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Epidemiology and Control of diabetes - tuberculosis comorbidity in Eswatini: protocol for the prospective study of tuberculosis patients on predictive factors, treatment outcomes and patient management practices

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ABSTRACT

Introduction Previous studies indicate people with diabetes mellitus (DM) may have varying treatment outcomes when receiving treatment for tuberculosis (TB) and that TB infection or its treatment may predispose them to develop an abnormal blood glucose or type 2 DM. This has implications for Eswatini which is a high TB burden country and with increasing cases of non-communicable diseases including DM. This study will describe the epidemiology of DM-TB comorbidity in a prospective cohort of patients receiving TB treatment and identify best practices for integration of care for non-communicable diseases into TB services in Eswatini.

Methods and analysis This study will employ a mixed-methods approach. Data from a prospective cohort of newly enrolled patients with TB at 12 health facilities from 1 June 2022 to 30 September 2022, and followed up to 30 April 2023, will be used. For the qualitative, key informants who provide TB services at the health facilities will be interviewed. Quantitative data from patients will be analysed descriptively and by tests of association and multivariate modelling. Key informant interviews from healthcare workers will be analysed using content analysis.

Ethics and dissemination This research has been approved by the Eswatini Health and Human Research Review Board and participant confidentiality will be maintained. COVID-19 safety measures to reduce the risk of infection or transmission by researchers and participants have been instituted. Key programmatic findings and how they can impact healthcare delivery and access will be presented to the specific programme in the Eswatini Ministry of Health and other relevant stakeholders.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The use of a prospective cohort design allows for the collection of more accurate and complete data.
⇒ Interview of key informants provides useful background to different factors which impact services access by patients with tuberculosis (TB).
⇒ Reduced sample size due to a reduced number of new patients with TB and short follow-up period.
⇒ Information on the incidence of diabetes mellitus (DM) or hyperglycaemia is limited due to a short follow-up period since DM may develop a few months after treatment.
⇒ Healthcare workers may provide limited information during the in-depth interview due to fear of reprimand by the health authorities.

INTRODUCTION

Background

The global pandemic caused by the novel coronavirus has affected all countries and territories of the world.[1 2] High daily cases and mortality have been recorded in the USA, India and Brazil, closely followed by countries in Europe and Asia.[3 4] Mortality data indicated a high mortality rate in patients with comorbidities such as diabetes mellitus (DM), cardiovascular and respiratory diseases, kidney and liver diseases, those recovering from transplants and the critically ill.[2 4 5] This indicates that non-communicable diseases (NCDs) have a propensity to coexist and complicate other disease conditions, most times, negatively altering the prognosis. Thus, the development of an appropriate context-specific method of managing commonly occurring NCDs is vital in the context of infectious disease.

In the last two decades, tuberculosis (TB) and HIV infection gained attention from global leaders, healthcare workers, researchers and non-governmental organisations. This was due to their impact on the

economy of high burden countries, the health of individuals and pressure on the health system. With concerted efforts from different stakeholders, the prevalence of these two diseases has been controlled in high-income countries while some low-income and middle-income countries are gradually achieving epidemic control with stable infrastructures for a sustained response.[6 7]

While all efforts concentrated on curtailing the impact of HIV/TB with visible results of its reduction globally, the NCDs, diverse with insidious onset, gradually increased and are now the highest cause of mortality globally.[8 9] NCDs now account for about 71% of global mortality.[10] This can partly be attributed to less-developed structures to combat NCDs with far less funding for NCD programmes compared with TB and HIV, especially in the low-income and middle-income countries which also have the highest incidence and prevalence of infectious diseases with high levels of poverty and social inequality.[11] This neglect of NCDs has become evident as the countries with a high burden of infectious diseases now record high mortality from NCDs. This indicates that both conditions (NCDs and infectious diseases) coexist in the community with each disease acting as an enabler for the other.[9 11 12] Major NCDs accounting for increased morbidity and mortality globally include cardiovascular diseases (17.9 million deaths—44%), cancers (23%), respiratory diseases (10%) and DM (1.5%).[10 13]

The coexistence of infectious diseases, particularly TB, with NCDs such as DM and hypertension has long been recognised by researchers with varying concepts on managing these conditions in the midst of dwindling resources for healthcare services.[14 15] People with DM have a greater risk of developing TB. This increased risk is possibly due to poor glycaemic control resulting in abnormal metabolism in macrophages and lymphocytes, which impacts the immune function of these cells. This predisposes to new TB infection or reactivation of latent TB in those who were previously infected.[12 14] On the contrary, the causes of impaired blood glucose during TB treatment are not clear. Current evidence points to an impaired glucose tolerance during TB treatment which may or may not resolve once treatment is completed.[16–18] This may be due to undiagnosed DM, stress response from infection which elevates stress hormones or abnormal functioning of the liver which results in abnormal endocrine function.[16 19]

Among known diabetics undergoing treatment for TB, there have been concerns of DM delaying sputum conversion leading to a poor outcome. This is yet to be fully confirmed.[12 14] A recent study from Ghana shows significantly fewer patients with hyperglycaemia had sputum conversion at 2 months of TB treatment compared with normoglycaemic patients, but not at 6 months.[20] Other factors that could impact TB treatment outcomes among people with DM include the non-integration of services that causes non-adherence, psychosocial factors such as stigma and increased economic burden of treatment for the two conditions which are paid for out-of-pocket in most low-income countries.[12 15] More recently, the COVID-19 pandemic impacted all service delivery and access to essential care. This was due to disruption in the supply of essential health commodities, widespread infection of healthcare workers with COVID-19 and restriction of movement which limited patients with TB from visiting health facilities. The impact of the pandemic and the different measures adopted to limit COVID-19 infection on access to TB services and treatment outcomes is yet to be quantified.

The Syndemics concept has been used to describe the symbiotic coexistence of diseases with associated inequity in access to health and social services, poverty and malnutrition resulting in increased morbidity and mortality in at-risk populations.[15 21] The Syndemics concept originated from high-income countries' observations that different disease conditions coexist and affect the communities, notably the minority populations and those with low socioeconomic status. Meanwhile, the concept has been extended to describe the comorbid conditions which exist in low-income and middle-income countries, like TB/HIV and NCDs.[15 21] With a gradual increase in lifespan in low-income and middle-income countries, the impact of NCDs particularly DM and hypertension, has become obvious. Morbidity and mortality due to TB and HIV have reduced because patients now access life-saving medications and observed morbidity and mortality is due to NCDs.[22–24]

In Eswatini, literature on DM in the population and DM-TB comorbidity is scarce with easily accessible data being estimates by WHO and International Diabetes Federation (IDF).[25] Available studies have centred on HIV-NCD comorbidity and developing effective integration models to address the increasing cases of NCDs among HIV patients.[26] A 2020 study on the prevalence of abnormal blood glucose metabolism in adults indicated a 3.9% prevalence of type 2 DM (T2DM) in adults who attended the outpatient department of a tertiary hospital but no data is available on associated comorbidities with TB or HIV.[25] Similarly, the IDF estimates the prevalence of DM in Eswatini is 3.6% in people aged 20–79 years while the age-adjusted prevalence for impaired glucose tolerance is 6.9%.[27]

Significant progress has been made in the Kingdom of Eswatini in the provision of HIV/TB services with HIV incidence in people 15 years and above reducing from 2.5% in 2011 to 1.4% in 2017.[28] Similarly, TB incidence reduced from 1069/100 000 in 2009 to 363/100 000 in 2019.[6] Despite these achievements in HIV/TB control, more is required to improve the quality of life of her citizens as more present with NCDs, notably cardiovascular diseases, DM and cancers.[29] Data from the Eswatini Ministry of Health indicate DM accounted for 12% of outpatient department visits in 2018 and 5.9% of all in-patient mortality.[29] Given the burden of TB in Eswatini, an increase in cases of DM due to lifestyle changes, obesity and ageing may limit further successes in TB prevention activities. Further complicating the dilemma is the

absence of reliable data on the prevalence of the common NCDs in the general population and diverse population groups, with the most recent reliable data on the burden of NCDs in Eswatini being the WHO STEPwise approach to surveillance (STEPS) Survey, conducted in 2014.[30] Therefore, research on DM in people receiving treatment for TB will provide insight into the different factors that may impact DM and TB treatment outcomes and provide direction for effective health services delivery. This will put Eswatini on track towards achieving WHO's target of reducing by a third, the burden of NCDs by 2025.[9] In this research, reference to diabetes means T2DM.

