# ADDIS ABABA UNIVERSITY

## EFFECTS OF COMORBID NON-COMMUNICABLE DISEASES ON TUBERCULOSIS TREATMENT OUTCOMES IN ETHIOPIA: A RETROSPECTIVE COHORT STUDY

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**A thesis submitted to Addis Ababa University (AAU), College of Health Sciences, Center for Innovative Drug Development and Therapeutic Trial for Africa (CDT-Africa), in partial fulfillment of the requirements for the Master of Science in Clinical Trials**

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## DECLARATION

I, Hanna Melesse, declare that this thesis, titled "**Effects of Comorbid Non-Communicable Diseases on Tuberculosis Treatment Outcomes in Ethiopia: A Retrospective Cohort Study**," is submitted in partial fulfillment of the requirements for the Master of Science in Clinical Trials at Addis Ababa University (AAU), College of Health Sciences, Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa). This work represents my research conducted during the academic year 2023/2024. I have prepared, collected, analyzed, and assembled this thesis in accordance with the ethical and technical standards of academia. All academic materials referenced in the thesis have been properly cited. I affirm that this thesis has not been submitted to any other institution for the purpose of obtaining any academic degree, diploma, or certificate.

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## ABSTRACT

**Background**: The intersection of tuberculosis (TB) and non-communicable diseases (NCDs) presents a major challenge in achieving global health targets, including the WHO's End TB 2030 strategy. In countries like Ethiopia where the TB burden is particularly high, the impact of NCDs on TB treatment remains insufficiently explored, limiting the development of informed interventions. Therefore, this study aimed to assess the effect of comorbid NCDs on TB treatment outcomes and identify underlying factors in Ethiopia.

**Methods**: This was a retrospective cohort study that utilized secondary data from the EXIT-TB project - an evidence-based, multiple-focus integrated intensified TB screening package. Participants were individuals with acute respiratory symptoms seeking outpatient care at four healthcare facilities in Ethiopia selected using stratified random sampling that account for urban and rural differences. Of these, all patients confirmed positive for TB and tested for NCDs were included. The patients were divided into two exposure groups: the exposed group, consisting of patients diagnosed with TB and one or more NCDs, and the non-exposed group, consisting of patients diagnosed with TB but without any NCDs. Their data were extracted from the EXIT-TB database, focusing on four key categories: sociodemographic variables, TB diagnosis and risk factor, NCD diagnosis, and TB treatment outcomes, classified as cured, treatment completed, treatment failure, loss to follow-up, transferred out, not assessed and death. The data were analyzed using SPSS version 20. A Chi-square ($X^2$) test was used to compare the baseline and clinical characteristics between the NCD-TB comorbid and TB-only patients groups, with a significance level of $p \leq 0.05$. Multiple logistic regression was used to investigate the association between independent and dependent variables.

**Results**: A total of 356 participants were included in the analysis, with 198 (55.6%) men, and the largest age group was between 15 and 30 years. The overall treatment success rate was 95.2%, with an unsuccessful treatment outcome of 4.8%. Patients with TB-NCD comorbidities

had a higher rate of unsuccessful treatment outcome, with 27.3% for those with TB-NCD comorbidity, compared to 4.0 % for those with TB only, resulting in an incident rate ratio of 6.8 (95% CI 2.4-19.5). Male gender (AOR=4.4 (CI 1.1-18.4)) and NCDs (AOR=8.9(CI (1.5-52.9)) were identified as significant risk factors for unsuccessful treatment outcomes.

**Conclusion**: The findings show that the incidence of unsuccessful treatment outcomes was nearly seven times higher in patients with TB-NCDs comorbidity compared to TB-only. This study underscores the importance of screening for and addressing NCD comorbidities in TB management. Healthcare systems should prioritize integrating TB care with the management of comorbid conditions to ensure patients receive comprehensive and coordinated treatment and better treatment outcomes.

**Keywords**: TB, NCD, Comorbidity, Tuberculosis, Non communicable diseases

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## LIST OF ACRONYMS/ABBREVIATIONS

| | |
|---|---|
| AAU | Addis Ababa University |
| AIDS | Acquired Immune Deficiency Syndrome |
| AFB | Acid Fast Bacilli |
| AOR | Adjusted odds ratio |
| ARR | Adjusted risk ratio |
| CDT Africa | Center for innovative drug development and therapeutic trial for Africa |
| COPD | Chronic obstructive pulmonary disease |
| COR | Crude odds ratio |
| CTC | Counselling and testing center |
| CVD | Cardiovascular diseases |
| DM | Diabetic mellitus |
| HIV | Human immune virus |
| IR | Incident rate |
| IRB | Institutional review board |
| LMICs | low-middle-income countries |
| NCD | Non-communicable diseases |
| NSP | National Strategic plan |
| OPD | Outpatient department |
| MCH | Maternal and child health |
| SOP | Standard operating plan |
| TB | Tuberculosis |
| TSR | Treatment success rate |
| WHO | World health organization |

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# 1. INTRODUCTION

## 1.1. Background

As the second most common infectious disease killer after COVID-19 and the 13th most common cause of death in 2020–2021, tuberculosis (TB) continues to be a major source of morbidity and mortality worldwide(1,2)**.** According to WHO 2024 report globally an estimation of 10.8 million new TB cases were reported in 2023, with an estimated increase of 4.6% IR between the year 2020 and 2023. The 87% of all incident cases were accounted by the 30 high TB burden countries. The TB incidence rate in the WHO African Region has declined every year since 2010.(3)

Ethiopia is one of the 30 countries with the highest TB burden, according to the World Health Organization's 2024 Global Tuberculosis Report(3), Ethiopia's national five-year TB strategic plan (NSP) was revised in 2020 with the goal of reducing TB incidence from 151 per 100,000 population in 2018 to 91 per population and mortality from 22 per 100,000 population in 2018 to 7 per 100,000 population by the end of the NSP, 2026..(4,5)

One of the key components of the global end-TB strategy is the treatment success rate (TSR); a 90% rate was established as the benchmark that all nations must meet. According to the WHO worldwide report from 2020, Ethiopia's TSR was 88% and the African region's was 82%(6) This partly can be attributed to the loss to follow ups and death during treatment.(7).Diabetes mellitus (DM), cardiovascular disease, cancer, and respiratory disorders are examples of non-communicable illnesses (NCDs) that greatly increase the risk of contracting tuberculosis (TB) and TB-related fatalities. These conditions also contribute to TB outbreaks at the population level, especially in LMICs(7,8).

