MAKERERE UNIVERSITY

SCHOOL OF PUBLIC HEALTH

EFFECT OF MOBILE HEALTH INTERVENTIONS ON ENHANCING COMPLETION OF THE DIAGNOSTIC PROCESS AMONG PEOPLE WITH PRESUMED TUBERCULOSIS IN CENTRAL UGANDA

BY

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I Rebecca Nuwematsiko declare that this research work is my original copy and has never been submitted for any academic award or publication in any University. I therefore submit this research for the award of Doctoral of Philosophy in Public Health undertaken at the School of Public Health, Makerere University. Reference to any work done by any other person, institution or any materials obtained from other sources has been appropriately cited and acknowledged.

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DEDICATION

This PhD thesis is dedicated to my parents, Mr. Myres Kweyamba and Mrs. Betsy Kweyamba, who supported me physically, emotionally, spiritually, and financially throughout my studies. Without them, there would have been no motivation and the energy to push forward. To my sisters; Charity Tumuhimbise Begumisa, Ziporah Musiime Twinobwengye, Christine Busingye Atumanya, Ruth Ikiriza Muhanguzi and my favourite brother, Kenneth Nuwarinda, you were my pillar and anchor upon which I found comfort and strength to carry on. Lastly, to my husband, Mr. Ivan Muramuzi who supported me throughout the journey up to the end, I am very grateful.

Psalm 27:13-14

13 I would have fainted, unless I had believed that I would see the goodness of the Lord in the land of the living.

14 Wait on the Lord; be of good courage, and He shall strengthen thine heart. Wait, I say, on the Lord!

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LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
CFIR	Consolidated Framework on Implementation Research
CHWs	Community Health Workers
COVID-19	Coronavirus Disease 2019
DOT	Directly Observed Therapy
HIV	Human Immunodeficiency Virus
LMICs	Low- and Middle-Income Countries
LTFU	Loss to Follow-up
mHealth	Mobile health
RCT	Randomized Controlled Trial
SDG	Sustainable Development Goal
SMS	Short message service
TB	Tuberculosis
UBOS	Uganda National Bureau of Statistics
UN	United Nations
USSD	Unstructured Supplementary Service Data
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Completion of the TB diagnostic process	This referred to undertaking the TB investigations required and obtaining results from the test within 30 days from the date of being presumed with TB
Confirmed TB patient	Patients who have been diagnosed with TB either bacteriologically or clinically. A bacteriologically confirmed TB patient is a person whose biological specimen tests positive by smear microscopy, culture or a WHO-approved rapid diagnostics, such as the Xpert MTB/RIF assay. A clinically diagnosed TB patients is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner based on the sign and symptoms, X-ray abnormalities, suggestive histology and extrapulmonary cases that do not have laboratory confirmation.
Contextually adapted intervention	An intervention whose design has been improved based on views and perceptions of the potential users.
Diagnosed TB patient	A patient who is bacteriologically positive for TB by either Xpert MTB/RIF, smear microscopy or TB Lipoarabinomannan (LAM) or those detected with an abnormal chest X-ray
mHealth interventions	Interventions which utilize mobile phone devices. These included mobile phone short message services (SMS), mobile phone calls and mobile health applications (Apps).
Pre-diagnosis loss to follow-up	This is the drop out of people with presumed TB before they are diagnosed for TB either through laboratory or radiological investigations within 30 days after being identified as presumptive. This will refer to either drop out before conducting the investigations or after by not receiving the results.

Person with presumed TB *(also known as Presumptive TB patient)*	A patient presenting with any or all of the cardinal symptoms and signs suggestive of TB. That is a persistent cough of more than two weeks, fever, night sweats, and unexplained weight loss
Pre-treatment loss to follow-up	This refers to drop out of confirmed TB patients before being initiated on treatment 30 days after being confirmed either through laboratory or radiological investigations.
TB presumption phase	Phase in the TB service provision continuum from when one is presumed to have TB until when they complete diagnosis.

PREFACE

Growing up, we were told that when you acquire tuberculosis (TB), you are given 60 injections, a thought that always scared me. Thankfully, today there are improved treatment regimens for TB including the recent move to shorten the treatment to four months as opposed to the standard six months. Because of the "60 injections" narrative, most people in my community feared to be tested or even be associated with TB. My parents were always health cautious telling us to avoid sharing plates, cups and sharp objects to avoid contracting diseases from other people. This sparked my interest into the health field to understand more about these diseases that people always talked about and dreaded. I set my mind out to become a Medical Doctor and understand more about these diseases and how to treat them. As I approached secondary school, I knew I had to study biology and chemistry to become a Doctor. But alas, my senior one biology lessons started deeming this dream because of how hard the subject was. But nonetheless, biology was that one subject that I always read to understand because it was so real, so practical and I didn't need to cram anything but rather look at an insect and know everything about it without cramming for example. So, because of this, my interest and passion for biology kept alive, and I pursued a path of reading textbooks to understand the subject more in close consultation with my teacher Mrs. Bonabaana (RIP). Mrs. Bonabaana believed in me and supported me until I turned from an average student to an A student in Biology which propelled me to keep on the path of health sciences. I vividly remember her words of affirmation in one of the biology classes when I mentioned a correct answer to a hard question after everyone else had failed it. She went *"Great, these are the future doctors we want……*". Those words, although told to me in senior two, have kept re-echoing in my mind till this day. These words have been the fuel/ push for pursuing my academics to this level.

I did not attain the points for medical school as hoped, and it was very disappointing. I knew one thing, I needed to work in the health sector, so I asked my sisters to advise on any other course that would lead me there and that's how I ended up with the Bachelors of Environmental Health Science and later on Masters in Public Health at Makerere University. At first, I lived in denial until I understood what public health was about- preventing diseases and promoting health. Only then did I truly know that it was what I always wanted to study and not just be confined in a clinical room treating the diseases. This changed everything because my childhood ambitions and desires to know more about diseases had come to pass.

Along my work and study, I engaged in research and projects on many diseases and there came a time for me to decide and specialise in one of them for my PhD and career pathway. I wanted to specialise in a disease that is "dynamic" in terms of presentation and treatment because then it would offer me a lot of learning and research opportunities. That's how I ended up focusing my research on TB after recalling my childhood stories of the treatment, stigma and also having gained a deeper understanding of its dynamics over the years. Coincidentally, at the time of my pre-PhD meditation, a scholarship opportunity came up under the MILEAGE4TB project at Makerere University School of Public Health and that is how the PhD Journey started.

I am very grateful that I have come to the end of this tough and trying journey. I hope that people with presumed TB in Uganda will brave the personal, social and health system barriers and test to know their status and if positive, start treatment. This will ultimately reduce deaths and complications associated with late treatment of TB and community spread of the infection.

DECLARATION 11: STATEMENT ON PUBLICATIONS

The publications and manuscripts that constitute this thesis are presented below:

Publication 1:

Pre-diagnosis and pre-treatment loss to follow-up and associated factors among patients with presumed tuberculosis and those diagnosed in Uganda. *BMC Health Serv Res. 2024 Dec 23;24(1):1638. doi: 10.1186/s12913-024-12115-4. PMID: 39710664; PMCID: PMC11665076.* **Nuwematsiko R,** Kiwanuka N, Wafula ST, Nakafeero M, Nakanjako L, Luzze H, Turyahabwe S, Sekandi JN, Atuyambe L, Buregyeya E (2024).

Publication 2:

Facilitators and barriers for completion of the diagnostic process among people with presumed tuberculosis in Central Uganda. *PLOS Glob Public Health. 2025 Sep 19;5(9):e0004808. doi: 10.1371/journal.pgph.0004808. PMID: 40971693; PMCID: PMC12449001.* **Nuwematsiko R,** Atuyambe L, Kasiita V, Kiwanuka N, Musiimenta A, Rutebemberwa E, Buregyeya E (2025)

Supplementary publication:

Effect of SMS Reminders, Telephone Calls, and Transport Incentives on Enhancing the Completion of Tuberculosis Diagnosis and Initiation of Treatment for Diagnosed Patients: Protocol for a Randomized Controlled Trial. JMIR Res Protoc. 2025 Nov 25;14:e70325. doi: 10.2196/70325. PMID: 41289571; PMCID: PMC12646550. **Nuwematsiko R**, Kiwanuka N, Atuyambe L, Wobusobozi I, Kasiita V, Kagongwe S, Ssenyonga R, Kalyango JN, Nankabirwa V, Buregyeya E (2025)

ABSTRACT

Background: In 2025, tuberculosis (TB) remained the leading infectious killer despite being preventable. The "*WHO End TB*" strategy calls for a reduction in TB incidence by 90% and deaths by 95% by 2035. However, progress towards achieving this strategy has been partly hampered by the continued loss to follow-up (LTFU) of patients along the TB care cascade. In the TB care cascade, patients can be lost either before they are screened or before they are diagnosed when presumed with TB or before they initiate treatment after testing positive for the infection or before completing treatment. At the health facility level, the biggest LTFU of patients happens between one being presumed to have TB and getting a diagnosis leading to loss to follow-up (LTFU) before completing the diagnostic process despite having reached the facility. Continuous LTFU of people with presumed TB before they are diagnosed propagates community transmission of mycobacterium tuberculosis (*Mtb*) and poor patient outcomes. There is therefore an urgent need to come up with interventions to reduce this LTFU of people with presumed TB before they are tested.