Rationale for the research

1. There is a lack of reliable data on the burden of DM in Eswatini, both in the general population and different population subgroups. This study at its conclusion will generate reliable information on DM-TB comorbidity and the prevalence of DM and hyperglycaemia in patients receiving treatment for TB.
2. With the availability of life-saving HIV/TB medications, people are living longer but are now exposed to developing diabetes due to changing lifestyles, ageing and possibly TB infection. This study will identify the risk factors for developing diabetes or hyperglycaemia in people receiving treatment for TB.
3. There is an absence of evidence on factors hindering effective management of diabetes at healthcare facilities providing TB services in Eswatini. This research will identify these factors and propose context-specific solutions to improve the integration of TB and DM care.

Conceptual framework

The study will be based on the Social-Ecological Model which examines different interactions which determine the health outcome of an individual.[31] The different individual, interpersonal, community, organisational and policy/environmental contexts which can influence health outcomes in Eswatini in line with the social-ecological model will be considered. This will be contextualised to ascertain how these affect the services received by people while receiving treatment for TB and how service delivery can be improved.

The conceptual framework presented in figure 1 highlights the possible interactions which determine the health outcome of an individual. The components of the socialecological model have been unpacked to show

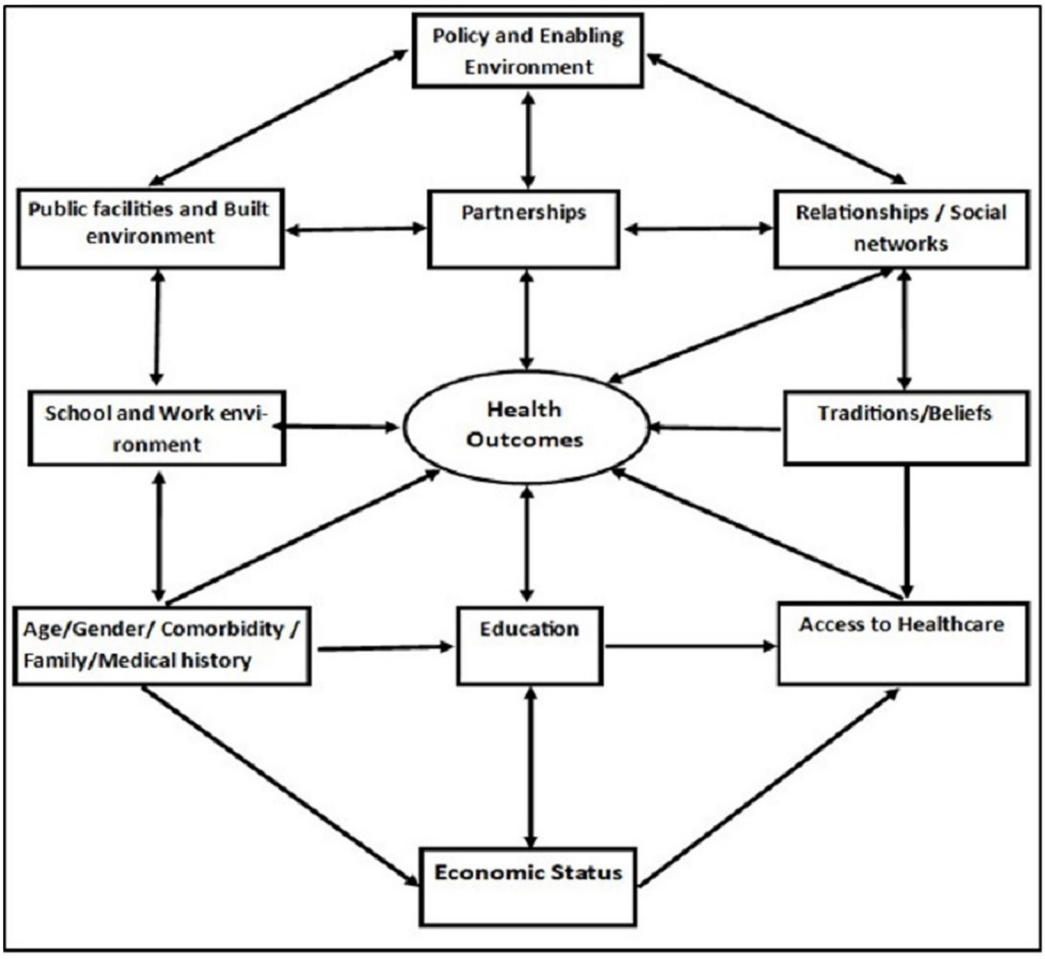

Figure 1 Conceptual framework for the study.

Table 1 Descriptive summary of different research questions and study requirements

S/n	Research question	Endpoint	Required variables	Proposed analysis method
1.	What is the prevalence and incidence of DM/hyperglycaemia in patients receiving treatment for tuberculosis in Eswatini?	► Prevalence of DM in diagnosed patients with TB ► Identified risk factors ► Incidence of elevated blood glucose in those receiving treatment for TB ► Identified predictive factors	► Sociodemographic variables ► Clinical variables ► Baseline and follow-up data	Descriptive: Frequency tables with percentages, Mean (SD) and/or median (IQR) Comparative analysis: Pearson $\chi 2$ test or Fischer's exact test for categorical variables. T-test or Mann-Whitney for continuous variables. Statistical analysis: Univariate and multivariate logistic regression and mixed-effects model. Missing data: If ≥10%, imputation of missing data will be done, and the results averaged across all the datasets imputed. Sensitivity analysis: Nested multilevel logistic regression analysis with random effects at two levels (region and individual) to account for clustering at regions. Model Fitness: Hosmer-Lemeshow goodness of fit test
2.	Does DM or hyperglycaemia affect TB treatment outcome in patients receiving treatment for tuberculosis in Eswatini?	► Findings of comparative analysis of TB treatment outcome in patients with diabetics/hyperglycaemia and those without	► Sociodemographic variables ► Clinical variables ► Baseline and follow-up data	Descriptive: Frequency tables with percentages, Mean (SD) and median (IQR) Comparative analysis: Pearson $\chi 2$ or Fischer's exact test for categorical variables. T-test or Mann Whitney for continuous variables. Statistical analysis: Univariate and multivariate logistic or linear regression models. Missing data: If ≥10%, imputation of missing data will be done, and the results averaged across all the datasets imputed. Model Fitness: Hosmer-Lemeshow goodness of fit test, residual sum of squares
3.	What factors limit the effective integration of diabetes care into TB Services provision at the health facilities providing TB care in Eswatini?	► Identified factors ► Recommendations for effective services delivery	► All the variables from the qualitative questionnaire	Descriptive: Frequency tables with percentages, Mean (SD) and median (IQR) Qualitative analysis: Analysis of both deductive and inductive codes from healthcare worker's interviews.

DM, diabetes mellitus; TB, tuberculosis.

the different direct and indirect relationships that exist between the components and the health outcome of an individual. Other determinants of the health outcome of an individual such as demand and supply factors are not included here. This is to enable easy interpretation and application of this framework to the context of Eswatini.

RESEARCH QUESTIONS AND OBJECTIVES

Research question

The study research questions with the desired endpoint and required variables are presented in table 1.

Objectives

This research aims to describe the epidemiology, predictive factors and control measures of diabetes in a prospective cohort of patients who will be treated for TB. The objectives are to:

1. Describe the epidemiology of diabetes-TB comorbidity in a prospective cohort of patients receiving TB treatment in Eswatini from 1 June 2022 to 30 April 2023.
2. Identify factors that predict the occurrence of diabetes (or hyperglycaemia) in patients receiving TB treatment in Eswatini from 1 June 2022 to 30 April 2023.
3. Describe the effect of blood glucose on TB treatment outcome in patients receiving treatment for TB in Eswatini from 1 June 2022 to 30 April 2023, and ascertain if diabetes is a precursor of first-line TB drug resistance.
4. Ascertain if there is a relationship between baseline BMI, HIV status, blood glucose level and TB treatment outcomes in patients treated for TB in Eswatini.
5. Identify factors that hinder effective DM care among diabetics receiving TB treatment in Eswatini and

propose a context-specific approach to address these factors.