The recent rapid rise of NCDs in Africa is worsening the existing burden of infectious disease (7). According to the WHO report, NCDs are the first cause of death and disability worldwide, killing 41million people every year, which is 71% of all deaths globally, with 77% occurring in LMICs. Cancer, cardiovascular disease, diabetes, and chronic respiratory disease account for two-thirds of this mortality (9,10). Fifteen million people aged 30 to 39 die from NCDs each year, with 85% of these premature deaths occurring at LMICs. Cardiorespiratory diseases are the most prevalent, followed by cancer, respiratory diseases, and DM, together representing 80% of all premature deaths due to NCDs (11).

In 2018 WHO reported, NCD accounted 39% of death in Ethiopia in 2016 and this was supported by the Ethiopia NCDI Commission 2018 report which indicated NCDs caused 43.5% of deaths. According to this report more than half (51%) of the NCDI mortality occurs before age 40, and 63% occurs before age 50.(12) NCD deaths across the countries region Addis Ababa accounted for 55% of total deaths, Tigray (51% ), Harari (45%), Amhara (43%), Dire Dawa (42%), and 29% to 33% of total deaths in Somali, Benishngul Gumuz and Afar regional states. In 2019, cardiovascular diseases, neoplasms, digestive diseases, chronic respiratory diseases, and diabetes mellitus were Ethiopia's leading causes of death rates. Overall CVD for 16%, cancers for 7%, respiratory disease for 2%, diabetes for 2%, injuries for 12% and other NCDs for 12% all causes of death..(12) The modifiable risk factors accounted for 52% (48-56%) of all NCD-caused mortality.(13)

## 1.2. Statement of the problem

Despite notable progress, TB remains a major public health challenge in Ethiopia, particularly for disadvantaged populations in the country. While Ethiopia continues to combat communicable diseases, it is now grappling with a growing threat from NCDs. The rapid

changes in demographics, sociocultural factors, nutrition, and economic conditions are driving an increase in the risk and occurrence of NCDs in Ethiopia and globally (14–16).

The intersection of TB and NCDs poses a significant challenge for Ethiopia in meeting global health targets, including the WHO End TB 2030 which targets to eliminate the TB epidemic by 2030. The global population level suggests that initiatives to control TB, such as expanding interventions to reduce TB prevalence, may be undermined by the interconnectedness of TB and NCDs (8,17), an issue that Ethiopia should investigate further.

The rise in NCDs significantly impacts TB epidemiology, case management, and treatment outcomes, prompting Ethiopia to enable effective and timely interventions, which are crucial for achieving the END TB 2030 targets. Data are limited to inform how and which NCDs in the country may increase susceptibility to *Mycobacterium tuberculosis* infection and weaken immune responses, raising the risk of TB infection.(14) Additionally, data are limited to inform if and how NCDs in Ethiopia may complicate TB detection, reduce the effectiveness of anti-TB drugs, worsen a patient's overall health, impede treatment adherence, and increase the likelihood of treatment failure, relapse, and mortality.(7) While the precise medical pathways connecting TB and NCDs remain unclear, it is evident that Ethiopia and other African countries will encounter the dual challenge of managing a heavy burden of infectious diseases alongside the rising prevalence of NCDs in the foreseeable future (15).

The Ethiopian National TB programme has often overlooked the effective management of this comorbidities for several reasons, including inadequate diagnosis of the comorbidity, weak existing services for NCDs, poor coordination between disease programmes, a reluctance within TB programmes to address additional health issues, and a lack of awareness regarding necessary interventions (7). However, studies have shown that bidirectional screening and integrated management can enhance early diagnosis and health outcomes for TB and NCDs

(2,7,15) More studies need to be done in Ethiopia to inform the Ethiopian National TB programme.

# 2. LITERATURE REVIEW

## 2.1. Impact of NCDs on TB treatment outcomes

The quick rise of NCDs in countries with high rates of TB has prompted the scientific community to actively investigate the association between NCDs and the impact of NCDs on TB treatment outcomes.

NCDs interact with TB by increasing both individual vulnerability to disease, increasing the chance of TB being sustained within a population (14) and it is associated with increased inpatient service utilization, a study indicated a higher rate of inpatient service utilization in pulmonary TB patients comorbidity with NCD (AOR 1.80; [CI] 1.66—1.96).(16)

Non-communicable diseases (NCDs) are linked with weakened immune defenses in the body, making it easier for infections to develop into diseases and resulting in unfavorable treatment results. (27) Studies indicate that the most common NCDs comorbid with TB include DM, hypertension, heart diseases, chronic obstructive pulmonary diseases (COPD), and cancer. These NCDs share common risk factors with TB, increasing the likelihood of co-occurrence and complicating the diagnosis and treatment of TB (9,11). Additionally, they can hinder effective and timely treatment, further contributing to the transmission of TB.