Objectives: The main objective of this thesis was to assess the magnitude of pre-diagnosis LTFU and the effect of mHealth interventions to enhance completion of the diagnostic process among people with presumed TB in Central Uganda so as to inform the design of interventions. Specific objectives were: i) to determine the proportion of pre-diagnosis LTFU and factors associated in Central Uganda **(sub-study 1)**; ii) to explore the facilitators and barriers to completion of the diagnostic process among people with presumed TB in Central Uganda **(sub-study 2)**; iii) to synthesize evidence on mHealth interventions used to reduce LTFU among people with presumed TB and those diagnosed **(sub-study 3)**; iv) to assess the effect of the SMS or phone call intervention to enhance completion of the diagnostic process among people with presumed TB **(sub-study 4)** and v) to explore factors that influence use of the SMS or phone call intervention to enhance completion of the diagnostic process among people with presumed TB **(sub-study 4).**

Methods: The study was implemented under four sub-studies based on the Socio-ecological (SEM) model using both quantitative and qualitative methods of data collection. In **sub-study 1,** a retrospective cohort analysis of secondary data was conducted among people with presumed TB who presented to the study facilities from 1st January 2019 to 31st December 2022 to determine the proportion of pre-diagnosis LTFU and factors associated. Modified Poisson regression modelling was used to estimate adjusted prevalence ratios (adj.PR) and factors associated with TB pre-diagnosis LTFU. In **sub-study 2**, twenty-five In-depth interviews (IDIs) with purposively selected people with presumed TB who either completed or dropped out of the diagnostic process were conducted to explore facilitators and barriers to completion of the diagnostic process using a qualitative descriptive design. In addition, six focus group discussions (FGDs) with patients who had recently initiated TB treatment and 20 key informant interviews (KIIs) with health workers were also conducted. Thematic analysis was used for analysis. In **sub-study 3**, a systematic review was conducted to synthesize evidence on what mHealth interventions have been previously used to reduce LTFU in the TB presumption phase. In **sub-study 4**, a mixed methods study was embedded in an individual randomised controlled trial (RCT) to assess the effect of Short Message Service (SMS) and phone call intervention on completing the TB diagnostic process and explore factors that influence their use.

Results:

From sub-study 1, overall 28.3% (3,699/13.064) experienced pre-diagnosis LTFU within 30 days from the day they were presumed with TB. Pre-diagnosis LTFU was more likely to occur among patients aged 0-14 years (adj.PR=1.1, 95% CI: 1.06, 1.24), females (adj.PR=1.06, 95% CI: 1.01, 1.12), those with no record of place of residence (adj. PR=2.7, 95% CI: 2.54, 2.93), and those with no record of phone contact **(Paper 1)**. In sub-study 2: the key facilitators for completion of the TB diagnostic process included; persistent symptoms, obtaining same day results, prior TB knowledge, social support and caring health workers. Barriers were; TB and HIV stigma, long turnaround time of results, stock out of supplies, unclear

appointment for collection of results, lack of transport to return to the health facility, and poor health worker attitude (**Paper 2**.

From the systematic review in sub-study 3, SMS, phone calls, WhatsApp messages and mobile applications (Apps) were the mHealth interventions utilised in the TB presumption phase. Phone calls and SMS were however the commonly used interventions mainly used as reminders to collect or deliver TB result, and for linkages and referrals to diagnostic centres.

The evaluation of the SMS and phone call interventions revealed that completion of the TB diagnostic process was highest among participants randomised to the phone call arm compared to those in the standard of care 74.3% (434/584). There was no statistically significant effect for those in the SMS arm (adj RR 0.99, 95% CI: 0.91,1.08). Individual factors, social influences, technological factors, intervention design factors, health system factors and participant experiences influenced the use of the SMS and phone call intervention (sub-study 4).

Conclusion: From the study findings in this thesis, more than a quarter of the people with presumed TB got lost before getting tested or before receiving their test results. Completion of the TB diagnostic process was facilitated by obtaining same day results, prior TB knowledge, social support, while TB and HIV stigma, long turnaround time of results and lack of transport to return to the health facility were barriers. SMS and phone calls were the commonly used mHealth interventions in the TB presumption phase. From the evaluation of the intervention, completion of the TB diagnostic process was highest among participants in the phone call reminders arm compared to the standard of care. Implementation of SMS or phone call interventions is influenced by social influences, technological factors and intervention design factors. To enhance completion of the TB diagnostic process, there is need for empowering laboratories with resources to avail same day results, short of which mHealth interventions that incorporate phone calls should be considered to communicate readiness of results to

the patients. Design of SMS and phone call interventions should take into consideration individual factors, social, technological factors, user experiences and localised design strategies. Social support and stigma reduction interventions should be embraced both in the community and at the health facility to support people with presumed TB to complete the diagnostic process.

CHAPTER ONE: INTRODUCTION AND BACKGROUND

1.1 GENERAL INTRODUCTION

1.1.1 Epidemiology of TB

Tuberculosis (TB) is an infectious disease caused by the bacteria *Mycobacterium tuberculosis* (Mtb). The Mtb is spread through aerosol mechanism when an infected person coughs, sneezes, or spits, releasing tiny droplets in air that can be inhaled by others (WHO, 2025a). The bacteria majorly affect lungs which is known as the pulmonary TB but can also affect other body parts such as the kidneys, spine, and brain which is referred to as the extrapulmonary type (WHO, 2025a). When infected with Mtb, some people progress to get ill with the TB disease (Active TB) while others remain harbouring the infection in a latent state (Latent TB). About a quarter of the global population is estimated to have latent TB, meaning that they have the infection but are not yet ill with the disease (WHO, 2025a). People with latent TB cannot transmit it to others but have a 5-10% lifetime risk of getting the disease. The risk for progression to TB disease is faster for individuals with compromised immunity such as those living with HIV, diabetics, malnutrition and tobacco users (WHO, 2025a, Zeru, 2021).

1.1.2 Global burden of TB

TB is both preventable and treatable yet it remains a significant global health challenge; it is ranked as the leading cause of death from a single infectious agent, a position it regained after 3 years of COVID-19 being the leading cause of death (WHO, 2025b). In 2024 10.7 million people fell ill with TB globally compared to 10.8 million in 2023, the first recorded decline in the incidence since the COVID-19 pandemic in 2020 (WHO, 2025b). Global TB incidence had been reducing at about 2% per year since 2015 until 2020 during the COVID-19 pandemic which reversed these previous gains in the decline

of TB incidence and deaths (Falzon et al., 2023, Kirby, 2021, WHO, 2022). Out of those who fell ill with TB in 2024, 1.23 million died (WHO, 2025b). TB disproportionately affects low- and middle-income countries (LMICs), men and people living with HIV (WHO, 2025b). In 2024, The TB burden remained high in low- and middle-income countries with 99% reporting incident cases. Most new TB cases were reported in the WHO South-East Asia Region (45%) followed by the Western Pacific, 27% and 25% in the African Region (WHO, 2025b).

Despite the high TB incidence, TB notification remains low signifying gaps in access to diagnostic services and reporting (WHO, 2025b). Globally, out of the 10.7 million people who fell ill with TB in 2024, only 8.3 million of them were diagnosed and notified to TB programs implying a LTFU of 2.4 million (22%) people (WHO, 2025b). The 22% loss includes those who were either not diagnosed or those who were not officially reported to national TB programs. Patients can be lost from the TB care cascade at different points, either after being presumed with TB and they do not test or at the testing point when they are diagnosed to have TB, but never start treatment. This is in addition to the number of patients who never access a TB diagnostic test (Subbaraman et al., 2020, Shah et al., 2022).

A previous study by Kim and colleagues on LTFU of patients along the TB care cascades from 30 high TB burden countries found that 35% of people incident with TB did not receive a diagnosis while 5% of people who were diagnosed did not initiate treatment (Kim et al., 2019). The burden of people with presumed TB getting lost before being diagnosed is shared across all TB-burden countries although it is highest in high-TB burden countries compared to low-burden countries (Kim et al., 2019).