METHODOLOGY

Study design

A mixed-methods prospective study design will be used for this study. For the quantitative part, a prospective cohort approach will be used to review data of consecutive newly diagnosed patients with TB enrolled on care and followed up from 1 June 2022 to 30 April 2023. The qualitative part will involve the interview of select clinical healthcare workers who provide direct care to patients with TB. Data from the prospective cohort will address objectives 1, 2, 3 and 4 while the healthcare worker's interview will address objective 5.

Setting

The study will be conducted at 12 health facilities providing TB services in the four regions of Eswatini (Mbabane Government Hospital, The Luke Commission, Phocweni Clinic, TB Centre, Siphofaneni clinic, Mankayane Hospital, AHF Lamvelase Clinic, Raleigh Fitkin Memorial Hospital, AHF Matsapha, Pigg's Peak Government Hospital, Nhlangano Health Centre, Hlathikulu Hospital TB Clinic). The health facilities are purposively selected because they see more patients with TB at any given time and have medical officers who review patients with TB with standard laboratories and X-ray facilities to aid patient investigations. Only complicated cases are referred to the National TB Referral Hospital. The National TB Referral Hospital is excluded from this study as it was converted to COVID-19 isolation and treatment centre and all patients relocated to one of these selected facilities. Eswatini is a landlocked country in Southern Africa with a population of about 1.2 million.[29] It is surrounded by South Africa, except in the North-East which is bordered by Mozambique.

Patients on drug-susceptible TB treatment in Eswatini receive treatment for 6–9 months depending on if they have received the first-line drug before and are followed up monthly till after two consecutive sputum conversions (expected in the second or third month). Monthly follow-up continues after sputum conversion till they complete treatment. Sputum microscopy for acid-fast bacilli (AFB) and culture are reviewed on each follow-up visit. Drug-resistant TB (DRTB) patients are initially admitted until they have two consecutive negative sputum culture tests (sputum conversion) before discharge and monthly follow-up visits for clinical evaluation which includes medication review, sputum AFB and culture results review, and general assessment. The duration of treatment for DRTB is varied and can last 12–24 months depending on the drug regimen and response to treatment.

Patients receive routine laboratory assessments during their treatment including random blood glucose at baseline, twice during treatment and at end of treatment before final discharge. Three follow-up visits postdischarge is advocated but most clients do not keep this appointment except those receiving antiretroviral medications from the same facility.

Study population

From 2015 to 2020, about 19 000 patients received treatment for TB in Eswatini and 6% of these were paediatric patients.[32] The male-female ratio ranged from 1.4 to 1.6 within the same period and the TB/HIV coinfection rate in 2020 was 64%.[32] Report of other comorbidities, for example, T2DM, or hypertension is not available. For the years 2015–2020, about 98% of all patients have a documented treatment outcome for all types of TB and the treatment success rate in 2019 and 2020 was 89% and 86%, respectively.[32] There are different cadres of healthcare workers who provide care for patients with TB but those who will participate in the key informant interview will be nurses and doctors.

Sampling and sample size

A consecutive sampling approach will be used to enrol newly diagnosed patients with TB on the study. Current TB programme data indicate that on average, in a period of 4 months, about 410 patients are enrolled on TB care at the 12 selected health facilities. Therefore, it is estimated that a minimum of 380–430 participants will be enrolled on this study. Using an estimated diabetes prevalence of 3.6% in Eswatini,[27] an effect size of 0.05 and an alpha of 5%, the estimated power of this study is 98%. A sample size range of 106–582 has been used in similar studies,[18 33–36] therefore, this anticipated sample size will be adequate for the different outcomes.

One doctor and one nurse will be purposively selected and interviewed per health facility until saturation is achieved in each group and no more new information is obtained from the healthcare workers.[37] Since the study will be conducted at 12 health facilities, there will be a minimum of 24 study participants for the qualitative study.

Inclusion criteria

New patients aged 18 and above who will initiate treatment for any form of TB at any of the 12 selected health facilities from 1 June 2022 up to 30 September 2022 will be eligible for inclusion irrespective of sex. Patients meeting the above criteria who are able and willing to provide informed consent will be included.

Healthcare workers to be included in the study must have clinical training (doctors or nurses), regularly review patients' medical records, have worked at the health facility for a minimum of 12 months, and be willing to provide informed consent to participate in the study.

Data collection

Data collection from patients (baseline and during follow-up) and interviews of healthcare workers will be conducted by two trained research staff conversant with TB data. Data from patients will be entered into an electronic form developed using Research Electronic Data

Capture (REDCap). Patients' demographic and clinical information will be extracted at baseline and during follow-up visits (month 2, month 5/end of treatment) till patients are discharged from care and have a treatment outcome documented in their case file per updated WHO guidance[38] (online supplemental file 1).

A structured questionnaire developed in REDCap will be administered electronically to healthcare workers to identify their views on DM-TB management and challenges to DM-TB services provision at the health facilities. This questionnaire has three sections that should take approximately 15 min to complete—demographic information, occupational information and patient care-related questions. An interview will complement the electronically administered questionnaire (online supplemental file 2) to obtain healthcare workers' perspectives on service delivery and recommendations for improvement. An interview guide has been developed to assist the interviewers during interviews (online supplemental file 3) to ensure the quality of the interview responses. The interview guide will be reviewed to ensure it is coherent and the questions asked directly operationalise the study research question. Before interviewing the healthcare workers, deductive codes will be discussed with the research team to act as a guide during the interviews and the final codes will include those raised by the participants. The interviewee will be allowed to respond with limited interruptions. Recorders will be used so that the correct information is transcribed once the interview is completed. The anticipated duration of the interview is 30–45 min.

Approach for patient data collection

The TB units at the different health facilities where patients with TB are enrolled and reviewed maintain patients' clinical information which will be available to the study team. Noting that some TB units may not have the facility for testing and recording baseline glucose measurements for patients and during follow-up, point of care Accu-Check Active Glucometer (Roche) (with test strips and lancets) will be placed at the different TB Units for the measurement and documentation of blood glucose at baseline and during the second and fifth month follow-up visits. Based on this, baseline data will be collected at enrolment, while follow-up data for the second-month visits will commence in the third month and that for the fifth-month visits will commence in the sixth month (figure 2). This is consistent with the guidelines for the recording of patient information when receiving treatment for TB in Eswatini (online supplemental file 4). The provision of Accu-Check Active Glucometer (Roche) is to ensure patients receive a blood glucose measurement at each visit and the study does not become an additional burden to the health facility. Study participants will not be required to fast before a blood glucose test as such a strict routine may not be achievable in programmatic conditions. All study participants with abnormal random baseline or follow-up glucose measurements will be referred to a clinician for further evaluation and care. At the end of the study, the glucometers will be donated to the TB unit for continued use with support from the health facility's laboratory.

The nurses in the TB unit will be oriented on how to use the Glucometer as a point of care test by a trained laboratory technician from the health facility's laboratory using a standardised guide (online supplemental file 5). The Glucometer will initially be calibrated by the health facility's laboratory technician at baseline, at the end of month 2 and the end of month 4. This is to ensure the quality of the results produced by the Glucometer is standardised and possible calibration errors are identified and rectified. Additional baseline patient sociodemographic information—educational status, marital status, occupation, smoking and alcohol status which is not routinely collected will be obtained for this study.

Staff at the TB clinic will be oriented on the study and one healthcare worker at each of the 12 health facilities will be trained on how to approach and consent new patients into the study. Facilities will be visited monthly with a follow-up call weekly for updates.