Various studies reported the prevalence of NCD in TB patients; a population study conducted in Indonesia found the prevalence to be 11.81%. In support of this another study conducted in Cameroon found that 10.2% of sputum-positive patients had at least one NCD comorbidity, the most common NCDs recorded in this study were DM 4.4%, kidney disease 2% hypertension 0.9%, and CVD 0.91% and around 0.6% had all the previous mentioned

NCDs in this study.(17) In another study conducted in tuberculosis-confirmed patients, hypertension and diabetes were diagnosed in 16·3% and 12·8%, respectively. The study further indicated diabetes was twice as high in tuberculosis patients compared to the non-tuberculosis patients.(18)

Furthermore, studies indicate a higher prevalence of TB with the increasing number of NCDs, in LMIC prevalence of TB increased with increasing numbers of NCDs, compared to those with no NCDs. (10,19) In a study conducted in 48 countries, those who had 1, 2, and 3 NCDs had 2.61 (95% CI = 2.14–3.22), 4.71 (95%CI = 3.67–6.11), and 6.96 (95%CI = 4.95–9.87) times higher In odds for TB.(19)

Patients with TB and NCD comorbidities have poor TB treatment outcomes resulting in a higher risk of treatment failure, recurrent TB, and worse outcomes. (2,15,20,21) When we see the treatment success reported in the different regions of Ethiopia, 84.9% Treatment success in Addis Ababa(22), 74.8% in the southern region(23), 87.8% in Bale zone southeast region(24), and 70.76% in Gambella (25). Another study conducted in Addis Ababa, Ethiopia; showed an overall high TB treatment success rate (94.0%) but those with TB/DM comorbidity had 14.8 (95% CI 3.5 – 62.7) times higher poor treatment outcome than the odds of patients without diabetes.(20). In support of this a systematic review reported the combined risk ratio of treatment failure and death for diabetes to be 1.69 (95% CI, 1.36 to 2.12). (26)

CVD and risk factors also need to be emphasized among active TB patients because they increase the risk of mortality and accounts for 20% of deaths among TB survivors after TB treatment completion which shows the bidirectional effect of these conditions. In addition to this cardiovascular risk factors such as smoking, alcohol, and diabetes mellitus are risk factors for poor TB treatment outcomes.(27)

Furthermore, studies also show TB affects the development and treatment of NCDs. TB aggravates the social and financial stress contributing to substance abuse and mental illness**.**(7), they are at increased risk of developing lung damage and all cause-mortality.(2,28–30) and contribute to the development of CVD. (15) A study showed a pooled RR of 1.51 (95% CI: 1.16–1.97) for major adverse cardiac events among those diagnosed with TB compared to non-TB controls (p = 0.0024). (31) In another study conducted in a post-TB survivor group. The post-TB survivor group had an increased 10-year ASCVD risk compared to the control groups (40.46% vs. 24.00%, $P < 0.001$).(32)

## 2.2. Factors associated with TB-treatment outcome

Studies indicated the different factors that contribute to TB treatment outcome including clinical diagnosis of patients(ARR= 0.8, CI: 0.53 - 0.94, P value =0.021), positive HIV/AIDS status (ARR= 0.7, CI: 0.43 - 0.88, P value =0.006),(33) reduced treatment success and having a community volunteer as a treatment supporter was associated with increased treatment success (ARR= 1.2, CI: 1.06 - 3.28, P value =0.028). TB retreatment (AOR = 0:31, 95%CI = 0:11 − 0:84),(34) comorbid illness (AOR: 2.8, 95% CI: 1.5–5.0), DOTS not performed (AOR: 2.5, 95% CI: 1.4–4.5), CXR showing multiple lesions (AOR: 3.0, 95% CI: 1.7–5.2) and unknown status of chest radiography in the first follow up (AOR: 48.1, 95% CI: 22.3–103.5) (35) age greater than 54, male sex,(23,36), anti-TB treatment side effect, weight(37), positive smear at the second-month follow-up (AOR 1.68, 95%CI 1.07–2.63) (23). These significant factors contributing to unsuccessful TB treatment outcomes needs to be dealt with to reach the goal of ending TB.