Loss to follow-up of patients before testing for TB and those diagnosed before starting treatment facilitates further spread of the infection in the community. An untreated smear-

positive TB patient for example is estimated to infect, on average, 10-15 contacts annually (WHO, 2018, Styblo, 1991). Completing the TB diagnostic process and starting treatment early leads to better treatment outcomes with a reduced rick of post-TB lung diseases, and reduces morbidity and mortality for those diagnosed (Tiemersma et al., 2011, Getnet et al., 2019, Mugauri et al., 2018, Zawedde-Muyanja et al., 2020a, MacPherson et al., 2013, Meghji et al., 2025). This LTFU of patients along the TB care cascade continues to hamper progress towards achieving the global target of ending the TB epidemic (Shah et al., 2022) given that completion of the TB diagnostic process is a key component towards the elimination of TB as a public health problem by 2035 (Gupta-Wright and Denkinger, 2024).

1.1.3 Global targets and ambitions to end the TB epidemic

Global efforts are all geared towards ending the TB epidemic by 2035 as stipulated by WHO in the End TB strategy. The End TB strategy aims to end the global TB epidemic by reducing incidence by 90%, deaths by 95% with zero catastrophic costs by 2035 (WHO, 2015a). In addition, the sustainable development goal (SDG) target 3.3 was also set to end the TB epidemic by 2030 through reducing incidence to <20 per 100,000 population (UN, 2015). These strategic documents and resolutions call for bold actions and funding to realise the set targets. Progress towards attaining these targets has however been slow over the years. The reduction in TB incidence rate since 2015 is 12%, far from the target of 90% and reduction in deaths at 29% far from the 95% target (WHO, 2025b). Even with the mid-term 2025 milestone of reduction of incidence by 50% and deaths by 75%, the progress remains very slow (WHO, 2015a).

In 2023, the second United Nations (UN) high-level meeting on the fight against TB adopted 2027 targets and milestones of reducing incidence and deaths to accelerate

progress towards achieving the 2030 and 2035 goals of ending TB (WHO, 2023a). These targets were aimed at enhancing equitable access to TB diagnostic and treatment services at 90% for all those who develop TB by 2027 and increasing Tuberculosis Preventive Treatment (TPT) coverage to 90% among others (WHO, 2023a). With two years left to 2027, progress towards achieving these targets remains far from reach with coverage of TB diagnosis and treatment at 78% in 2025 versus the target of 90% (WHO, 2025b).

1.1.4 What has been done

Several interventions are on-going to reduce the LTFU of people with presumed TB before they complete the diagnostic process including community health worker programs to increase awareness of TB symptoms, provide home screening and support tracking of patients (Garg et al., 2020, Garg et al., 2021); integration of TB services with HIV(Burnett et al., 2018, Uyei et al., 2011); increasing availability of point-of-care diagnostics to enable faster turn-around time of results (Byrne et al., 2024); programmatic quality improvements for patient flow, data and laboratory processes; counselling and health education (Marley et al., 2023); use of transport incentives and mobile health (mHealth) technologies such as SMS, phone calls, mobile applications and Unstructured Supplementary Service Data (USSD) codes (Marx et al., 2022, Chadha et al., 2017, Bassett et al., 2019, Wagstaff et al., 2019).

However, most of these interventions have not yielded the expected results to reduce LTFU before TB testing. This is because the interventions are often implemented in isolation ignoring the underlying barriers of TB testing such as economic constraints, stigma, gender norms affecting healthcare access and competing household priorities (Li et al., 2013, Mulaku et al., 2024a). Furthermore, health system challenges remain unaddressed such limited access to diagnostics, long laboratory turnaround times, referral

systems weak and long distances to health facilities, all of which continue to increase the LTFU before TB testing even when other interventions are implemented (Fenta et al., 2023, Teibo et al., 2024). There is therefore a need for multi-component interventions (Marley et al., 2023).

The WHO recommends use of mHealth in TB care for improved service delivery and continuation of care given its timeliness, popularity and affordability (WHO, 2015b, WHO, 2017). Increased ownership and use of mobile phones has further accelerated and favoured the use of mHealth in health care settings (Ibeneme et al., 2020). As of 2025, 82% of the global population aged 10 years and above own a mobile phone with people in LMICs at 74% ownership (ITU, 2025). Most of these mHealth interventions have however been commonly used in the TB treatment phase fostering adherence to medication (Lester et al., 2019, Mohammed et al., 2016, Musiimenta et al., 2020, Iribarren et al., 2014) as compared to TB presumption phase where increasingly most people are lost (Kim et al., 2019). The TB presumption phase offers an opportunity for early detection of TB and treatment initiation (Yayan et al., 2024, Gordin et al., 1989).

In the TB pre-diagnosis phase, very few studies have utilised mHealth interventions to reduce LTFU. The few studies conducted have utilised SMS, WhatsApp messaging, phone calls, mobile applications (Apps) and combined approaches of mHealth tools with community health worker support (Marx et al., 2022, Wagstaff et al., 2019, Tumuhimbise and Musiimenta, 2021, Mudzengi et al., 2024). These interventions have mainly been used for active case finding, screening, result notification, reminders for results collection and clinic appointments and linkage to treatment initiation (Marx et al., 2022, Wagstaff et al., 2019, Mudzengi et al., 2024). However, few of these studies have tested for the effect of these mHealth interventions on patient outcomes such as sample submission and results collection with most testing for feasibility and others are program evaluations (Mudzengi

et al., 2024, Nglazi et al., 2013, Liu et al., 2014). Implementation barriers such as training requirements, phone availability and accessibility, and network connectivity have been reported to hamper feasibility (Tumuhimbise et al., 2023, Babirye et al., 2019).

Evidence suggests that mHealth interventions in the TB pre-diagnosis phase are feasible, and potentially effective for attending appointments and follow-up within the diagnostic pathway (Tumuhimbise et al., 2023, Babirye et al., 2019). However, there is insufficient high-quality evidence to conclude that mHealth interventions reduce pre-diagnosis LTFU since most studies focus on process indicators rather than patient outcomes with very few randomised controlled trials hence the need for rigorous effectiveness studies on mHealth interventions across the pre-diagnostic pathway (Mudzengi et al., 2024, Nglazi et al., 2013).

There is mixed evidence on the effect of these mHealth interventions with some showing effect and others none (Nglazi et al., 2013, Hall et al., 2014, Marcolino et al., 2018). These interventions were possibly not successful because they did not address underlying barriers such as counselling needs, transport costs, and health-system inefficiencies. The differences in evidence may have resulted from differences in message frequency, modality of SMS delivery that is one-way versus two-way, content, and continued interactivity (Nglazi et al., 2013). Hence a need remains for further contextually-designed studies on the effect of mHealth interventions in improving TB care especially in the presumption phase before one is tested.

1.2 BACKGROUND

Uganda is ranked among the 30 high TB/HIV burdened countries and continues to suffer a high incidence of TB at 197 cases per 100,000 people (WHO, 2025b). This incidence

represents a 2.4% reduction since 2015, way below the End TB target of 50% reduction by 2025. In addition to being a high TB burden country, Uganda is grappling with high levels of missing TB cases who are either not presenting to health facilities or not diagnosed or diagnosed but not notified (WHO, 2025b). Out of the 99,000 people who fell ill with TB in 2024 in Uganda, only 88,861 were diagnosed leaving out 10,139 (11.4%) of the people undiagnosed and untreated (WHO, 2025b). The LTFU of people with presumed TB before diagnosis has been previously estimated in a study in Uganda at 40.7% (Ekuka et al., 2020).

In order to improve case detection and notification, Uganda adopted the WHO TB systematic screening and testing strategy at all health facilities but its implementation is at 75.1%, below the 100% target (NTLP, 2023, GOU, 2017). In addition to improving diagnostics, the country has also continued to implement community campaigns such as TB Catch-up and Community Awareness, Screening, Testing, prevention and treatment to end TB Campaign (CAST TB) all aimed at reducing the LTFU of patients before they are diagnosed (MOH, 2021a). These campaigns involve community awareness of TB, intensified screening and diagnosis of patients for TB, (MOH, 2021a). Although these interventions are in place to foster increased diagnosis, people with presumed TB continue to be lost in Uganda before completing the diagnostic process and initiating treatment.

Some of the reasons for the LTFU of patients before diagnosis include limited access to the diagnostics, high out of pocket expenditure to go to the health facility, distance to the health facility, stigma, failure to get a result from the testing laboratory, and stigma (Ekuka et al., 2020, Buregyeya et al., 2014). These reasons have however not been studied empirically in the TB presumption phase. The challenges to completing the TB diagnostic process are more evident in rural and semi urban areas where the diagnostic services are limited, lack of transport to the facility rampant and community members less aware of

availability of the services (Buregyeya et al., 2014). This study was conducted in Central Uganda which is one of the regions grappling with a high TB/HIV burden amidst over population and few health facilities which are distant to the general population (NTLP, 2024). The TB screening and diagnostic capacity in Central Uganda are also limited especially on the access of the Xpert MTB/RIF (NTLP, 2024). All these factors contribute to LTFU of people with presumed TB.