Statistical methods and analysis

Baseline characteristics of variables in the patients' dataset will be presented in a table. Prevalence of DM or impaired glucose will be determined based on the number of patients with DM or impaired glucose at baseline and during the treatment period expressed as a proportion of all the patients treated in the same period. This will be determined overall and by the type of TB disease (drug-sensitive TB, rifampicin-resistant TB, DRTB or extra drug-resistant TB). The occurrence of abnormal

Description	Timeline										
	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11
	Jun-22	Jul-22	Aug-22	Sep-22	Oct-22	Nov-22	Dec-22	Jan-23	Feb-23	Mar-23	Apr-23
Baseline	Recruit	Recruit	Recruit	Recruit							
Follow up data 1 (Month 2)			Month 1 Recruits	Month 2 Recruits	Month 3 Recruits	Month 4 Recruits					
Follow up data 2 (Month 5)						Month 1 Recruits	Month 2 Recruits	Month 3 Recruits	Month 4 Recruits		
Follow up data for end of treatment								Month 1 Recruits	Month 2 Recruits	Month 3 Recruits	Month 4 Recruits

Figure 2 Schedule for data collection at baseline and during follow-up.

glucose during treatment will be determined based on the number of patients who had normal values at baseline but developed abnormal values during treatment or at the end of treatment. This will be determined overall, and by type of TB disease with additional analysis to estimate the mean and median time between TB diagnosis and identification of abnormal measurements. A logistic regression (or mixed effect model for repeated data) will be used to predict the occurrence of DM or hyperglycaemia.

Statistical tests will be significant if $p<0.05$. Different subanalysis, comparative and sensitivity analyses will be done to identify possible interactions which may exist between the different patient characteristics (eg, age, sex, HIV status) and hyperglycaemia, for example, testing to ascertain if there is an association between timing of culture conversion and blood glucose. The proposed statistical methods for the different research questions are presented in table 1.

Qualitative analysis in form of analysis of identified codes will be done to identify factors that hinder the care of diabetics receiving TB treatment. Recommendations for improvement will be coded and similar codes will be analysed and presented.

Study data entered into REDCap[39] will be extracted in Stata format and imported into Stata V.15 (Stata) for analysis. The software NVivo[40] will be used for the analysis of transcribed information from healthcare workers' interviews.

Patient and public involvement

Patients and members of the public were not involved in the study design and the development of this protocol. However, TB programme priorities were considered in the design of the study and protocol. Patients during their routine visits will be informed if their blood glucose measurement is within the normal values. Those with abnormal values will be referred for further review and care. Participating health facilities, healthcare workers, the TB programme and relevant stakeholders will be provided with feedback on the outcome of the study with direct recommendations on how to improve access to TB services and integrate NCD care into TB services.

ETHICS AND DISSEMINATION

Ethical considerations

Approval for the study has been obtained from the Eswatini Health and Human Research Review Board (Protocol Reference Number: EHHRRB036/2021).

Participation in the study will be optional. Patients and healthcare workers who will be interviewed will be oriented and provided with a study information sheet (online supplemental files 6 and 7). They will be required to provide informed consent before participating (online supplemental files 6 and 7) and healthcare workers' consent will include consent for the recording of their comments. Researchers administering the interviews will be required to attest they read out the information sheet to the study participants and answered all questions to their satisfaction before commencing the interview.

Data will be deidentified to ensure confidentiality. Each patient record and healthcare worker interviewed will be assigned a unique identification code. This code will assist with retrieving information in case there is missing data during analysis or a follow-up question. Identifiable information will only be available to the principal investigator and the deidentified data will be accessible to the study team for monitoring of data quality. All project data will be stored in a password protected hard drive to ensure data safety. Transcription will be done without linking names to comments to ensure confidentiality. Healthcare workers will be free to stop participating in the interview at any time without providing a reason. The risks to study participants are minimal and measures have been instituted to ensure confidentiality and safety of data and information from the patients and healthcare workers. Researchers who will access patient data and interview healthcare workers will be required to sign a confidentiality and non-disclosure document (online supplemental file 8).

Standard COVID-19 control measures will be adopted during data extraction and a virtual interview option will be available to limit infection and transmission of SARS-COV-2.

Dissemination

Several articles will be generated from this study for presentation either as a poster or oral presentation at local and international conferences and for publication in peer-reviewed journals.

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REFERENCES

1 World Health Organisation. Novel Coronavirus (2019-nCoV) situation report - 1. 21 January 2020 Geneva, 2020. Available: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf?sfvrsn=20a99c10_4 [Accessed 30 Oct 2021].
2 Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054–62.
3 Johns Hopkins University. Coronavirus resource center, 2021. Available: https://coronavirus.jhu.edu/map.html [Accessed 20 Oct 2021].
4 World Health Organisation. Coronavirus disease (COVID-19) situation report – 114. May 13 2020 Geneva, 2020. Available: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200513-covid-19-sitrep-114.pdf?sfvrsn=17ebbbe_4 [Accessed 25 Oct 2021].
5 Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ* 2020;368:m1198.
6 World Health Organisation. Global tuberculosis report 2020 Geneva, 2020. Available: https://www.who.int/tb/publications/global_report/en/ [Accessed 30 Oct 2021].
7 The Joint United Nations Programme on HIV/AIDS. Global HIV & AIDS statistics - 2019 factsheet, 2019. Available: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf [Accessed 30 Oct 2021].
8 Allen L. Are we facing a noncommunicable disease pandemic? *J Epidemiol Glob Health* 2017;7:5–9.
9 World Health Organisation. Global action plan and the prevention and control of non-communicable diseases, 2013–2020. Geneva, 2013. Available: https://www.who.int/nmh/events/ncd_action_plan/en/ [Accessed 20 Oct 2021].
10 World Health Organisation. Noncommunicable diseases: key facts Geneva, 2018. Available: https://www.who.int/es/news-room/fact-sheets/detail/noncommunicable-diseases [Accessed 20 Oct 2021].
11 Reubi D, Herrick C, Brown T. The politics of non-communicable diseases in the global South. *Health Place* 2016;39:179–87.
12 Niazi AK, Kalra S. Diabetes and tuberculosis: a review of the role of optimal glycemic control. *J Diabetes Metab Disord* 2012;11:28.
13 Patel P, Rose CE, Collins PY, *et al*. Noncommunicable diseases among HIV-infected persons in low-income and middle-income countries: a systematic review and meta-analysis. *AIDS* 2018;32:S5–20.
14 Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis* 2009;9:737–46.
15 Mendenhall E, Kohrt BA, Norris SA, *et al*. Non-communicable disease syndemics: poverty, depression, and diabetes among low-income populations. *Lancet* 2017;389:951–63.
16 Magee MJ, Salindri AD, Kyaw NTT, *et al*. Stress hyperglycemia in patients with tuberculosis disease: epidemiology and clinical implications. *Curr Diab Rep* 2018;18:1–10.
17 Luies L, du Preez I. The echo of pulmonary tuberculosis: mechanisms of clinical symptoms and other disease-induced systemic complications. *Clin Microbiol Rev* 2020;33:20. doi:10.1128/CMR.00036-20
18 Krishnappa D, Sharma SK, Singh AD, *et al*. Impact of tuberculosis on glycaemic status: a neglected association. *Indian J Med Res* 2019;149:384.
19 Yorke E, Atiase Y, Akpalu J, *et al*. The bidirectional relationship between tuberculosis and diabetes. *Tuberc Res Treat* 2017;2017:1–6. doi:10.1155/2017/1702578
20 Yorke E, Boima V, Dey ID, *et al*. Transient impact of dysglycemia on sputum conversion among smear-positive tuberculosis patients in a tertiary care facility in Ghana. *Clin Med Insights Circ Respir Pulm Med* 2021;15:11795484211039830
21 Singer M. *Introduction to syndemics: a critical systems approach to public and community health*. John Wiley & Sons, 2009.
22 Achwoka D, Waruru A, Chen T-H, *et al*. Noncommunicable disease burden among HIV patients in care: a national retrospective longitudinal analysis of HIV-treatment outcomes in Kenya, 2003-2013. *BMC Public Health* 2019;19:372.
23 Coetzee L, Bogler L, De Neve J-W, *et al*. HIV, antiretroviral therapy and non-communicable diseases in sub-Saharan Africa: empirical evidence from 44 countries over the period 2000 to 2016. *J Int AIDS Soc* 2019;22:e25364.
24 Haacker M, Bärnighausen T, Atun R. HIV and the growing health burden from noncommunicable diseases in Botswana: modelling study. *J Glob Health* 2019;9:010428.
25 Gbadamosi MA, Tlou B. Prevalence of abnormal glucose metabolism among adults attending an outpatient department at a tertiary referral hospital in Swaziland: a cross-sectional study. *BMC Public Health* 2020;20:1–12.
26 Matanje Mwagomba BL, Ameh S, Bongomin P, *et al*. Opportunities and challenges for evidence-informed HIV-noncommunicable disease integrated care policies and programs: lessons from Malawi, South Africa, Swaziland and Kenya. *AIDS* 2018;32:S21–32.
27 International Diabetes Federation. *IDF diabetes atlas tenth edition 2021 Brussels*. Belgium: International Diabetes Federation, 2021. https://diabetesatlas.org/en/resources/
28 Nkambule R, Nuwagaba-Biribonwoha H, Mnisi Z. *Substantial progress in confronting the HIV epidemic in Swaziland: first evidence of national impact*, 2017.
29 Eswatini Ministry of Health. *2020 annual NCD report*. Mbabane: Government of Eswatini, 2021.
30 Swaziland Ministry of Health. WHO STEPS - noncommunicable disease risk factor surveillance report Mbabane: Government of Swaziland, 2015. Available: https://www.who.int/ncds/surveillance/steps/Swaziland_2014_STEPS_Report.pdf?ua=1 [Accessed 25 Oct 2021].
31 Stokols D. Translating social ecological theory into guidelines for community health promotion. *Am J Health Promot* 1996;10:282–98.
32 Eswatini Ministry of Health. *2020 annual national tuberculosis control program (NTCP) report*, 2021.
33 Jawad F, Shera AS, Memon R, *et al*. Glucose intolerance in pulmonary tuberculosis. *J Pak Med Assoc* 1995;45:237–8.
34 Tabarsi P, Baghaei P, Marjani M, *et al*. Changes in glycosylated haemoglobin and treatment outcomes in patients with tuberculosis in Iran: a cohort study. *J Diabetes Metab Disord* 2014;13:1–6.
35 Moreira J, Castro R, Lamas C, *et al*. Hyperglycemia during tuberculosis treatment increases morbidity and mortality in a contemporary cohort of HIV-infected patients in Rio de Janeiro, Brazil. *Int J Infect Dis* 2018;69:11–19.
36 Diarra B, Tolofoudie M, Sarro YS, *et al*. Diabetes mellitus among new tuberculosis patients in Bamako, Mali. *J Clin Tuberc Other Mycobact Dis* 2019;17:100128.
37 Hennink M, Hutter I, Bailey A. *Qualitative research methods*. Sage, 2020.
38 World Health Organization. Meeting report of the WHO expert consultation on drug-resistant tuberculosis treatment outcome definitions, 17-19 November 2020 2021.
39 Harris PA, Taylor R, Minor BL, *et al*. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
40 QSR International Pty Ltd. NVivo (released in March 2020), 2020. Available: https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home [Accessed 30 Oct 2021].