## 3. CONCEPTUAL FRAMEWORK

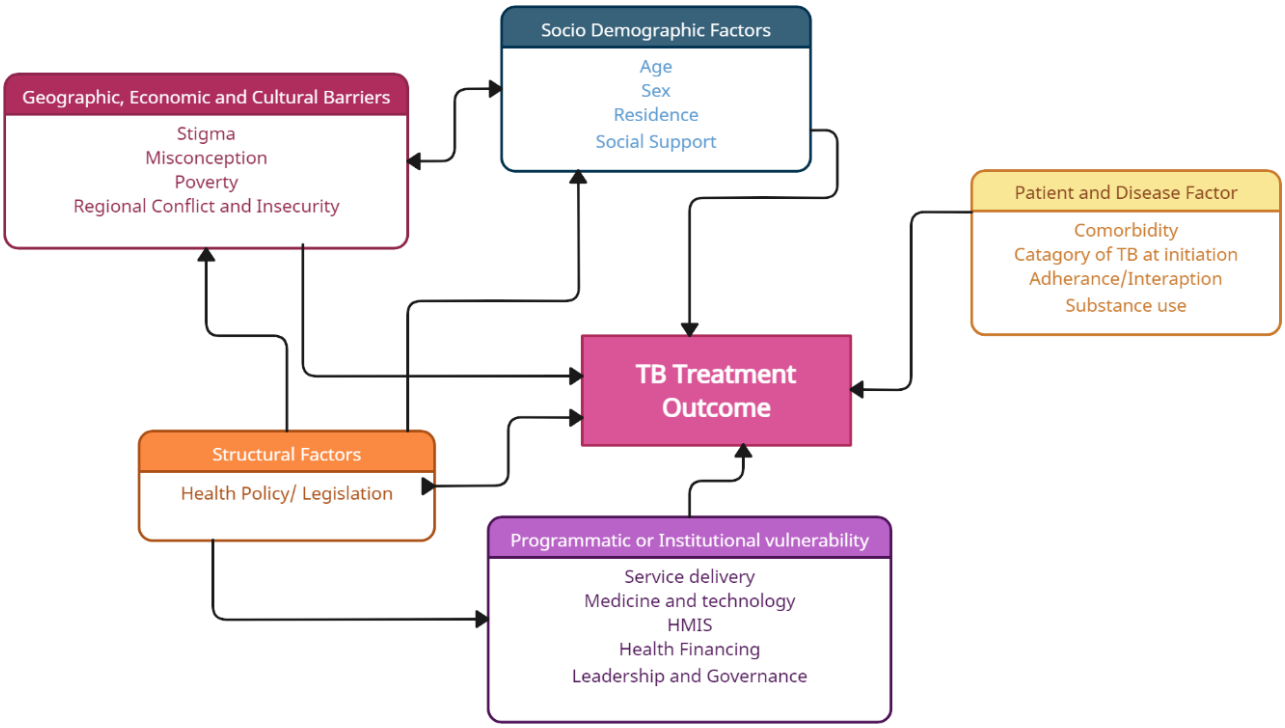


*Figure 1 - Conceptual frame work of factors that affected TB Treatment Outcome(38–40)*

## 4. Significance of the study

Ethiopia is one of the 30 high burden countries targeting to reduce TB mortality by the end of 2026 as per the national TB strategy, in this context, it is crucial to identify any potential modifiable factor that may be causing a poor outcome. This study will serve to show the incidence of unsuccessful treatment outcome among NCD patients, and effect of the different factors contributing to the treatment outcome. It will identify patients with high risk of unsuccessful treatment outcome and serve as evidence for stake holders aiming to improve tuberculosis treatment outcome.

# 5. OBJECTIVE

## 5.1. General objective

- To assess the effect of comorbid NCDs on TB treatment outcomes and associated factors in Ethiopia.

## 5.2. Specific objective

- To determine the effect of NCDs on TB treatment outcomes in Ethiopia.
- To describe the factors associated with TB treatment outcomes in Ethiopia.

# 6. METHODS

## 6.1. Study design and setting

A retrospective cohort study was conducted using secondary data collected as part of a project called EXIT TB collected from four health facilities. These facilities include Zewditu Memorial Hospital in Addis Ababa City Administration, Melka Jebdu Health Center in Dire Dawa City Administration, Chelenko Primary Hospital in the Oromia region, and Hiwot Fina Specialized University Hospital in the Harari Regional State.

The EXIT-TB Project - an Evidence-Based, Multiple-focus Integrated Intensified TB Screening to End TB. This prospective multi-center implementation project sought to assess the effectiveness of the EXIT-TB package in increasing TB case detection in the East African region. The package included screening all patients who report any cough regardless of duration, testing for TB irrespective of symptoms in HIV clinic attendees, and conducting household contact tracing for children with a household member with TB and performing symptoms screening followed by CXR.

## 6.2. Study population

The study population consisted of individuals seeking healthcare at the outpatient departments (OPDs), reproductive and child health clinics, antiretroviral therapy units, and diabetes mellitus (DM) clinics in the study facilities.

The study population was divided into the following exposure groups:

- Exposed group: This group included patients diagnosed and confirmed positive for TB and one or more of NCDs
- Non-exposed group: This group included patients diagnosed and confirmed positive for TB, but negative for any of the NCDs

## 6.3. Eligibility criteria

### 6.3.1. Inclusion criteria

- All patients confirmed to be positive for TB and underwent NCD diagnosis.
- Clinical care and treatment for their TB and NCDs have been monitored at the study sites, as documented in the EXIT-TB study database.

### 6.3.2. Exclusion criteria

- Patients confirmed to be negative for TB
- Patients confirmed to be positive for TB but did not underwent NCD diagnosis
- Patients confirmed to be positive for TB and underwent NCD diagnosis, but their clinical care and treatment have been monitored elsewhere.

## 6.4. Sample size determination

The sample size was calculated using Epi Info statistical software using a two-population proportion sample size calculation for cohort study with a confidence level of 95% ($\alpha = 0.05$) and statistical power of 80% ($\beta = 0.20$). Using treatment outcomes from a prior study conducted in Thailand(35), we estimated unsuccessful treatment outcomes would occur in 23.5% of comorbid patients and 9.3% of the non-exposed. The ratio was estimated at 3:1 non-exposed to exposed patients. Based on these assumptions the initial sample size was calculated to be 295. Considering a 10% non-response rate and a 5% loss to follow-up, the final sample size was 340.

*Table 1 - Sample size calculation for the exposure*

| Variables as exposure | Assumptions | | | | Sample size (controls + cases) |
|---|---|---|---|---|---|
| | Risk in unexposed | Ratio (Cases, Controls) | Power% | CI% | |
| NCD | 9.3 | 1:3 | 80 | 95 | 295 |
| Previous TB treatment | 16.1 | 1:3 | 80 | 95 | 255 |

Ratio = cases to control & CI = confidence interval.

## 6.5. Data collection and procedure

Secondary data was collected using data extraction sheet from EXIT-TB survey database which was conducted from July 2019 to May 2022 at the selected study health facilities in Ethiopia. The data was accessed by requesting the survey team and upon approval the data management team provided the data base for this study. The Excel sheet used for data collection is included as an annexure at the end of the thesis (**Annexure 1: Data Collection Tool**).

Data relevant to this study were extracted from the EXIT-TB database on four major categories:

- Sociodemographic variables: Age, sex, marital status, educational level, occupation, and residence
- TB diagnosis and risk factors : Diagnostic methods used (CXR, AFB sputum smear microscopy, and Gene Xpert MTB/RIF assay), clinical manifestations, and risk factors
- NCD diagnosis: diagnosis results
- TB treatment outcomes: Outcomes classified as cured, treatment completed, treatment failure, loss to follow-up, transferred out, not assessed or death as applicable.

