)	0.8%	2.1	(0-4.8)	0.8%
	Direct non-medical costs	Accommodation	0.06	(0-0.1)	0.0%	0.5	(0.2-0.7)	0.2%	0.3	(0.2-0.4)	0.1%	0.4	(0.2-0.7)	0.1%
		Food	3.6	(2.6-4.6)	1.2%	7.6	(3.5-10.6)	2.9%	7.6	(3.6-11.7)	2.8%	7.0	(3.5-10.6)	2.6%
		Travel	19.2	(16.2-22.1)	6.3%	33.4	(22.9-47.3)	12.6%	32.9	(22.1-43.8)	12.1%	35.1	(22.9-47.3)	12.9%
		Nutrition supplement	45.8	(40.0-51.7)	14.9%	51.7	(44.2-60.0)	19.6%	57.5	(48.4-66.7)	21.1%	52.1	(44.2-60.0)	19.2%
	Indirect costs		136.7	(96.7-176.8)	44.5%	97.4	(71.4-123.4)	36.9%	97.2	(72.1-122.3)	35.7%	98.4	(74.0-122.9)	36.3%

Total direct medical costs	32.3	(23.3-41.3)	10.5%	18.1	(16.5-23.4)	6.8%	20.4	(16.0-24.8)	7.5%	20.0	(16.5-23.4)	7.4%
Total direct non-medical costs	97.7	(87.6-107.8)	31.8%	111.6	(0-136.4)	42.2%	118.1	(0-136.4)	43.4%	118.1	(0-136.4)	43.5%
Indirect costs (human capital approach)	176.9	(134.5-219.2)	57.6%	134.5	(105.6-163.3)	50.9%	131.9	(104.4-159.4)	48.5%	133.6	(107.3-159.8)	49.2%
Total cost	307.1	(257.1-357.1)	100.0%	264.3	(224.8-303.7)	100.0%	272.1	(232.7-311.6)	100.0%	271.3	(232.3-310.4)	100.0%

Table 29. Composition and phase of costs incurred by TB-affected households in the Philippines, 2018-2020 USD, output approach

During TB treatment, DR-TB patients incurred higher direct non-medical costs compared to DS-TB patients at intensive phase (DR-TB: USD 78.7, DS-TB 19.9, p<0.001), middle of continuation phase (DR-TB: USD 44.5, DS-TB USD 18.2, p=0.001) and end of continuation phase (DR-TB: USD 41.9, DS-TB: USD 17.5, p<0.001). DR-TB patients also faced larger income loss in intensive phase (DR-TB: USD 722.0, DS-TB: USD 341.8. p<0.001).

Costs associated with accessing care for TB, US$		**Drug-susceptible TB**		**Drug-resistant TB**		**All TB patients**		**p-value***
		Mean	**(95% CI)**	**Mean**	**(95% CI)**	**Mean**	**(95% CI)**	
Cost category | Phase of incurred costs								
Direct medical	Before TB diagnosis	26.3	(20.7-32.0)	46.2	(0.0-104.8)	28.7	(20.1-37.3)	0.510
	Intensive phase	0.8	(0.3-1.3)	10.7	(0.0-31.5)	2.0	(0-4.5)	0.351
	Middle of continuation phase	0.8	(0.2-1.3)	0.0	(0.0-0.0)	0.7	(0.2-1.2)	0.007
	End of continuation phase	1.0	(0.2-1.8)	0.2	(0.0-0.5)	0.9	(0.2-1.6)	0.067
Direct non-medical	Before TB diagnosis	28.2	(22.9-33.4)	35.7	(25.0-46.4)	29.1	(24.3-33.9)	0.219
	Intensive phase	19.9	(17.6-22.2)	78.7	(54.6-102.8)	26.9	(23.0-30.8)	<0.001
	Middle of continuation phase	18.2	(15.9-20.6)	44.5	(30.0-59.1)	21.4	(18.6-24.2)	0.001
	End of continuation phase	17.5	(15.4-19.6)	41.9	(32.0-51.7)	20.4	(18.1-22.7)	<0.001
Income loss	Before TB diagnosis	219.7	(155.8-283.6)	216.5	(94.8-338.3)	219.3	(161.2-277.4)	0.964
	Intensive phase	341.8	(277.5-406.2)	722.0	(516.9-927.1)	387.1	(324.4-449.9)	0.001
	Middle of continuation phase	83.5	(63.0-104.1)	146.2	(62.3-230.1)	91.0	(70.3-111.8)	0.156
	End of continuation phase	103.3	(79.0-127.6)	113.6	(50.3-177.0)	104.6	(81.9-127.3)	0.766
Total	Direct medical costs	28.9	(23.1-34.8)	57.0	(0.0-118.7)	32.3	(23.3-41.3)	0.374
	Direct non-medical costs	83.8	(75.0-92.6)	200.8	(155.1-246.4)	97.7	(87.6-107.8)	<0.001
	Income loss	748.4	(609.2-887.7)	1 198.4	(853.8-1 543.0)	802.0	(672.0-932.1)	0.018
	Total	861.1	(719.8-1 002.5)	1 456.2	(1 077.5-1 834.8)	932.0	(798.4-1 065.7)	0.004