Supplementary file 1: Proposed variables list for the study

Facility name: _____
Date of visit: DD/MM/YY

Baseline*: Sociodemographic*

1. Assigned unique id
2. Age
3. Sex
4. Weight
5. Height
6. Educational status
7. Marital status
8. Occupation
9. Region
10. Smoking
11. Alcohol
12. Family history of DM

Baseline*: Clinical*

13. HIV status
14. Year HIV Diagnosis
15. Past TB Treatment
16. Date TB diagnosis
17. Type of TB (Drug Sensitive, Rifampicin Resistant, Drug-Resistant, Extra-Drug Resistant)
18. TB Drugs Regimen
19. HIV Drugs Regimen
20. Last Viral Load result
21. DM on admission
22. DM Treatment

Baseline and follow-up variables

23. Visit Date (DD/MM/YY)
24. Fasting Blood Sugar (FBS) (mmol/l)
25. Systolic Blood Pressure (SBP) (mmHg)
26. Diastolic Blood Pressure (DBP) (mmHg)
27. Sputum Acid-Fast Bacilli (AFB)
28. Sputum Culture
29. Adverse Event
30. Adverse Event Type
31. DM Diagnosis
32. Treatment Outcome

Supplementary file 2: Healthcare Workers Interview Questionnaire

Date: _____

Health facility description (To be filled in by the researcher)

1. Questionnaire Identification Number: _____
2. Facility type: Hospital/Health centre/ Clinic
3. Facility location: Urban/Semi-urban/Rural

Section A: INTRODUCTIONS

- The researcher introduces herself and confirms the healthcare worker is the right one who is scheduled for the interview.
- The researcher gives an overview of the study to the healthcare worker and hands her a copy of the study information sheet (the healthcare worker would have received one by email some days before the interview).
- If the healthcare worker accepts to participate in the study, s/he is given the consent form to review and endorse.

Section B: SURVEY

Sociodemographic Details

1. Date of Birth: _____
2. Gender: Male/Female/Other
3. Region of residence: Hhohho/Lubombo/Manzini/Shiselweni

Occupational History

1. Region hospital is located: Hhohho/Lubombo/Manzini/Shiselweni
2. Occupation/profession type e.g., a. Nurse b. Doctor
3. Nature of work a. direct patient care c. Other
4. Highest qualification a. Certificate b. Diploma c. Degree d. Post-graduate
5. Total number of years in your profession _____
6. Duration of years providing care for TB patients _____
7. Received training for Non-communicable diseases Yes/No
8. Received specific training in TB/NCD care. Yes/No
9. Received specific training in TB/Diabetes care. Yes/No
10. Number of in-service training received in the last twelve-months _____

Patient Care related Questions

1. In a month how many TB patients on the average present with a non-communicable disease (NCD) in your hospital e.g. of NCD – hypertension, diabetes, asthma, cancers _____
2. What is the commonest NCD they present with? _____
3. In a month how many TB patients present with Diabetes Mellitus (This is baseline blood glucose >7.0 mmol/dl)? _____
4. Indicate Yes/No if the following are readily available at your health facility:
    a. Policy document on TB care
    b. Current National TB Treatment guidelines
    c. Standard Operating Procedure (SOP) for the care of TB patients with diabetes mellitus
    d. Training requirement for staff on non-communicable diseases
    e. Essential medicines list
5. Describe the protocol or give a summary of the protocol followed if "Yes" to 4C above.

_____

_____

6. If a TB patient has DM, is the treatment offered at the same consultation room? Yes/No
7. Where a TB patient is HIV positive and has diabetes mellitus, is the treatment for the three conditions offered at the same consultation room? Yes/No
8. Does your facility provide Hba1c? Yes/No
9. If Yes to 8 above, describe the referral process:

_____
_____

10. Indicate Yes/No if the following services are offered to TB clients at baseline:
    a. HIV Testing
    b. Fasting/random blood glucose
    c. Blood Pressure measurement
11. Indicate Yes/No if the following services are offered to TB clients during follow-up visits:
    a. HIV Testing
    b. Fasting/random blood glucose
    c. Blood Pressure measurement
12. Indicate if the following are available or not available for TB patient screening at your OPD:
    a. Sphygmomanometer
    b. Weighing scale
    c. Glucometer
    d. Urinalysis test strips
13. Indicate Yes/No if the following medications are available for dispensing at your facility:
    a. Insulin
    b. Oral DM drugs
    c. Antihypertensive medication
14. Indicate Yes/No if there has been a stock-out of the following medications at your hospital in the last six months:
    a. Glucometer test strips
    b. Urinalysis test strips
    c. Insulin
    d. Oral DM medication
    e. Antihypertensive medication
    f. At least one 1st line TB medication
15. How many clinical staff (doctors and nurses) provide care for TB patients in your hospital?
    _____

Section C: Qualitative Interview

Healthcare Providers Perspective

1. Considering the number of TB Patients seen daily at your TB department, do you think your department has enough clinical staff? _____

2. What best practices have your unit adopted that has improved the care of TB clients receiving treatment for Diabetes Mellitus?

_____
_____

3. What is your view of the current standard of care for TB patients? _____
4. Do you feel you are well trained and prepared to provide the required care for TB clients with DM?