## 6.6. Operational definitions

- NCDs- is a medical condition or disease that is by definition non-infectious and non-transmissible among people. It has a prolonged course, that does not often resolve spontaneously, and for which a complete cure is rarely achieved.(12)
- **Treatment outcome:** Categorized based on World Health Organization (WHO) definition; treatment success (cured or treatment completed), un successful treatment (failure, death, loss to follow-up).(41,42)
- **Cured:** A patient with pulmonary TB with bacteriologically confirmed TB at the beginning of treatment who completed treatment as recommended by the national policy, with evidence of bacteriological response b and no evidence of failure.
- **Treatment completed:** A patient who completed treatment as recommended by the national policy but whose outcome does not meet the definition for cure or treatment failure.
- **Treatment failure:** A patient whose treatment regimen needed to be terminated or Permanently changed to a new regimen or treatment strategy.
- **Dead:** A patient who died before starting treatment or during the course of treatment.
- **Loss to follow-up:** A patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.

## 6.7. Variables

### 6.7.1. Dependent variable

- TB treatment outcome

### 6.7.2. Independent variable

- Sociodemographic variables-- Age, Sex, , residence,
- Previous TB treatment

- Bacteria confirmation
- NCD and risk factors
- HIV status

## 6.8. Data analysis and management

Data management and analysis was conducted by using the software Statistical Package for Social Sciences software (SPSS) version 20. Descriptive analysis was conducted to summarize the base line characteristics of the respondents and clinical factors that contribute to the tuberculosis treatment outcome and this was presented in the form of tables.

Comparison of the baseline and clinical characteristics of respondents among the NCD TB comorbid patients and no NCD TB patients groups was conducted by using the Chi-square($X^2$) test with significance level $p \leq 0.05$

Incidence rate ratio was calculated to determine the impact of NCDs on TB treatment outcome and presented in a table. The factors associated with TB treatment outcomes were examined using Logistic regression model. Logistic regression model was preferred because the Unsuccessful treatment outcome was below 10%. A crude and adjusted odds ratio with the corresponding 95% confidence intervals were used to interpret the group difference for the dependent and independent variables. P-value ≤0.25 was considered to decide on significance of the variable on the univariate logistic regression model and to be included in the final model. P-value ≤0.05 was considered statistically significant association on the multivariable regression model in this study.

## 6.9. Data quality

|These data used in this study was taken from EXIT TB study conducted by CDT Africa in collaboration with other stake holders. All collaborators adhered to established protocols,

standardized tools and procedures for data collection and management. The data was evaluated for its relevance for this study objectives and only those data that are relevant for this study were included.

Date collectors involved in the data collection were trained. The tool was also pretested to check for clarity of the contents. All the samples were collected and processed according to the WHO and the national guidelines. In addition to this SOPs were prepared and provided for smear, and GeneXpert. The data collection was supervised with a frequent visit to the sites and observation while the data collectors conduct the interview and checked the completeness of the data collected in addition to regular check-ups of the files sent to the center.

These measures collectively ensured that the data used in this study were of high quality, reliable, and appropriate for the research objectives.

## 7. ETHICAL CONSIDERATION

Ethical approval for the study has been granted by the Scientific and Ethics Review Committee of the Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa) at the College of Health Sciences, Addis Ababa University. In the process of abstracting patient data from the EXIT-TB study database, no patient identifiers were utilized, ensuring that patients were not identifiable.

The initial EXIT TB study protocol had obtained IRB approval from Institutional Review Board of the College of Health Sciences, Addis Ababa University and permissions were sought from authorities of participating sites. Written informed consent was obtained from each participant or parents as applicable, and assent was sought from children under the age of 18.

# 8. RESULT

## 8.1. Baseline characteristics of study participants

A total of 356 participants were included in the analysis: of these, 138 (38.8%) are from Challanko Primary hospital, 119 (33.4%) from Hiwot Fana Specialized Teaching Hospital, 72 (20.2%) from Zewiditu Memorial Hospital, and 27 (7.6%) from Melka Jebdu Health Center. Among the participants, 198 (55.6%) were men and the largest age group was between 15 and 30 years, comprising 214 (60.1%) of the participants. Additionally, 248 (69.7%) were from rural areas, 156 (43.8%) had no formal education, 185 (52.0%) were married, and 197 (55.3%) were employed (**Table 2**).

*Table 2 - Baseline characteristics of study participants*

| Characteristics | Frequency (%) |
|---|---|
| **Residence** | |
| **Rural** | 248(69.7) |
| **Urban** | 108(30.3) |
| **Facility** | |
| **Zewiditu Memorial Hospital** | 72(20.2) |
| **Hiwot Fana Teaching Hospital** | 119(33.4) |
| **Challanko Primary Hospital** | 138(38.8) |
| **Melka Jebdu Health Center** | 27(7.6) |
| **Age** | |
| **0-14** | 28(7.9) |
| **15-30** | 214(60.1) |
| **31-45** | 67(18.8) |
| **45+** | 47(13.2) |
| **Sex** | |
| **Male** | 198(55.6) |
| **Female** | 158(44.4) |
| **Marital status** | |
| **Married** | 185 (52.0) |
| **Divorced** | 6 (1.7) |
| **Separated** | 10 (2.8) |
| **Widow/Widower** | 13 (3.7) |
| **Single** | 142 (39.9) |
| **Educational status** | |

| | |
|---|---|
| **No formal education** | 156 (43.8) |
| **Primary** | 111 (31.2) |
| **Secondary and above** | 89(25.0) |
| **Employment** | |
| **Unemployed** | 159(44.7) |
| **Employed** | 197(55.3) |

## 8.2. Clinical characteristics of study participants

The presenting symptoms were cough in 351 (98.6%), fever in 142 (39.9%), bloody sputum in 56 (15.7%), weight loss in 152 (42.7%), night sweat in 245 (68.8%) and other symptoms which included chest pain, SOB, nausea and vomiting 139 (39.0%). Of the total participants, 12 (3.4%) had concomitant NCD, DM accounts 6(1.7%), Asthma 3(0.8%), mental illness 2 (0.6%) and hemiparesis $2^0$ to ICSOL 1 (0.3%) (**Table 3**).