This thesis therefore aimed at assessing the magnitude pre-diagnosis LTFU and the effect of mHealth interventions in enhancing completion of the diagnostic process among people with presumed TB in Central Uganda so as to inform the design of interventions to address the problem of LTFU of patients before diagnosis.

1.3 STATEMENT OF THE PROBLEM AND JUSTIFICATION

1.3.1 PROBLEM STATEMENT

1.3.1.1 The problem

Globally, much attention has been focused on the LTFU of TB patients before completing treatment yet increasingly most patients are lost before they are tested and or diagnosed (Kim et al., 2019). TB notifications remain low indicative of either limited access to diagnostic services or missed diagnosis of patients at the health facility or poor reporting (WHO, 2025b). Twenty two percent (22%) of the patients who fell ill with TB worldwide in 2024 were not diagnosed (WHO, 2025b). In high TB burden countries, it was estimated that 35% of people incident with TB do not receive a diagnosis (Kim et al., 2019). Undiagnosed and untreated TB patients continue to spread the infection in the community and experience high morbidity and mortality (Tiemersma et al., 2011, Getnet et al., 2019, Mugauri et al., 2018, Zawedde-Muyanja et al., 2020a, MacPherson et al., 2013).

1.3.1.2 Magnitude of the problem

At the time of this study, Uganda too was experiencing high loses of people with presumed TB before they are tested contributing to spread of the infection in the community. In 2024, 11.4% of people with TB remained undiagnosed (WHO, 2025b). A previous study in-country also showed a pre-diagnosis loss to follow up (LTFU) of as high as 40.7% (Ekuka et al., 2020). Those commonly LTFU before completing TB diagnosis and include females, HIV positive patients and young people aged 15 years and below (Ekuka et al., 2020, Zawedde-Muyanja et al., 2020b).

1.3.1.3 What has been done

Few interventions have been implemented to reduce the LTFU before completing diagnosis and before treatment initiation with most efforts being focused on estimating the magnitude of this LTFU in previous studies. Some of the interventions include community campaigns, use of SMS reminders, phone calls, mobile apps, systems strengthening, improving the diagnostics, intensifying follow-up and providing incentives (Zawedde-Muyanja et al., 2020a, Musiimenta et al., 2020, Babirye et al., 2019, NTLP, 2024, Meyer et al., 2018, Nalugwa et al., 2020). Use of mHealth interventions has been recommended by WHO and from previous research to guide improvement of TB care (Babirye et al., 2019, Meyer et al., 2018, Kiberu et al., 2017, WHO, 2019). Previous m-Health interventions like SMS, mobile apps and phone calls have shown potential for great impact in improving retention in care for patients on treatment (Sekandi et al., 2020a, Hermans et al., 2017).

1.3.1.4 Study gap

Although these interventions have been put in place to reduce the LTFU before completing diagnosis, people with presumed TB have continued to be LTFU and there is limited information on why and how completion of TB diagnosis can be fostered (Ekuka et al.,

2020). Previous studies have been conducted in limited settings, mainly among TB patients, in few health facilities and urban centres yet greater problems lie at the lower health facility levels and in rural areas (Dowhaniuk, 2021, Konde-Lule et al., 2010).

Few studies in the TB pre-diagnosis phase have implemented mHealth interventions as a potential tool for reducing the pre-diagnosis LTFU yet it has been successfully used in improving healthcare seeking especially for TB and HIV treatment. SMS and phone calls are the commonly used mHealth tools in the pre-diagnosis phase mainly used for TB screening, adherence to appointments, diagnostic follow-up and linkages to treatment initiation. SMS reminders and phone-calls have been associated with better screening, active case finding, appointment's attendance and follow-up compliance among people with presumed TB.

SMS reminders and phone-calls have proved feasible and acceptable among stakeholders but with limited evidence on the actual effect on patient-level outcomes such as sample submission, turnaround time and overall pre-diagnosis LTFU. This could be because most studies have either been observational or program evaluations thus lacking rigorous evaluations for measuring the intervention effect on patient outcomes. More so, most mHealth interventions have remained at the pilot level with no process evaluations conducted to explore factors that influence implementation and use hence they have not been scaled up due to the limited evidence (Marcolino et al., 2018, Lee et al., 2020).

1.3.1.5 Consequences

People with presumed TB who do undiagnosed continue to transmit the infection within their communities, perpetuating the spread of TB and undermining control efforts (WHO, 2025a). In addition, delayed diagnosis of people with presumed TB who are positive for the disease may have poor treatment outcomes and greater socioeconomic hardship due to

prolonged illness and loss of productivity (Zawedde-Muyanja et al., 2020a). Moreso, lack of process evaluations during implementation limits availability of evidence on mechanisms of impact for interventions hampering scale up (Rathod et al., 2024, Skivington et al., 2021).

1.3.1.6 What was done

This study therefore assessed the magnitude of pre-diagnosis LTFU and the effect of mHealth interventions to enhance completion of the diagnostic process among people with presumed TB in Central Uganda.

1.3.2 JUSTIFICATION

The TB burden continues to be high in Uganda with an estimated incidence of 197 cases per 100,000 people per year (WHO, 2025b). In 2024, Uganda was still ranked among the top 30 TB high burden countries which calls for urgent action (WHO, 2025b). Efforts to reduce the burden and achieve the 2035 target to eliminate the epidemic have however been halted by continued transmission due to LTFU for TB patients both before TB diagnosis and starting treatment (Ekuka et al., 2020, Zawedde-Muyanja et al., 2020b). Hence the need for this study to provide evidence on some interventions that may be effective in reducing the TB burden.

The study focused on SDG 3 three on good health and well-being which aims at ensuring healthy lives and promotion of well-being for all at all ages. Specific focus was on target 3.3 to fight communicable diseases and to end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases by 2030. Evidence from this study provided reasons why patients are lost before they test for TB and some potential interventions that are effective in reducing this LTFU of patients who could potentially continue to spread TB in the community, further increasing the epidemic. Therefore, these findings may be

adapted to address these barriers to TB testing and support the design of strategies to improve the TB diagnostic process hence preventing the spread of TB in the community.

The study aligned to the Uganda Health Information and Digital Health Strategic Plan 2020/21 –2024/25 that aims to leverage digital health technologies to optimize health service delivery in order to achieve universal health coverage by 2030 (MOH, 2021b). The strategic plan emphasizes implementing patient-centred digital health interventions at points of care which this study sought to address by using SMS and phone call reminders to enhance completion of the diagnostic process. Strategy 4.2.4 of the Uganda Vision 2040 also encourages use of science and technology and innovations to drive health and economic development. Findings from this study may therefore provide information on ways how technology can be embedded in the routine health care system for improved service delivery at health facilities.

The WHO and Stop TB partnership recommend use of mHealth interventions to support TB care and increase patient-centred care (WHO, 2015b, WHO, 2017, WHO, 2019). In practice, this recommendation however stops at research studies and pilot projects with limited scale up and sustainability. This therefore supports our need to conduct the process evaluation of these interventions to identify opportunities that can be enhanced for scale up and sustainability. This study will likely contribute to pillar 3 of the WHO's End TB strategy on intensified research and innovation by providing information to add to the evidence base on what may foster completion of TB diagnosis.

1.4 RESEARCH QUESTIONS AND OBJECTIVES

1.4.1 RESEARCH QUESTIONS

1. What is the proportion of pre-diagnosis LTFU and the factors influencing it in Central Uganda?

2. What mHealth interventions have been used to enhance completion of the TB diagnostic process and treatment initiation in LMICs?
3. What is the effect of an SMS or phone call intervention on the completion of the TB diagnostic process in Central Uganda?
4. What factors influence use of an SMS or phone call intervention to foster completion of the TB diagnostic process in Central Uganda?

1.4.2 GENERAL OBJECTIVE

To assess the magnitude of the pre-diagnosis LTFU and effect of mHealth interventions to enhance completion of the diagnostic process among people with presumed TB in Central Uganda so as to inform design strategies for reducing this LTFU before completing the diagnostic process.