_____
_____

5. Are there any challenges that hinder you from providing effective care to TB Patients in your hospital?

_____
_____

6. Are there any challenges that limit the provision of diabetes mellitus care to TB patients in your hospital?

_____
_____

7. What would you suggest that can improve services delivery for TB patients with diabetes mellitus?

_____
_____

8. In the last 18 months, how has the COVID-19 Pandemic affected your ability to provide care to TB patients with diabetes mellitus?

_____
_____

9. Other comments _____

Supplementary file 3: Interview guideline

This guideline provides an outline of the different questions the healthcare worker should be asked based on the different sections of the questionnaire. The researcher should adapt the questions and may not need to necessarily ask exactly the way it is written and should observe the healthcare worker for guiding cues during the interview.

This interview aims to obtain the healthcare workers perspectives on services accessed by the TB clients, those who are also being treated for DM, and those who develop DM during treatment. The interview will also identify best practices instituted by the healthcare workers to improve services, challenges they encounter during services delivery and some recommendations on what they think can be done to address the challenges.

Section A: Introduction

The first part of the interview aims to develop a rapport with the participant you are interviewing. It is important to develop a non-judgemental tone throughout the interview and to convey that there are no right or wrong answers.
Start by ensuring the participant is comfortable and at ease. Introduce yourself and confirm you have the right healthcare worker for an interview. Provide a recap about the study and give the healthcare worker a copy of the Study information sheet to review and the consent form to sign if they accept to participate in the study.

Turn the digital recorder on.

Example introduction – adapt as appropriate
Thank you for agreeing to be interviewed for our study today. As I explained earlier, we are studying the different processes involved in the provision of services for TB clients and, those with DM or those who develop DM during treatment. We are interviewing you to better understand this process and some challenges you encounter. This will enable us to develop recommendations that can help improve services delivery in the future.

We are interested in your opinion today; everything you say is very important to us. I will not talk much, but I want you to talk freely, and as much as you want. There are no “good” or “bad” answers.

Section B: Survey to provide a background on the healthcare worker and services delivery

This part of the interview aims to understand the background of the healthcare worker, processes adopted in the care of TB patients with TB, and availability of optimal work conditions which can enhance services provision.
Open the structured questionnaire on the tablet and allow the healthcare worker to respond to the short survey questions.

Provide clarity for any question that may not be clear.

Section C: Healthcare providers perspectives on services delivery

This part of the interview aims to understand how well equipped and confident health practitioners are in providing care for TB clients also receiving treatment for DM. This section will also elicit challenges encountered by health providers, innovative approaches adopted to solve problems and their recommendations for improving services delivery for TB clients and those also receiving treatment for DM. There will also be a further enquiry on the impact of the COVID-19 pandemic on the provision of TB services and how this has impacted services delivery for TB clients with DM.

Now, I would like to ask you some questions about your work, potential challenges, and some recommendations for improvement.

Considering the number of TB Patients seen daily at your TB department, do you think your department has enough clinical staff to attend to them?
Probes:

What is your view of the current standard of care for TB patients?
Probes: Any frustrations?

What best practices have your unit adopted that has improved the care of TB clients receiving treatment for Diabetes Mellitus?
Probes:

Do you feel you have adequate training to care for TB clients with DM?
Probes: Please elaborate on some areas you would like more training in.

What would you suggest that can improve services delivery for TB clients with DM?
Probes:

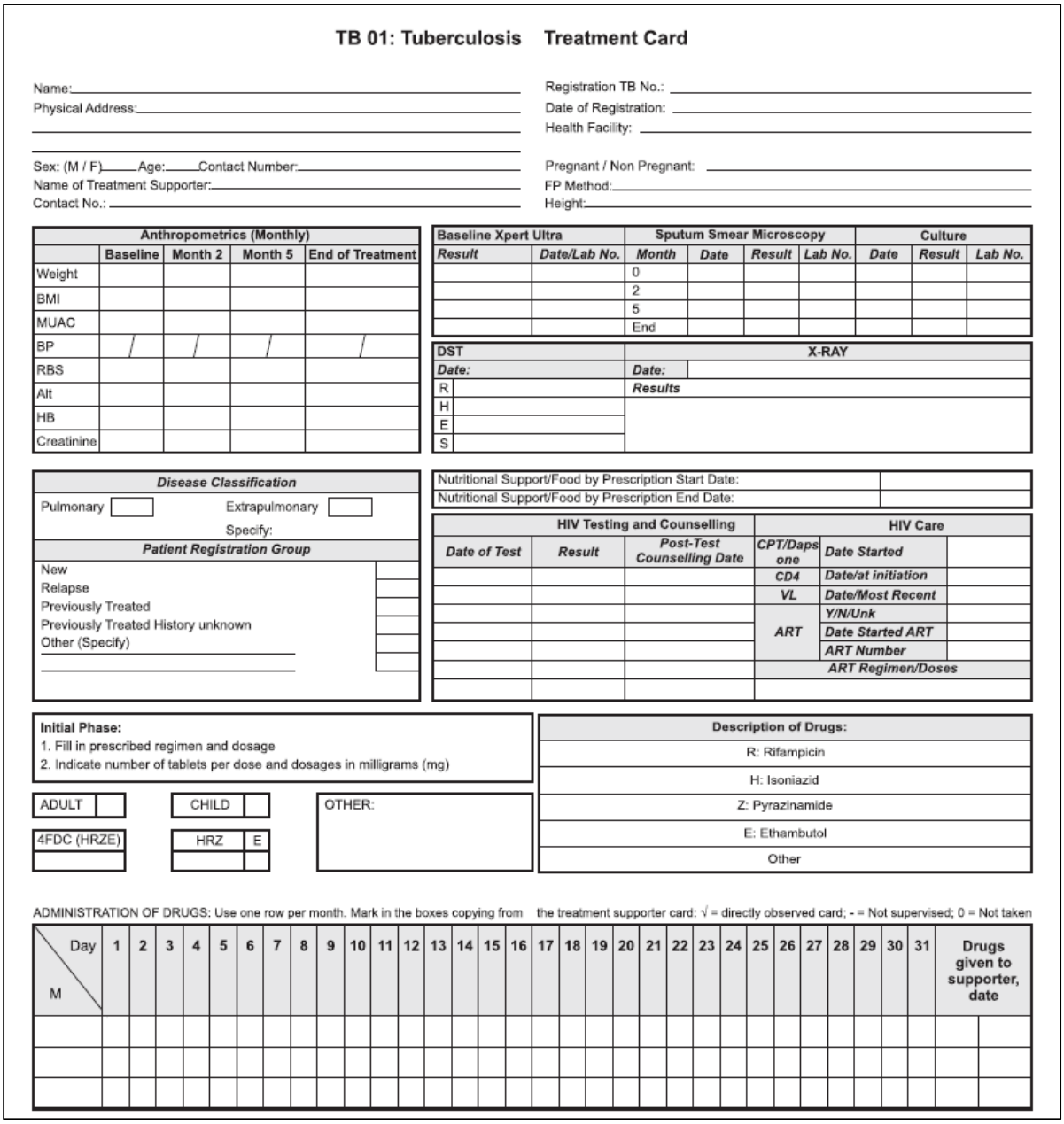
How has the COVID-19 Pandemic affected your ability to provide care to TB patients with DM?
Probes: Did you have to screen all your clients before attending to them?

Ending the Interview

Before closing the interview, allow the participant to make any further comments about the topics discussed or to ask questions.
Thank the participant for his/her time and for sharing experiences and views.