*Table 3 - Clinical characteristics of study participants*

| Clinical characteristics | Frequency (%) |
|---|---|
| **Clinic** | |
| **OPD** | 333(93.5) |
| **Diabetic** | 3(0.8) |
| **CTC** | 18(5.1) |
| **MCH** | 2(0.6) |
| **Cough** | |
| **Yes** | 351(98.6) |
| **No** | 5(1.4) |
| **Fever** | |
| **Yes** | 142(39.9) |
| **No** | 214(60.1) |
| **Bloody sputum** | |
| **Yes** | 56(15.7) |
| **No** | 258(72.5) |
| **Weight loss** | |
| **Yes** | 152(42.7) |
| **No** | 204(57.3) |
| **Night sweat** | |
| **Yes** | 242(68.8) |
| **No** | 111(31.2) |
| **TB contact history** | |

| | |
|---|---|
| **Yes** | 44(12.4) |
| **No** | 312(87.7) |
| **Other symptoms[a]** | 139(39.1) |
| **Yes** | 217(61.0) |
| **No** | |
| **NCD** | 12(3.4) |
| **Diabetes** | 6(1.7) |
| **Asthma** | 3(0.8) |
| **Mental illness** | 2(0.6) |
| **ICSOL** | 1(0.3) |
| **No NCD** | 344(96.6) |
| **Tobacco use** | |
| **Yes** | 18(5.1) |
| **No** | 338(95.0) |
| **Alcohol use** | |
| **Yes** | 18(5.1) |
| **No** | 338(95.0) |
| **Drug use** | |
| **Yes** | 79(22.2) |
| **No** | 277(77.8) |
| **HIV status** | |
| **Positive** | 23(17.7) |
| **Negative** | 107(82.3) |
| **Previous TB Treatment** | |
| **Yes** | 39(11.0) |
| **No** | 317(89.0) |
| **CXR** | |
| **Suggestive** | 234(81.0) |
| **Not suggestive** | 55(19.0) |
| **Sputum smear microscopy** | |
| **Positive** | 20(52.6) |
| **Negative** | 18(47.4) |
| **Sputum Gene Xpert** | |
| **Positive** | 258(88.1) |
| **Negative** | 35(11.9) |
| **TB treatment outcome (original)** | |
| **Cured** | 227(63.8) |
| **Treatment completed** | 91(25.6) |
| **Death** | 8(2.2) |
| **Loss to follow up** | 7(2.0) |
| **Treatment failure** | 1(0.3) |
| **Transferred out** | 4(1.1) |
| **Not assessed** | 18(5.1) |

**Other symptoms include:** Chest pain, SOB, Back pain, Vomiting, headache and Appetite loss

## 8.3. Comparison of baseline characteristics of study participants

When the base line characteristics of participant among the NCD comorbid TB patients and with no comorbid TB patients groups. A statistically significant difference was observed in the residence of participants, HIV status, previous TB treatment and the facility where they were diagnosed and treated for TB. A significantly higher proportion of NCD (58.3%) participants living in urban area compared to rural residents (41.7%), significant level p-value = 0.03. Participants with comorbid TB and NCD had positive HIV status (33.3%) than those with No NCD (5.5%), significant level p-value = 0.01. Participants with previous TB treatment and NCD were 33.3% compared to No NCD group (10.2%), significant level p-value = 0.01. In terms of facility, Zewditu memorial hospital had 50% of the TB and NCD compared to 19.2% in the TB with no NCD group, significant level p-value = 0.05.

*Table 4 - Comparison of baseline characteristics of study participants among the treatment outcome groups, Ethiopia, 202(n=356)*

| | **NCD** | | **P-value** |
|---|---|---|---|
| **Characteristics** | Yes (%) | No (%) | |
| **Residence** | | | |
| **Urban** | **7(58.3)** | **101(29.4)** | **0.03*** |
| **Rural** | **5(41.7)** | **243(70.6)** | |
| **Age** | | | |
| **0-14** | 1(8.3) | 27(7.8) | 0.20 |
| **15-30** | 4(33.3) | 210(61.0) | |
| **31-45** | 4(33.3) | 63(18.3) | |
| **45+** | 3(25.0) | 44(12.8) | |
| **Sex** | | | |
| **Male** | 4(43.6) | 194(56.4) | 0.10 |
| **Female** | 8(66.7) | 150(33.3) | |
| **Educational status** | | | |
| **No formal education** | 5(41.7) | 151(43.9) | 0.70 |
| **Primary** | 5(41.7) | 106(30.8) | |
| **Secondary and above** | 2 (16.7) | 87 (25.3) | |
| **Employment** | | | |
| **Unemployed** | 5(41.7) | 154(44.8) | 0.80 |

| | | | |
|---|---|---|---|
| **Employed** | 7(63.6) | 190(55.1) | |
| **Previous TB Treatment** | | | |
| **Yes** | **4(33.3)** | **35(10.2)** | **0.01** |
| **No** | **8(66.7)** | **309(89.8)** | |
| **HIV status** | | | |
| **Positive** | **4(33.3)** | **19(5.5)** | |
| **Negative** | **3(25.0)** | **104(30.2)** | **0.01*** |
| **Unknown status** | **5(41.7)** | **221(64.2)** | |
| **Bacteria confirmed** | | | |
| **Positive** | 11(91.7) | 269(78.2) | 0.30 |
| **Negative** | 1(8.3) | 75(21.8) | |
| **Alcohol use** | | | |
| **Yes** | 0(0.0) | 18(5.2) | 0.40 |
| **No** | 12(100.0) | 326(94.8) | |
| **Facility** | | | |
| **Zewiditu memorial hospital** | **6(50.0)** | **66(19.2)** | **0.05*** |
| **Hiwot Fana teaching Hospital** | **1(8.3)** | **118(34.3)** | |
| **Challanko $1^0$ hospital** | **4(39.0)** | **134(33.3)** | |
| **Melka Health center** | **1(8.3)** | **26(7.6)** | |

## 8.4. Incidence and subgroup analysis of TB treatment outcome

The overall treatment success rate was 95.2%, with an unsuccessful treatment outcome of 4.8%. Patients with TB-NCD comorbidities had a higher rate of unsuccessful treatment outcome, with 27.3% for those with TB-NCD comorbidity, compared to 4.0 % for those with TB only, resulting in an incident rate ratio of 6.8 (95% CI 2.4-19.5).