1.4.3 SPECIFIC OBJECTIVES

1. To determine the proportion of pre-diagnosis LTFU among people with presumed TB and factors associated in Central Uganda **(sub-study 1)**
2. To explore the facilitators and barriers to completion of the diagnostic process among people with presumed TB in Central Uganda **(sub-study 2)**
3. To synthesize evidence on what mHealth interventions have been used to enhance completion of the tuberculosis diagnostic process and treatment initiation **(sub-study3)**
4. To assess the effect of an SMS or phone call intervention on the completion of the TB diagnostic process in Central Uganda **(sub-study 4)**
5. To assess factors that influence use of an SMS or phone call intervention to foster completion of the TB diagnostic process in Central Uganda **(sub-study 4**

CHAPTER TWO: LITERATURE REVIEW

2.1 LITERATURE REVIEW

2.1 Introduction

In this section, existing literature on the magnitude and factors for LTFU before completing the TB diagnostic process and use of mHealth interventions was searched and synthesized. From the literature I synthesize the findings, context of the studies, opportunities, strengths, weaknesses and gaps.

2.2 The TB care cascade and magnitude of pre-diagnosis LTFU

Understanding the phenomena of LTFU of patients with presumed TB starts with critically understanding their flow in the health care system once they start to feel the symptoms of TB. This flow of health care for such patients is known as the TB care cascade. The TB care cascade comprises of four phases namely; i) Screening, ii) Diagnosis, iii) treatment initiation, and iv) treatment (Subbaraman et al., 2020). The cascade begins with people in the community recognizing that they have symptoms of TB and seeking care at health facilities where they are presumed with TB. A person presumed with TB is one who presents to a health facility with all or any of the four cardinal symptoms and signs suggestive of TB - persistent cough of more than two weeks, fever, night sweats, and weight loss. At the health facility, screening of people with presumed TB is conducted using the cardinal symptoms of TB that is fever, night sweats, unexplained weight loss and cough (screening phase). Once one is presumed to have TB, they are sent for evaluation using either laboratory (using either Xpert MTB/RIF or microscopy or urine lipoarabinomannan [LAM]) or radiology investigations (X-ray) for TB diagnosis (diagnosis phase). People with presumed TB who test positive for TB are initiated on treatment (treatment initiation). Confirmed TB patients are expected to adhere to the TB drugs for the six months treatment course (treatment phase) as shown in figure 1 below;

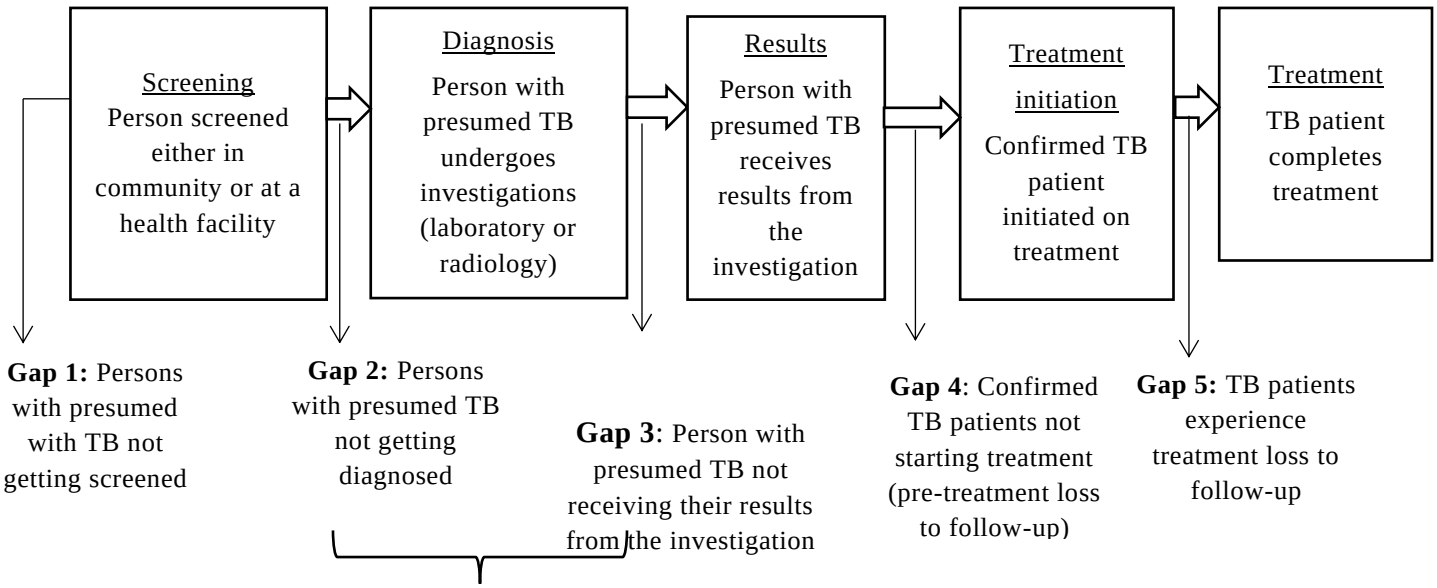


Figure 1: Schematic diagram of the TB care cascade and gaps at each stage (Subbaraman et al., 2020)

Over the years, significant gaps have been identified in this TB care cascade leading to LTFU of patients *(Subbaraman et al., 2020, Feasey et al., 2021, Oga-Omenka et al., 2020, Karamagi et al., 2018)*. Some of the gaps highlighted in the literature include; limited ability to detect and track infected TB patients in the community; delayed and or failure of the presumptive TB patients to come to a health facility to seek care; inability to access diagnostic services for those who reach the health facility, failure of patients to return and get their test results or initiate treatment if positive and loss to follow up of those on treatment (Subbaraman et al., 2020, Oga-Omenka et al., 2020, Lienhardt et al., 2012).

At the screening level, a systematic review by Divala et al., showed that screening for TB is not done for 33-96% of participants with symptoms (Divala et al., 2022). For patients who make effort to come

to health facilities and are presumed with TB by health workers but still don't make it for TB examination, the extent of their loss ranges from 9% in India to as high as 80% in Nigeria (Garg et al., 2020, Ekuka et al., 2020, Oga-Omenka et al., 2020, Murongazvombo et al., 2019, Jayasooriya et al., 2023, Ismail et al., 2020, Mando et al., 2023). Most of the evidence available on this LTFU is from Africa and Asia regions which are LMICs but also double as high-TB burden countries (Kim et al., 2019, MacPherson et al., 2013, Ekuka et al., 2020). Higher LTFU is reported in settings with limited diagnostic access or referral compliance, such as Ethiopia (Milkias et al., 2023), Zimbabwe (Murongazvombo et al., 2019) and Tanzania (Mgina et al., 2022) while lower proportions of LTFU observed in studies with on-going interventions such as Pakistan (Fatima et al., 2015) and India (Thomas et al., 2018).

Information on pre-diagnosis LTFU in Uganda is still limited and evolving. A study conducted at a health centre IV facility in Jinja district revealed a pre-diagnosis LTFU of 40% (Ekuka et al., 2020). Another study by Kakame et al., revealed that 55.9% of the patients who had presented to public health facilities did not undergo sputum and/or chest X-ray examinations (Kakame et al., 2021). This included both patients who mentioned the symptoms to health care workers and those who did not. Much of the available evidence is based on secondary data with limitations of missing data and there is paucity of data on both pre-diagnosis and pre-treatment LTFU from the same setting. It is therefore important to add onto the existing evidence on pre-diagnosis and pre-treatment LTFU from other districts in Uganda, throughout the TB care cascade from diagnosis to treatment.

2.3 Factors associated with pre-diagnosis LTFU

Pre-diagnosis LTFU in TB programs is driven by socio-demographic vulnerabilities (young age, sex, rural residence, low-income level), access barriers (transport, distance), clinical features (HIV infection, lower symptom severity) and health-system inefficiencies (missing contact data, limited

diagnostics) (MacPherson et al., 2013, Zawedde-Muyanja et al., 2020b, Murongazvombo et al., 2019, Milkias et al., 2023, Mulaku et al., 2024b).

Evidence shows that younger patients are more likely to experience pre-diagnosis LTFU for TB compared to other ages. A study in Uganda by Ekuka et al., showed that those aged 18 years and below were more likely to drop out before completing the diagnostic process (Ekuka et al., 2020). In another study in India, pre-diagnosis LTFU was highest among those aged below 15 years (Pala et al., 2018). In a health-seeking behaviour study in Zambia among people with presumed TB, the older age groups were 1.6 times more likely to seek care than the younger ones (Chanda-Kapata et al., 2016). Lower completion rates among younger patients may be because of the dependency in decision making and existing diagnostic challenges of TB among children, such as difficulty obtaining sputum and a lack of functional radiological investigations (X-rays) at health facilities (Gunasekera et al., 2022, An et al., 2023, Shitol et al., 2023). Early detection of TB especially in children and adolescents is crucial for improving treatment outcomes and preventing post TB lung impairment (Getnet et al., 2019, Meghji et al., 2025).