Williams V, *et al. BMJ Open* 2022; 12:e059254. doi: 10.1136/bmjopen-2021-059254

Supplementary File 4: TB Treatment Card



TB 01: Tuberculosis Treatment Card

Name: _____ Registration TB No.: _____
Physical Address: _____ Date of Registration: _____
_____ Health Facility: _____
_____
Sex: (M / F)____Age:____Contact Number: _____ Pregnant / Non Pregnant: _____
Name of Treatment Supporter: _____ FP Method: _____
Contact No.: _____ Height: _____

Anthropometrics (Monthly)				
	Baseline	Month 2	Month 5	End of Treatment
Weight				
BMI				
MUAC				
BP	/	/	/	/
RBS				
Alt				
HB				
Creatinine				

Baseline Xpert Ultra		Sputum Smear Microscopy				Culture		
Result	*Date/Lab No.*	*Month*	*Date*	*Result*	*Lab No.*	*Date*	*Result*	*Lab No.*
		0						
		2						
		5						
		End						

DST		X-RAY	
Date:		*Date:*	
R		*Results*	
H			
E			
S			

Disease Classification	
Pulmonary ☐ Extrapulmonary ☐	
Specify:	
Patient Registration Group	
New	
Relapse	
Previously Treated	
Previously Treated History unknown	
Other (Specify)	

Nutritional Support/Food by Prescription Start Date:	
Nutritional Support/Food by Prescription End Date:	

HIV Testing and Counselling			HIV Care	
Date of Test	*Result*	*Post-Test Counselling Date*	*CPT/Dapsone*	*Date Started*
			CD4	*Date/at initiation*
			VL	*Date/Most Recent*
			ART	*Y/N/Unk*
				Date Started ART
				ART Number
				ART Regimen/Doses

Initial Phase:
1. Fill in prescribed regimen and dosage
2. Indicate number of tablets per dose and dosages in milligrams (mg)

ADULT ☐ CHILD ☐ OTHER:

4FDC (HRZE)	HRZ	E

Description of Drugs:
R: Rifampicin
H: Isoniazid
Z: Pyrazinamide
E: Ethambutol
Other

ADMINISTRATION OF DRUGS: Use one row per month. Mark in the boxes copying from the treatment supporter card: √ = directly observed card; - = Not supervised; 0 = Not taken

Day / M	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Drugs given to supporter, date	

2. Continuation Phase: Prescribed regimen and doses

Day / M	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Drugs given to supporter, date	

Remarks:

Administration of IPT: *Use one row per contact, document date refill taken. *Dosage should be 30 tabs per month*

In case treatment has been interrupted, extend to month 7

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7
Contact 1							
Contact 2							
Contact 3							

Treatment Outcome ***(document date outcome assigned)***

Cured		Completed	
Failed		Lost to follow-up	
Died		Not evaluated	

Is treatment supporter present at end of treatment? Y N

Post Treatment Follow-up										
Visits	Anthopometrics								Smear	Culture
	Weight	BMI	MUAC	BP	RBS	Alt	HB	Creatinine		
Visit 1										
Visit 3										
Visit 2										

Supplementary file 5: Guidelines for Capillary Blood Glucose (CBG) Testing

Preparation

- Gather equipment required for the procedure
    - Gloves
    - Disposable lancet
    - Glucometer test strips
    - Glucose monitoring device (Glucometer)
    - Gauze/tissue
    - Sharps disposal box
    - Patients register and pen
- Check the expiry dates on the glucometer test strips.
- Ensure that the glucometer and the test strips have been calibrated together. Each batch of glucometer test strips will require calibration to the machine.

Patient preparation

- Obtain informed consent from the patient for the procedure – explain the need for the test and the benefits to the patient.
- Wash and dry hands to be tested.
- Note: The recommended site is the side of the distal ends of fingertips to minimize pain and injury to the bone. Avoid the little finger as the tissue may not be deep enough to prevent injury to the bone. Avoid the index finger and thumb as these are highly sensitive areas compared to other fingers. Avoid the arm if an intravenous infusion is underway or is the side of the body where a recent mastectomy, if any, was performed.

Process

- Bring out the glucometer from its packing and place it on the table
- Remove the glucose testing strip without touching the sensor tip from the container and insert it into the glucometer. This often leads to the glucometer turning itself on.
- Prime the lancet to no more than 2.0 mm to minimize the risk of bone injury.
- Firmly apply lancet to the site of sample collection and release the trigger on the lancet to pierce the skin. Dispose of the lancet in the sharps box.
- Wipe away the first drop of blood with a clean gauze or tissue as this drop of blood may contain intracellular or interstitial fluid, or is hemolyzed, both of which could affect the blood sample.
- Apply a gentle downward pressure close to the puncture site to facilitate blood flow and collection of the second drop of blood.
- Collect the second drop of blood as it forms by touching the tip of the glucose testing strip.
- Place the glucometer down and cover the site of skin puncture with a clean tissue. Pressure may need to be applied to stop further bleeding from the puncture site.
- The glucometer will provide a result at this stage unless there have been errors in collection; for example, insufficient sample, low battery, wrong code, or the machine times itself out.

- If an error displays on the glucometer, troubleshoot as appropriate.
- Document the patient's blood glucose measurement in the patient register and the date the test was conducted.
- Dispose of the glucose test strip in the sharps box.
- Wash hands and replace equipment in storage bag container.
- Inform the patient if the results is within normal values
- Where the reading falls outside the normal values, refer the patient to a doctor for immediate review.

Adapted from: Mathew TK, Tadi P. Blood glucose monitoring. In StatPearls [Internet] 2020 Aug 14. StatPearls Publishing.

Supplementary file 6: Patient information and consent form

Part 1: Study Information Sheet for patients

Patient guidance: ***Please read this document carefully and ask for clarity where it is required.***

Introduction

Previous studies conducted in other parts of the world have indicated that people with diabetes may have varying treatment outcomes when receiving treatment for tuberculosis and that treatment for tuberculosis may predispose them to develop diabetes. This study will verify the status of these claims in patients receiving TB treatment in Eswatini and also identify means of improving treatment outcomes for diabetic persons receiving treatment for tuberculosis. The title of this study is ***"Diabetes-Tuberculosis comorbidity: Epidemiology, Predictive factors, and Control in Eswatini"***. The principal investigator of this study, Dr Victor Williams will also utilise findings from this study to fulfil part of the requirement for the award of a Doctor of Philosophy degree (PhD) by the University Medical Centre, Utrecht University, Utrecht, Netherlands.

This research will be implemented at the different hospitals and health centres that provide TB services in Eswatini. These include Mbabane Government Hospital, The Luke Commission, Phocweni Clinic, TB Center, Siphofaneni clinic, Mankayane Hospital, AHF Lamvelase Clinic, Raleigh Fitkin Memorial Hospital, AHF Matsapha, Pigg's Peak Government Hospital, Nhlangano Health Center, Hlathikulu Hospital TB Clinic.

Aim of the research

The study aims to describe the epidemiology, predictive factors, and control measures of diabetes in patients who are being treated for tuberculosis in Eswatini. The study has four objectives and one of them is to identify factors that hinder effective Diabetes Mellitus care for diabetics receiving TB treatment in Eswatini and to propose a context-specific approach to address these factors. To achieve this objective, health care workers who directly provide care for these patients will be interviewed. As healthcare personnel who is experienced in the care of TB patients, you are invited to participate in this study.

If you agree to participate in the study, a convenient date and time will be arranged for you to be interviewed.

Potential benefits and risks

There will be no direct benefit for you from taking part in the interview. However, the information you provide will help the researcher understand the best practices and challenges in the care of TB clients with diabetes and provide recommendations that will help improve services delivery for these clients. Participating in the interview carry's a low risk for you as a participant if there is a breach of confidentiality but the researchers have been trained in research ethics to ensure your confidentiality. Comments you make will not be directly linked to your name in the final study report. Also, there is a possibility that the interview may evoke sad memories concerning your patients. Kindly let the interviewer know if you feel this way and would like to end the interview.

Voluntary participation

Your participation in this interview is voluntary. There are no right or wrong answers. You can at any time choose to withdraw from the study completely (including deletion of audio-recording and transcript of interview if you wish). You can decide not to take part or to stop taking part in this study at any time, without giving a reason, and without any impact on your work. We would like to record the interview, if you consent to this, solely for the study, to ensure we capture everything you say.

Confidentiality

The information you provide during the interview will be confidential and accessible only to the research team. The audio recording will only be heard by the research team. This will be transcribed onto paper and the original recording will be kept securely for the duration of the study. All written information collected (transcripts of interviews, notes, signed informed consent form) will be kept privately and anonymously (including password-protected storage) for about 10 years or as recommended by the Eswatini Health and Human Research Review Board (EHHRRB).

The researchers will make every effort to ensure that the information you provide as part of this study remains confidential. When using quotes from an interview, the researcher will make sure that the identity of the cited person cannot be revealed. Any information you share during the interview will be confidential and your privacy will be maintained. Also, the research assistants and interviewers conducting this research have been made to sign a confidentiality agreement to further ensure your confidentiality and privacy.