*results of t-test

Table 30. Composition and phase of costs incurred by TB-affected households in the Philippines, 2018-2020 USD, output approach, by drug-resistance

TB patient costs, US$			Drug susceptible TB								Drug resistant TB							
			Longitudinal		Cross-sectional						Longitudinal		Cross-sectional					
					20:80		35:65		50:50				20:80		35:65		50:50	
			Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Pre-TB diagnosis	Direct medical costs		26.3	(20.7-32.0)	13.7	(12.2-15.2)	16.2	(14.2-18.3)	18.0	(16.1-20.0)	46.2	(0.0-104.8)	14.7	(10.1-19.3)	16.3	(12.8-19.7)	8.3	(5.4-11.2)
	Direct non-medical costs		28.2	(22.9-33.4)	17.4	(16.1-18.7)	17.9	(15.3-20.5)	23.7	(19.3-28.0)	35.7	(25.0-46.4)	24.4	(20.7-28.2)	30.7	(23.7-37.7)	22.1	(17.2-26.9)
	Income loss		219.7	(155.8 - 283.6)	N/A		N/A		N/A		216.5	(94.8-338.3)	N/A		N/A		N/A	
Post-TB diagnosis	Direct medical costs	Drug pickup	0.06	(0.0-0.1)	0.002	(0.0-0.007)	0.004	(0.0-0.01)	0.01	(0.001-0.02)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)
		Directly observed therapy	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)
		Follow-up	2.0	(1.0-3.0)	1.8	(0.6-2.9)	2.3	(0.9-3.6)	1.4	(0.2-2.6)	0.2	(0.0-0.5)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)
		Hospitalization	0.5	(0.1-1.0)	0.8	(0.0-1.8)	0.5	(0.0-1.0)	0.8	(0.0-1.8)	10.7	(0.0-31.5)	14.5	(0.0-39.9)	13.0	(0.0-38.4)	9.9	(0.0-29.3)
	Direct non-medical costs	Accommodation	0.07	(0.0-0.1)	0.5	(0.2-0.8)	0.2	(0.1-0.3)	0.4	(0.09-0.7)	0.0	(0.0-0.0)	0.9	(0.3-1.5)	0.7	(0.2-1.3)	0.7	(0.2-1.3)
		Food	2.6	(1.9-3.2)	2.7	(1.7-3.6)	2.7	(1.7-3.7)	2.5	(1.5-3.4)	11.2	(4.9-17.5)	38.3	(14.3-62.4)	38.8	(11.0-66.5)	36.0	(11.9-60.1)
		Travel	12.2	(11.0-13.4)	13.5	(11.7-15.3)	12.7	(11.0-14.5)	12.5	(10.8-14.3)	70.3	(52.4-88.2)	157.2	(106.0 - 208.4)	159.3	(89.3-229.2)	178.8	(98.4-259.2)
		Nutrition supplement	40.7	(35.6-45.9)	45.7	(38.5-52.9)	47.5	(40.8-54.1)	43.9	(38.1-49.6)	83.6	(54.4-112.7)	89.3	(56.8-121.8)	120.5	(71.9-169.1)	104.6	(62.1-147.1)
	Income loss		528.7	(437.3 - 620.1)	396.9	(312.0 - 481.7)	599.4	(401.8 - 797.0)	716.9	(514.9-918.9)	981.8	(676.0-1287.7)	601.0	(325.0 - 877.0)	715.1	(396.1 - 1034.1)	690.0	(404.4 - 975.5)