There is inconsistent evidence on which sex is more likely to be LTFU before completing the TB diagnostic process with most literature showing women as more likely and others showing men mainly attributing it to their poor health seeking behaviours (Chanda-Kapata et al., 2016, Arja et al., 2022). For example, in a study in Tanzania by Mhalu et al., females were 3.8 times more likely to be LTFU (Mhalu et al., 2019). Although females are likely to experience pre-diagnosis LTFU, males on the other hand are more likely to drop out before initiating treatment (MacPherson et al., 2013, Daka et al., 2022, Chilembo et al., 2020). On the contrary, another study found no association between sex and LTFU (Ekuka et al., 2020).

Residing in rural residence has also been linked to high pre-diagnosis and pre-treatment LTFU (Tumuhairwe et al., 2025, Padingani et al., 2018). This is linked to increased distance to health facility, limited transport and low-income levels to access health services. In Ghana, a distance to a laboratory that was greater than 10 kilometers was associated with pre-diagnosis LTFU (Der et al., 2020). Similarly, in Zimbabwe, Murongazvombo et al., found that a distance greater than 2 kilometers is associated with pre-diagnosis LFTU for people with presumed TB (Murongazvombo et al., 2019). Distance to the health facility consequently determines the amount of transport required which was also reported as a barrier to completing the diagnostic process. Patients mentioned lack of transport to health facilities as a barrier aligning to the fact that TB is a disease of the poor (Dixit et al., 2021, Zawedde-Muyanja et al., 2022).

Studies show mixed evidence on the association between HIV and pre-diagnosis LTFU. Some studies indicate that those who are HIV positive are most likely to be LTFU before completing the TB diagnostic process (Ekuka et al., 2020, Zawedde-Muyanja et al., 2020b, Padingani et al., 2018). For example a study in Zimbabwe showed that HIV positive presumptive tuberculosis patients were 40% more likely to be LTFU than HIV negative patients (Padingani et al., 2018). On the contrary, studies in South Africa showed no difference in LTFU between those who are HIV positive and those who are negative (Mwansa-Kambafwile et al., 2017, Burger et al., 2021). Although there is mixed evidence on if HIV patients are more likely to be LTFU, it still emphasizes the need to strengthen integration of TB services across all health facility departments especially in chronic care clinics where patients are likely to have health facility fatigue due to repeated visits.

2.4 Facilitators and barriers for completing the TB diagnostic process

Facilitators and barriers for completing the TB diagnostic process among people with presumed TB differ across different countries and regions within the same countries (MacPherson et al., 2013, Garg

et al., 2020, Ekuka et al., 2020, Murongazvombo et al., 2019, Pala et al., 2018, Padingani et al., 2018, Der et al., 2020). From the review of literature, these factors have been categorized according to patient factors, health system factors and environmental factors.

Patient factors

Studies show patient factors that lead to LTFU as low severity of symptoms, poor health seeking behaviours, lack of social support, limited knowledge on TB, lack of transport to the health facility, stigma and failure to submit sputum samples on the day of hospital visit (Garg et al., 2020, Buregyeya et al., 2014, Der et al., 2020, Zawedde-Muyanja et al., 2022, Mulaku et al., 2023).

For long, healthcare seeking of patients has been tagged to the severity of the symptoms and delaying with anticipation of symptoms reducing (Arja et al., 2022). The less severe or the less the pain and discomfort the less likely someone will seek care appropriately (Arja et al., 2022, Daneshvari et al., 2021). This has been the case across all diseases and TB is not spared with studies showing that some patients don't seek care to completion because their symptoms are not severe hence, they think it's not serious as seen in a systematic review from India and studies elsewhere (Arja et al., 2022, Padingani et al., 2018, Jhaveri et al., 2024).

Poor patient knowledge and attitude on TB have also been associated with non-completion of the TB diagnostic process (MacPherson et al., 2013, Mulaku et al., 2023, Cattamanchi et al., 2015, Nalugwa et al., 2025). Studies show that limited awareness of TB is associated with delays in healthcare seeking (Teibo et al., 2024, Mulaku et al., 2023, Marahatta et al., 2020). Moreso, some studies report patients' inability to understand the diagnostic process as a key barrier for completion (Der et al., 2020).

Systematic reviews show low economic status of patients as also a major contributor to patient LTFU before completing the TB diagnostic process (MacPherson et al., 2013, Arja et al., 2022, Cai et al.,

2015, Ahmad et al., 2024). Low economic status implies no or limited transport to the health facilities to test for TB which often leads to delay in seeking care or non-completion of the TB diagnostic process especially if it involves making several visits to the health facility (Cattamanchi et al., 2015). The lack of transport is further amplified by long distances to health facilities for patients who stay far (Murongazvombo et al., 2019, Ahmad et al., 2024).

More so, studies report lack of patient support both social and health provider as key contributors for pre-diagnosis LTFU (Mulaku et al., 2023, Nalugwa et al., 2025). Lack of support from family members is reported to either motivate or hinder someone from completing the diagnostic process (Mulaku et al., 2023). This social support is crucial given that TB is a highly stigmatized disease which could deter one from testing if not supported and motivated by a significant person in their life (Fenta et al., 2023, George, 2019, George et al., 2020). Participants in a qualitative study in Uganda mentioned that having support, encouragement and empathy from their family during their illness is a critical component to progressing through the TB care cascade to the end (Nalugwa et al., 2025).

TB stigma is also a key barrier to completing the TB diagnostic process as has been found in studies in Uganda, Kenya and across the globe (Arja et al., 2022, Mhalu et al., 2019, Zawedde-Muyanja et al., 2022, Mulaku et al., 2023, Cattamanchi et al., 2015, Nalugwa et al., 2025). The stigma is commonly anticipated and due to the misconception that whoever has TB has HIV hence the fear is more on being associated with HIV. HIV remains highly stigmatized despite on-going efforts which is now consequently affecting the opportunistic infections complicating their control and management (George, 2019, George et al., 2020).

Health system factors

Limited diagnostic services and infrastructure at health facilities were found as a key facilitator to pre-diagnosis LTFU since the patient must leave the facility in search of the service elsewhere which

sometimes isn't cost free (Cattamanchi et al., 2015). A study in Zambia showed that patients who were diagnosed with smear microscopy were more likely to be LTFU compared to those of Gene Xpert (Chilembo et al., 2020). The Gene Xpert assay has a short turnaround time for results but is expensive hence not available in all health facilities. Relatedly, limited infrastructure also hinders quality diagnostic services for TB. In a study by Cattamanchi et al., with health workers in Uganda, the clinic staff described that limited private space for assessing and counseling clients and lack of waiting areas are barriers to providing high quality care which could hence send away some people with presumed TB before finishing the diagnostic process (Cattamanchi et al., 2015).

Long turnaround time of the results also contributes to LTFU since patients have to wait for long hours for the results or even return another day for the results (Zawedde-Muyanja et al., 2022, Cattamanchi et al., 2015). This necessitates more transport and time off work which may not be possible especially for those in employment and those with limited income (MacPherson et al., 2013, Zawedde-Muyanja et al., 2022). The long turnaround time of results is attributed to insufficient laboratory personnel, staff absenteeism, lack of staff motivation, Xpert MTB/RIF errors, poor sample tracking, stock out of supplies, limited and impaired diagnostic machines and delays in processing samples and validating results (Mbuh et al., 2025, Dey et al., 2013, Shiferaw and Yismaw, 2019).

The type and level of health facility are key factors affecting pre-diagnosis LTFU, as shown by studies from Zimbabwe, private facilities were more likely to have people with presumed TB dropping out before completing diagnosis as compared to public facilities (Padingani et al., 2018). On the other hand, receiving care from a regional health facility also contributes to pre-diagnosis LTFU (Murongazvombo et al., 2019). Poor documentation of patient tracker information at the health facilities such as telephone number and physical address was also found as key facilitators for LTFU (Zawedde-Muyanja et al., 2020a, Arinaitwe et al., 2025).

2.5 mHealth interventions in TB care

mHealth has increasingly gained popularity for patient communication, monitoring treatment adherence, improving service delivery and health education all aimed at improving access to health services and clinical diagnosis (Wagstaff et al., 2019, Tetra Dewi et al., 2019, Sekandi et al., 2020b, Owiti et al., 2012). No standard definition exists for mHealth but common terms are used by WHO to define mHealth as medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices (WHO, 2011). The commonly used mHealth interventions include SMS, drug monitors, phone calls, mobile applications (Apps), digital bill boxes and personal assistance devices (WHO, 2017, WHO, 2011, Yoeli et al., 2019, Subbaraman et al., 2018).