*Table 5 - Incidence and subgroup analysis of TB treatment outcome among patients visiting study treatment centers in Ethiopia*

| **Variable** | **TB Treatment outcome** | | **Total** |
|---|---|---|---|
| | Unsuccessful | Successful | |
| **NCD** | | | |
| **Yes** | 3(IR-27.3%) | 8(IR-72.7%) | 11 |
| **No** | 13(IR-4.0%) | 310(IR-96.0%) | 323 |
| **Total** | 16(IR-4.8%) | 318(IR-95.2%) | 334 |

## 8.5. Factors associated with TB treatment outcome

The variables are included in the final model based on their significance level on the binary regression model taking significance level ≤0.25 and clinical significance of the variables

Factors significantly associated with unsuccessful TB treatment outcome in the unadjusted model were residence, previous TB treatment, sex, and NCD comorbidity.

The multivariable binary logistic regression model reveal that males had 4.4 times higher risk of unsuccessful treatment outcomes keeping the other variables constant, adjusted odds ratio (AOR) of 4.4(CI=1.1-18.4).Those with NCD comorbidity had 8.9 times higher risk of unsuccessful treatment outcome compared to those with no NCD comorbidity AOR of 8.9(1.5-52.9).

The crude and adjusted odds ratios and the multivariable binary logistic regression findings for associated factors are presented in **Table 6**.

*Table 6 - Factors associated with TB treatment outcome among patients visiting study treatment centers in Ethiopia (n=334)*

| **Characteristics** | **Treatment outcome** | | **COR** | **AOR** |
|---|---|---|---|---|
| | Unsuccessful (%) | Successful (%) | | |
| **Residence** | | | | |
| **Urban** | 10(9.5) | 95(90.5) | 3.9(1.4-11.1) | 3.9(0.9-16.9) |
| **Rural** | 6(2.6) | 223(97.4) | 1 | 1 |
| **Age** | | | | |
| **0-14** | 1(4.5) | 21(95.5) | 1 | 1 |
| **15-30** | 6(2.9) | 198(97.1) | 0.6(0.1-5.5) | 0.5(0.05-4.5) |
| **31-45** | 5(7.7) | 60(92.3) | 1.8(0.2-15.9) | 0.8.3(0.1-8.7) |
| **46+** | 4(9.3) | 39(90.7) | 2.2(0.2-20.5) | 1.1(0.1-12.9) |
| **Sex** | | | | |
| **Male** | 13(6.9) | 175(93.1) | 3.5(1.0-12.7) | **4.4(1.1-18.4)** |
| **Female** | 3(2.1) | 143(97.9) | 1 | **1** |

| | | | | |
|---|---|---|---|---|
| **Previous TB Treatment** | | | | |
| **Yes** | 5(13.5) | 32(86.5) | 4.1(1.3-12.4) | 1.7(0.4-7.0) |
| **No** | 11(3.7) | 286(96.3) | 1 | 1 |
| **NCD** | | | | |
| **Yes** | 3(27.3) | 8(72.7) | 8.9(2.1-37.7) | **8.9(1.5-52.9)** |
| **No** | 13(4.0) | 310(96.0) | 1 | **1** |
| **Alcohol use** | | | | |
| **Yes** | 2(11.1) | 16(88.9) | 2.7(0.6-12.9) | 1.1(0.2-6.2) |
| **No** | 14(4.4) | 302(95.6) | 1 | 1 |
| **HIV status** | | | | |
| **Positive** | 3(13.0) | 20(87.0) | 2.3(0.5-9.9) | 1.3(0.2-7.8) |
| **Negative** | 6(6.2) | 91(93.8) | 1 | 1 |
| **Bacteria confirmed** | | | | |
| **Yes** | 10(3.9) | 248(96.1) | 0.5(0.2-1.3) | 0.3(0.1-1.2) |
| **No** | 6(7.9) | 70(72.1) | 1 | 1 |

## 9. DISCUSSION

This study's findings revealed that among participants with tuberculosis, 3.4% also had concomitant non-communicable diseases, which included diabetes mellitus, asthma, mental illness, and ICSOL. A comparison of baseline characteristics between participants with TB and NCDs and those without NCDs showed statistically significant differences in residence, HIV status, previous TB treatment, and treatment facilities. Most patients with NCDs resided in urban areas, and this group also had a higher prevalence of positive HIV status. The study reported an overall incidence rate of unsuccessful TB treatment outcomes at 4.8% of patients. Notably, the incidence of unsuccessful treatment outcomes was almost seven times higher in patients with both TB and NCDs compared to those with TB alone. Additionally, factors such as the patient's sex, and NCD comorbidity were associated with unsuccessful treatment outcomes.

The unsuccessful TB treatment rate of this study is lower than other studies done in Gondar University (28.5%)(43), Motta Town, Northwest Ethiopia (11.6%)(44), south Gondar zone (11%)(45), Arsi zone (16%)(46), Nigeria (47%)(47)(5), Namibia (49.4)(48) and Ireland (10.7)(49). This difference can be due to region differences influenced by factors such as healthcare access, population demographics, and the burden of chronic diseases in different settings.