Total direct medical costs	28.9	(23.1-34.8)	16.3	(14.0-18.7)	19.0	(16.4-21.5)	20.2	(17.6-22.9)	57.0	(0.0-118.7)	29.1	(0.9-57.3)	29.3	(1.7-56.9)	18.3	(0.0-37.6)
Total direct non-medical costs	83.8	(75.0-92.6)	79.7	(71.5-87.9)	81.0	(72.2-89.7)	82.9	(74.1-91.7)	200.8	(155.1-246.4)	310.2	(232.5-387.9)	349.9	(245.9-454.0)	342.2	(235.1-449.2)
Income loss	748.4	(609.2-887.7)	396.9	(312.0-481.7)	599.4	(401.8-797.0)	716.9	(514.9-918.9)	1198.4	(853.8-1543.0)	601.0	(325.0-877.0)	715.1	(396.1-1034.1)	690.0	(404.4-975.5)
Total cost	861.1	(719.8-1002.5)	492.9	(406.6-579.2)	699.3	(500.2-898.4)	820.0	(616.0-1024.1)	1456.2	(1077.5-1834.8)	940.3	(628.9-1251.8)	1094.4	(731.2-1457.5)	1050.4	(715.3-1385.5)
Total cost (excluding income loss before TB diagnosis)	641.4	(547.7-735.2)	492.9	(406.6-579.2)	699.3	(500.2-898.4)	820.0	(616.0-1024.1)	1239.6	(895.6-1583.7)	940.3	(628.9-1251.8)	1094.4	(731.2-1457.5)	1050.4	(715.3-1385.5)

Supplementary material 4. Additional analysis for diabetes outpatient provider costs

Table 31. Unit costs for diabetes interventions by sampled facility

Study site	Risk assessment	HbA1c	Referral service		FBS		RPG		OGTT	Drug prescription	Consultation
			General	Complication	Glucometer	Chemistry analyser	Glucometer	Chemistry analyser			
Rural health unit #1	0.75		0.82	3.00	2.45	4.60	2.15			1.94	3.38
City health office #1	0.72		0.58	1.43	2.65		2.28			1.45	1.35
City health office #2	0.83		1.00	1.82	1.33	2.50	1.28			2.04	3.56
Rural health unit #2	0.33		0.60	1.02	0.91	3.02	0.90			1.10	1.31
City health office #3	0.63		0.67	0.72	0.84	2.88	0.75			1.72	0.75
Rural health unit #3	0.27		0.25	1.12	1.85	2.76	1.85			1.12	1.26
Rural health unit #4	0.27		0.65	0.94	1.52		1.50			0.65	1.57
Hospital #1						3.94	1.94			1.05	1.63
Hospital #2	0.51	2.91	0.50	2.06	3.32	2.42	0.15	3.28	23.72	1.24	2.06
Rural health unit #5	0.57		1.74	2.22	0.77	2.10	0.71			0.80	2.23
Rural health unit #6	0.39		1.02	1.66	1.04	2.66	1.05			1.05	1.70

FBS: Fasting blood glucose, HbA1c: Glycated haemoglobin, OGTT: Oral glucose tolerance test, RPG: Random plasma glucose, SD: Standard deviation USD: United States Dollar, PHP: Philippine Peso