Short message service (SMS) and phone call reminders have been previously used to improve prevention and treatment adherence of different health conditions such as HIV/AIDS, tobacco control and others (WHO, 2015b, Hermans et al., 2017, Haberer et al., 2016, Ware et al., 2016, Devi et al., 2015). However, in the recent past, SMS interventions also gained popularity in the TB field all aimed at improving retention in care and patient-centred care for the TB patients. Most mHealth interventions which have been conducted in the TB treatment phase use SMS or phone calls for reminders to TB patients either to take medicine or come for clinical appointments (Babirye et al., 2019, Majella et al., 2021, Choun et al., 2017). There is less attention to the presumption phase (the period before one is diagnosed with TB) yet increasingly that is where most patients are LTFU (Iribarren et al., 2014, Mwansa-Kambafwile et al., 2022, Liu et al., 2015). The TB presumption phase presents an opportunity for early diagnosis and treatment initiation which are key components in TB control but also lead to better outcomes (WHO, 2010, Migliori et al., 2012).

A synthesis of the literature showed scanty evidence on effectiveness of SMS reminders and phone calls in improving treatment adherence for TB patients (Nglazi et al., 2013, Choun et al., 2017, Meira et al., 2025, Ngwatu et al., 2018). A few studies have shown increased adherence to TB treatment (Tetra Dewi et al., 2019, Yoeli et al., 2019, Fang et al., 2017, Gashu et al., 2020). On the contrary, some studies in Argentina, Uganda and Pakistan have not found a significant increase in adherence to treatment for those who received SMS reminders (Mohammed et al., 2016, Hermans et al., 2017, Meira et al., 2025, Iribarren et al., 2012). However, there are variations in methodologies and the design and delivery of SMS across different study settings especially on frequency, content, model of delivery and continued patient engagement resulting in different effects (Nglazi et al., 2013, Ngwatu et al., 2018). These variations largely contribute to the mixed evidence. Hence there remains a need for further high-quality studies on the effect of mHealth interventions in improving TB treatment.

In the TB presumption phase before one is diagnosed with TB, few mHealth interventions have been piloted, implemented and scaled up. The few mHealth interventions in this phase have so far been used for four purposes that is i) to improve surveillance and contact tracing; ii) provide health information on TB; iii) reminding patients to return to the clinics and complete diagnosis and iv) deliver test results to patients who have gone through the diagnosis (Wagstaff et al., 2019, Liu et al., 2014, Babirye et al., 2019, Meyer et al., 2018, Maraba et al., 2018a, Ggita et al., 2020). From the literature, the commonly piloted mHealth interventions in this presumption phase were SMS, phone calls and mobile applications. For example, a 2022 study in South Africa tested the use of WhatsApp-based reminders to prompt individuals with presumptive TB to return for a scheduled follow-up appointment to receive their sputum test results (Marx et al., 2022). Similarly, another study used SMS reminders to see their effects on patients' return to the clinic to get their test results and start appropriate treatment (Wagstaff et al., 2019). However, there is scanty consolidated evidence of all the mHealth interventions used thus far in this phase, their effectiveness, potential for scale up and

their sustainability. The most commonly studied intervention in the TB pre-diagnosis phase is the use of automated SMS messages to inform patients when results are available or to directly communicate test results. Evidence shows that the SMS is a feasible and acceptable tool for supporting TB care, however it produces limited and inconsistent outcomes especially when used alone (Mudzengi et al., 2024, Nglazi et al., 2013, Babirye et al., 2019). Greater benefits are observed when SMS is integrated into other interventions (Meira et al., 2025, Ggita et al., 2020). In Uganda, an automated SMS platform linked to GeneXpert testing was used to send TB test results to patients and referring health facilities. The intervention demonstrated technical feasibility, with high message delivery rates among patients whose phone numbers were correctly recorded. However, only about half of all enrolled patients ultimately received results through the SMS pathway because of failures at multiple steps, including missing phone numbers and data-entry errors (Babirye et al., 2019). Similarly, among household contacts undergoing TB evaluation, SMS-delivered results were intended to improve awareness of TB status and reduce delays in receiving results. Participants reported appreciating the speed and convenience of receiving results by text message. However, some mentioned lack of confidence in the results delivered by SMS and some were worried that negative results were incorrect (Ggita et al., 2020).

Phone calls from health workers to patients are also a common mHealth intervention in the TB pre-diagnosis phase. Phone calls are often used to notify patients that results are available, encourage return visits and facilitate referrals and treatment initiation. Phone call-based interventions are shown to provide greater opportunities for clarification and interaction than SMS alone (Majella et al., 2021, Choun et al., 2017). Systematic reviews of mobile communication interventions have found that phone-based communication can improve patient-provider interaction and continuity of care (Kashgary et al., 2016, Alkhuzaimi et al., 2025, Qudah and Luetsch, 2019).

2.6 Factors that influence implementation of an SMS or phone call interventions in the TB care

Findings from almost all studies show high acceptability and positive perceptions towards use of SMS based interventions in TB care and other health conditions (Wagstaff et al., 2019, Musiimenta et al., 2020, Babirye et al., 2019, Ggita et al., 2020, Albino et al., 2014). This high acceptability does not however translate to uptake and sustained usability of the interventions which calls for innovations into sustainable solutions and how the effect of acceptability studies can be maximized (Ggita et al., 2020, St-Jules et al., 2021). In terms of implementing SMS and phone call interventions especially in the presumption phase where the patients are not accountable or bound, not much information is available in terms of factors that would influence implementation. However, in other TB phases, different literature revealed a few implementation factors to consider when using SMS based interventions.

Knowledge and perceptions of users and implementers od SMS and phone calls plays a great role in implementation (Meyer et al., 2020). This determines how much they can appreciate the need and importance of the intervention. Also lack of knowledge and poor perceptions means not engaging with the intervention despite an enabling environment and availability of all necessary resources. Health care workers not trained on the importance and delivery of SMS based interventions may for example shun the implementation or not give it the due attention it deserves (Iribarren et al., 2015).

Mobile phone access is also reported by some studies as a potential factor that can influence implementation of SMS based-interventions (Hermans et al., 2017). The challenges associated with mobile phone access and usage include lack of ownership, loss and or damage of phones and complete lack of and or unreliable/unstable network coverage. Technological issues concerning SMS based interventions may also lead to either success or failure of an intervention (Iribarren et al., 2015). A study in Uganda showed that even though the users had knowledge and positive perceptions, technological failures led to reduced uptake and loss of trust in the intervention. Technological failures

may results from the SMS sending platforms or alert systems for prompts to send SMS and make phone calls (Hermans et al., 2017, Meyer et al., 2020).

Design of the SMS intervention also determines implementation success. For example, two-way SMS interventions have shown better results than one-way SMS. This has been attributed to the fact that patients feel ignored and not given chance to provide feedback hence they ignore the intervention. More so, due to challenges in storage space requirements and phone specifications, text SMS have been more successful compared to the voice texts (Lester et al., 2019, Ggita et al., 2018). Delivery methods of the SMS intervention were also mentioned as critical factors for implementation success. This was often expressed in terms of frequency of delivery of the SMS and language of delivery. A modest number of reminders per week, at least once was required so that they don't appear too many or too few for the user and use of a language that is not familiar with the users often hampered comprehension of the messages (Hermans et al., 2017).

Privacy and security of the users play a key role in uptake and continuity of SMS based interventions (Lester et al., 2019, Iribarren et al., 2015). TB is a disease highly stigmatized in the community hence patients never want to disclose their status or engage in activities that may make others suspicious of their status (Macq et al., 2006). Ensuring privacy of the users, using techniques that ensure privacy and assuring them of this therefore provides confidence to the users (Ggita et al., 2018). More so, in LMICs, some people share phones hence the risk of third parties accessing information in the SMS is high and could disrupt the intervention in case such happens (Lester et al., 2019). Although these factors were found to influence implementation and uptake of SMS based interventions in the other phase of the TB care cascade, it was not clear as to whether these factors would also potentially affect implementation in the TB presumption phase which has dynamic and unaccountable patients.

TABLE 1.0: Synthesis of the knowledge gap

Study objective	What is known	What gaps remain	What gaps the study sought to fill
1. To determine the proportion of pre-diagnosis LTFU among people with presumed TB and factors associated in Central Uganda	-Pre-diagnosis LTFU of people with presumed TB ranges from 9% to 80%. In Uganda, it was estimated in only one health facility, a health centre IV in Jinja district at 40.7%. Pre-treatment LTFU in one study in Uganda is 20%	-National, regional and district estimates of pre-diagnosis and pre-treatment LTFU remain limited.	-Estimating the Pre-diagnosis LTFU and factors associated among patients in Central Uganda
2. To explore the facilitators and barriers to completion of the diagnostic process among people with presumed tuberculosis in Central Uganda	- Barriers to completing the diagnostic process include; poor health seeking behaviours, limited knowledge on TB, stigma the need failure to produce sputum, lack of understanding of the diagnostic process and health system inefficiencies.	Context-specific qualitative facilitators and barriers to completing the TB diagnostic process among people with presumed TB	Documenting the context and population specific facilitators and barriers to completing the TB diagnostic process among people with presumed TB in Central Uganda
3. To synthesize evidence on mHealth interventions used to reduce LTFU among people with presumed TB and those diagnosed	-SMS, mobile applications and Phone calls are some of the commonly used mHealth interventions - SMS interventions are used for three major functions, as reminders to clinic appointments, deliver testing results and to create awareness -Most mHealth interventions are used in the treatment phase and very few in the presumption phase.	-Information on use of mHealth interventions in the TB presumption phase is limited	Providing information on what mHealth interventions have been used in TB presumption phase and their role.