Contact for additional information

If you have any questions regarding this study, please contact the study's Principal Investigator Dr Victor Williams at +268 7618 4334; victormw55@gmail.com or P.O Box 9482, Mbabane, H100, Eswatini.

OR

The Secretariat of Eswatini Health and Human Research Review Board (EHHRRB) on (00268) 2404 0865 / (00268) 24044905.

Part 2: Patient Consent form

Thank you for considering taking part in this study. The person organising the interview must explain the study to you before you agree to take part. If you have any questions, from the information sheet above or the explanation given to you, please ask the researcher before you decide to take part. You wi/ll be given a copy of the information sheet to keep if you wish.

Informed consent

□□I have been informed by the undersigned person of the purpose of this study, and the possible benefits and risks of my participation.

□□Any questions, I had about my participation in this study have been answered to my satisfaction. I will receive a copy of the document I have signed if I wish.

□□I was given enough time to decide if I will participate in the study.

□□I am participating in this study voluntarily. I may withdraw at any time without giving a reason and my decision not to take part will not affect my access to health services.

□□I permit the researchers and the Ethics Committee to see my anonymised data, with the understanding that this data will remain confidential.

I, _____ consent voluntarily to being a participant of this study.

I consent to this interview being recorded
□Yes □No
I consent to be contacted for a follow-up interview
□Yes □No

_____
Signature of the study participant with Date (**or thumbprint if cannot sign**)

_____
Name and Signature of researcher with Date

Supplementary file 7: Healthcare worker Information and consent form for qualitative interviews

Part 1: Study Information Sheet for participants

Guidance for study participants: ***Please read this document carefully and ask for clarity where it is required.***

Introduction

Previous studies conducted in other parts of the world have indicated that people with diabetes may have varying treatment outcomes when receiving treatment for tuberculosis and that treatment for tuberculosis may predispose them to develop diabetes. This study will verify the status of these claims in patients receiving TB treatment in Eswatini and also identify means of improving treatment outcomes for diabetic persons receiving treatment for tuberculosis. The title of this study is ***"Diabetes-Tuberculosis comorbidity: Epidemiology, Predictive factors, and Control in Eswatini"***. The principal investigator of this study, Dr Victor Williams will also utilise findings from this study to fulfil part of the requirement for the award of a Doctor of Philosophy degree (PhD) by the University Medical Centre, Utrecht University, Utrecht, Netherlands.

This research will be implemented at the different hospitals and health centres that provide TB services in Eswatini. These include Mbabane Government Hospital, The Luke Commission, Phocweni Clinic, TB Center, Siphofaneni clinic, Mankayane Hospital, AHF Lamvelase Clinic, Raleigh Fitkin Memorial Hospital, AHF Matsapha, Pigg's Peak Government Hospital, Nhlangano Health Center, Hlathikulu Hospital TB Clinic.

Aim of the research

The study aims to describe the epidemiology, predictive factors, and control measures of diabetes in patients who are being treated for tuberculosis in Eswatini. The study has four objectives and one of them is to identify factors that hinder effective Diabetes Mellitus care for diabetics receiving TB treatment in Eswatini and to propose a context-specific approach to address these factors. To achieve this objective, health care workers who directly provide care for these patients will be interviewed. As healthcare personnel who are experienced in the care of TB patients, you are invited to participate in this study.

If you agree to participate in the study, a convenient date and time will be arranged for you to be interviewed.

Potential benefits and risks

There will be no direct benefit for you from taking part in the interview. However, the information you provide will help the researcher understand the best practices and challenges in the care of TB clients with diabetes and provide recommendations that will help improve services delivery for these clients. Participating in the interview carry's a low risk for you as a participant if there is a breach of confidentiality but the researchers have been trained in research ethics to ensure your confidentiality. Comments you make will not be directly linked to your name in the final study report. Also, there is a possibility that the interview may evoke sad memories concerning your patients. Kindly let the interviewer know if you feel this way and would like to end the interview.

Voluntary participation

Your participation in this interview is voluntary. There are no right or wrong answers. You can at any time choose to withdraw from the study completely (including deletion of audio-recording and transcript of interview if you wish). You can decide not to take part or to stop taking part in this study at any time, without giving a reason, and without any impact on your work. We would like to record the interview, if you consent to this, solely for the study, to ensure we capture everything you say.

Confidentiality

The information you provide during the interview will be confidential and accessible only to the research team. The audio recording will only be heard by the research team. This will be transcribed onto paper and the original recording will be kept securely for the duration of the study. All written information collected (transcripts of interviews, notes, signed informed consent form) will be kept privately and anonymously (including password-protected storage) for about 10 years or as recommended by the Eswatini Health and Human Research Review Board (EHHRRB).

The researchers will make every effort to ensure that the information you provide as part of this study remains confidential. When using quotes from an interview, the researcher will make sure that the identity of the cited person cannot be revealed. Any information you share during the interview will be confidential and your privacy will be maintained. Also, the research assistants and interviewers conducting this research have been made to sign a confidentiality agreement to further ensure your confidentiality and privacy.

Contact for additional information

If you have any questions regarding this study, please contact the study's Principal Investigator Dr Victor Williams at +268 7618 4334; victormw55@gmail.com or P.O Box 9482, Mbabane, H100, Eswatini.

OR

The Secretariat of Eswatini Health and Human Research Review Board (EHHRRB) on (00268) 2404 0865 / (00268) 24044905.

Part 2: Consent form for participants

Thank you for considering taking part in this study. The person organising the interview must explain the study to you before you agree to take part. If you have any questions, from the information sheet above or the explanation given to you, please ask the researcher before you decide to take part. You will be given a copy of the information sheet to keep if you wish.

Informed consent

□□I have been informed by the undersigned person of the purpose of this study, and the possible benefits and risks of my participation.

□□Any questions, I had about my participation in this study have been answered to my satisfaction. I will receive a copy of the document I have signed if I wish.

□□I was given enough time to decide if I will participate in the study.

□□I am participating in this study voluntarily. I may withdraw at any time without giving a reason and my decision not to take part will not affect my position, career or reputation as a healthcare worker.

□□I permit the researchers and the Ethics Committee to see my anonymised data, with the understanding that this data will remain confidential.

I, _____ consent voluntarily to being a participant of this study.

I consent to this interview being recorded
□Yes □No
I consent to be contacted for a follow-up interview
□Yes □No

_____
Signature of the study participant with Date

_____
Name and Signature of researcher with Date

Part 3: Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and the best of my ability made sure that the participant understands that the following will be done:

1. The interview will be recorded in a tape recorder and later transcribed for use.

2. The information obtained from the interview will be used to provide recommendations for the improvement of health services delivery and care of TB patients.

3. All comments and responses by the participant will be confidential and when a reference is made to a statement, it will be anonymous.

I confirm that the participant was allowed to ask questions about the study, and all the questions asked by the participant have been answered correctly and 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 ICF has been provided to the participant.

Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____
Day/month/year

Supplementary File 8: Confidentiality and Non Disclosure Statement

As a member of this research team, I understand that I may have access to confidential information about research sites and study participants. By signing this statement, I am indicating my understanding of my responsibilities to maintain confidentiality and agree to the following:

- I understand that names and any other identifying information about research sites and participants are completely confidential.
- I agree not to divulge, publish, or otherwise make known to unauthorized persons or the public any information obtained during this research that could identify the persons who participated in the research.
- I understand that all information about research sites or participants obtained or accessed by me during this research is confidential. I agree not to divulge or otherwise make known to unauthorized persons any of this information unless specifically authorized to do so by approved protocol or by the local principal investigator acting in response to applicable law or court order, or public health or clinical need.
- I understand that I am not to read information about research sites or participants, or any other confidential documents, nor ask questions of research participants for my personal information but only to the extent and to perform my assigned duties on this research project.
- I agree to notify the local principal investigator immediately should I become aware of an actual breach of confidentiality or a situation that could potentially result in a breach, whether this is on my part or the part of another person.

_____	_____	_____
Name of researcher	Signature	Date
_____	_____	_____
Name of principal investigator	Signature	Date