Tuberculosis patients with concomitant NCDs faced a higher risk of unsuccessful treatment that was 8.9 times greater than that of patients without NCDs. This finding is consistent with a study conducted in Poland, which reported increased odds ratios for unsuccessful treatment outcomes among TB patients with specific comorbidities: diabetes (OR = 1.7), cancer (OR = 2.49), alcoholism (OR = 3.86), undergoing immunosuppressive therapy (OR = 1.8), and drug addiction (OR = 3.09)(50). A study conducted in South Asia also found that patients with

tuberculosis and diabetes had higher odds of treatment failure compared to non-diabetic TB patients, with an odds ratio of 1.7(51).

Moreover, being male was also associated with an increased risk of unsuccessful treatment, reflected in an odds ratio of 4.4. This finding aligns with other studies conducted in Motta Town (44) and Brazil(52), which reported an odds ratio of 2.4 and 1.28 respectively. This indicates that male patients may encounter specific barriers to successful treatment, such as socioeconomic factors, health-seeking behaviors, or potential differences in the management of TB compared to female patients which need further investigation.

This study tried to see TB treatment outcomes by using data collected from different parts of Ethiopia which included both urban and rural areas but under powered because few participants were diagnosed with NCD.

## Conclusion

This study's objective is to assess the effect of comorbid NCDs on TB treatment outcomes and associated factors in Ethiopia so that the relevant body can enhance TB treatment. The findings show that the incidence of unsuccessful treatment outcomes was nearly seven times higher in patients with TB-NCDs comorbidity compared to TB-only and underscores the significance of addressing NCD comorbidities in the management of tuberculosis and male gender as associated factors. Effectively tackling the challenges associated with comorbidities in TB patients necessitates a multifaceted approach.

## Recommendation

Recognizing these factors is crucial, as it highlights the need for targeted strategies to overcome the specific challenges faced by these populations. Healthcare systems must prioritize the integration of TB care with the management of comorbid conditions including enhanced

screening and monitoring to ensure that patients receive comprehensive and coordinated treatment for all their health needs. By developing interventions tailored to these unique circumstances, healthcare professionals can enhance treatment success rates for TB and improve overall patient outcomes.

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# ANNEXURE 1: DATA COLLECTION TOOL

☐☐☐☐☐
Patient/index enrolment number

Hospital number ..... Visit Date ☐☐/☐☐/☐☐☐☐
DD MM YYYY

CLINIC OPD ☐ CTC ☐ DIABETIC ANC ☐ ☐ PMCT ☐ LABOUR WARD ☐ FP ☐ Post-natal/MCH ☐

CLIENT IDENTIFICATION

Age ☐☐☐ Gender Male ☐ Female ☐

Marital Status

Single ☐ Married ☐ Divorced ☐ Separated ☐ Cohabited ☐ Widow/Widower ☐

Occupation
- ☐ None
- ☐ Employed
- ☐ Peasant
- ☐ Business/Vendor/Petty traders
- ☐ Housewife
- ☐ Student
- ☐ Not applicable

Education level
- ☐ never attended
- ☐ Primary education
- ☐ Secondary education
- ☐ Tertiary education
- ☐ Adult education
- ☐ Vocational training
- ☐ Religious education

Location, Place of Residence Urban Rural ☐ Urban Rural ☐

PAST MEDICAL HISTORY AND TB RISK FACTORS ASSESSMENT

| S/N | Past medical History/ Risk factor(s) | Responses(s) | | | |
|---|---|---|---|---|---|
| 1 | (a) has the client ever tested for HIV? | ☐ Yes | ☐ No | | |
| | (b) If yes, what was the result? | ☐ Positive | ☐ Negative | I don't want to disclose | ☐ |
| 2 | Has the client had history of contact with an infectious TB case in the past 2 years? | ☐ Yes | ☐ No | ☐ Not Sure | |
| 3 | Does the client have a chronic illness? | ☐ Yes | ☐ No | If yes specify | ..... |
| 4 | Does the client have a Current use of? | | | | |
| | i) Alcohol | ☐ Yes | ☐ No | ☐ NA | |
| | ii) Tobacco | ☐ Yes | ☐ No | ☐ NA | |
| | iii) Drug use | ☐ Yes | ☐ No | ☐ NA | |
| 5 | Has the client ever been treated for TB? | ☐ Yes | ☐ No | | |

**TUBERCULOSIS SYMPTOM SCREENING**

| | | Response | |
|---|---|---|---|
| (i) | Cough of any duration | ☐ Yes | ☐ No |
| (ii) | Coughing up blood stained sputum | ☐ Yes | ☐ No |
| (iii) | Fever | ☐ Yes | ☐ No |
| (iv) | Noticeable weight loss or failure to thrive in children | ☐ Yes | ☐ No |
| (v) | Excessive sweating at night | ☐ Yes | ☐ No |
| (vi) | Others Specify ……. | | |

6. Results

(i) **GeneXpert Results (Sputum)**

(T) ☐ (Ti) ☐ (TA) ☐ (RR) ☐ (N) ☐ (I) ☐

(ii) **GeneXpert (Stool)**

(T) ☐ (Ti) ☐ (TA) ☐ (RR) ☐ (N) ☐ (I) ☐

*(T) – MTB detected, Rifampicin resistance not detected*
*(RR) – MTB detected, Rifampicin resistance detected*
*(TI) – MTB detected, Rifampicin resistance indeterminate*
*(N) –MTB not detected*
*(TA) – MTB Positive Trace Call, Rifampicin resistance*
*(I) – Invalid/no result/error Indeterminate*

*(iii) Smear microscopy* ☐ *Positive* ☐ *Negative*

*(iv) Chest X-ray results* ☐ *TB suggestive* ☐ *Not suggestive*

*(vi) Clinically diagnosed to have TB* ……

*(v) Bacteria confirmed* ☐ Yes ☐ No

*(Vii) Treatment Outcome* ☐ Cured ☐ Treatment completed ☐ Death ☐ Loss to follow up

☐ Treatment failure ☐ Transferred out ☐ Not assessed