	-Evidence on the effect of SMS and phone call interventions is mainly from high income countries		
4. To assess the effect of an SMS or phone call intervention to foster completion of the TB diagnostic process	- Evidence on the effect of the SMS and phone call interventions in the TB presumptive phase is scanty and mixed - Most studies on the effect of SMS and phone call focus on treatment adherence rather than the pre-diagnosis phase. -SMS and phone calls have been mainly used for TB screening, adherence to appointments, diagnostic follow-up and linkages to treatment initiation. -SMS reminders and phone-call communication have been associated with better clinic attendance and follow-up compliance among people with presumed TB.	-Limited evidence on the effect of SMS reminders and phone calls in the TB presumptive phase in LMIC settings. -Differences exist in types of SMS and phone calls implemented, implementation strategies and outcome measures which further complicate the consolidation of evidence. For example, some studies send one way SMS and others two-way and some use direct phone calls which others use automated voice calls. -Some studies have measured process indicators of feasibility and	Generating evidence on the effect of SMS reminders and phone calls in fostering completion of the TB diagnostic process using a randomised controlled trial.

		acceptability with limited evidence on the actual effect on diagnostic outcomes such as time to sample submission, turnaround time, time to completing the diagnostic process and overall pre-diagnosis LTFU. -Most studies are either observational or pilot projects or program evaluations which lack rigorous evaluations for measuring the intervention effect on patient outcomes. Few randomized controlled trials have been conducted in this pre-diagnosis phase.	

		-Cost-effectiveness studies are limited	
5. To explore factors for the use of an SMS or phone call intervention to foster completion of the TB diagnostic process	-Success of interventions depends on; individual factors for users and implementers, mobile phone access by users, design of the SMS intervention, delivery methods of the intervention in terms of frequency of delivery of the SMS and language of delivery and Privacy and security of the users	-Factors that influence implementation of mHealth interventions in rural and semi-urban settings where mobile phones access is limited -Process evaluations not embedded in the implementation	Exploring factors for the use of an SMS or phone call intervention to foster completion of the TB diagnostic process

2.2 THEORETICAL FRAMEWORK

Behavioural change theories provide a systematic way of understanding the research problem and its components. Several theoretical models exist to predict human behaviour for preferred health actions. Potential theories to guide this study were identified and these include the health belief model (Strecher and Rosenstock, 1997), the theory of reasoned action (Fishbein, 1979), the theory of planned behaviour (Ajzen, 1985), the Transtheoretical Model (Prochaska and Velicer, 1997), the socio-ecological model (Bronfenbrenner, 1994), the social cognitive theory (Bandura, 1991), and the Capability, Opportunity, Motivation and Behaviour (COM-B) model (West and Michie, 2020) among others (Shete et al., 2015).

The health belief model (HBM) is one of the oldest and most used models that focuses on one's perceptions and beliefs about a health threat (Strecher and Rosenstock, 1997). Anchored in the constructs of perceived susceptibility, perceived severity, perceived benefits, perceived barriers and cues to action, it has been widely used to predict why people fail to participate in programmes aimed at preventing or detecting disease such as Tb prevention behaviour, TB medication adherence and cancer screening (Yirsaw et al., 2024, Parwati et al., 2021, Gebremariam et al., 2021, Khamai et al., 2024, Yoshitake et al., 2019). The HBM describes the connection between an individual's beliefs, their understanding of health threats, and the perceived barriers and benefits associated with performing health behaviours. Although the model highlights how beliefs and not just knowledge, influence behaviour, it ignores the social, cultural, economic, and environmental factors that influence behaviour such as poverty, social pressures and access to services yet these are inherent within a person's environment.

The theory of reasoned action was designed to predict volitional behaviours and to help us understand their psychological determinants why people do not behave as expected (Fishbein, 1979). It indicates

that behaviours are as result of internalising available information and implications of behaviours connecting attitudes, intention and social influences. However, the theory assumes people carefully weigh consequences, ignoring emotion, impulse, habits and does not consider broader influences such as culture, socioeconomic status, or policy (Kippax and Crawford, 2015). This theory provided the basis for the Theory of Planned Behaviour to address some of these limitations.

The theory of planned behaviour proposes that actions are controlled by intentions emphasizing the fact that not all intentions lead to the action, some are followed with or without adjustments while others abandoned (Ajzen, 1985). The theory also states that intentions to perform a behaviour are shaped by attitudes, subjective norms such as social pressures and perceived behaviour controls. The theory acknowledges the role of social pressure and adds a predictive component of intention to attitudes improving on the highly individualistic models like the HBM. The theory has been previously used to predict behaviours based on intentions (Ggita et al., 2020, Chaisson et al., 2015, Lock et al., 2011). Chaisson et al., used the theory to evaluate the impact of performance feedback and same-day smear microscopy on the quality of TB evaluation in Uganda (Chaisson et al., 2015). Ggita et al., also used the theory to explore how household contacts experience test results delivered via SMS, and how these experiences influence follow-up intentions (Ggita et al., 2020). However, the theory neglects environmental and structural factors such policy, access, costs among others which largely play a role in taking up behaviours (Sniehotta et al., 2014). The theory also underplays the role of emotional and habitual factors (Sniehotta et al., 2014, Conner et al., 2013, McEachan et al., 2011).

The Transtheoretical Model views change as a process rather than a single event giving room for dynamic stages of change (Prochaska and Velicer, 1997). It assumes that individuals are at different levels of readiness to change. It involves pre-contemplation, contemplation, preparation, action, maintenance of behaviour and termination. The model has been used in integrated smoking cessation and TB care programs (Awaisu et al., 2011, Lin et al., 2019) and in designing an integrated nursing

care model for multi-drug resistant TB patients (Wei and Duan, 2021). Whereas the model gives flexibility of change and decision making, it does not explicitly mention how to measure attainment of each stage and also does not recognise the fact that individuals may not fit neatly into a single stage. More so, the model underplays contextual, environmental, social, and economic factors which predict behaviour.

The social cognitive theory emphasizes the reciprocal interaction between person, environment, and behaviour (Bandura, 1991). It suggests that people learn not just through their own experiences, but by observing others in their environment. Whereas the theory accounts for social and environmental influences, it includes many constructs, which can make it difficult to operationalize and test comprehensively but lo over emphasizes personal factors compared to other constructs (Beauchamp et al., 2019). This model has not been largely used in TB research.

The COM-B model stipulates that behaviour change results from an interaction of three domains that is; Capability, Opportunity, Motivation which should be a focus of any behaviour change intervention. Capability refers to the individual's physical and psychological capacity to engage in the behaviour; opportunity, the physical and social factors that lie outside of the control of the individual; and motivation, the automated and reflective brain processes that direct behaviour. Connected to this model is the behaviour change wheel (BCW) which proposes nine intervention and policy functions which can potentially address identified facilitators and barriers. According to the BCW, the potential interventions include training, social influence, incentives and environmental restructuring. The COM-B model has been previously used in exploring facilitators and barriers to initiating TB treatment, chlamydia testing and designing interventions for piloting (Zawedde-Muyanja et al., 2022, Khalilollahi et al., 2022, McDonagh et al., 2018, Bennett et al., 2022) (West and Michie, 2020).

However, most of those theories predict health-related behaviour with no aspects of behaviour maintenance which leads to no sustainability and wastage of resources (Kwasnicka et al., 2016). Behaviour maintenance is mentioned to be predicted by five aspects; maintenance motives, self-regulation, resources, habits and contextual influences which package lacks in most theories. This study was therefore guided by the socio-ecological (SEM) model which states that behaviour is influenced by multiple, interacting factors at different levels [Figure 2) (Bronfenbrenner, 1994). The model was considered as most suitable because it allows understanding of behaviours at different levels and their interactions. This can consequently guide the design and implementation of multi-level interventions since no single level is sufficient to cause change. The SEM suggests that individual, social, environmental, and policy factors influence behaviour without placing much emphasis on individual or social factors alone as seen in previous models. Because of the different levels that influence behaviour, the SEM encourages use of interdisciplinary approaches of interventions.

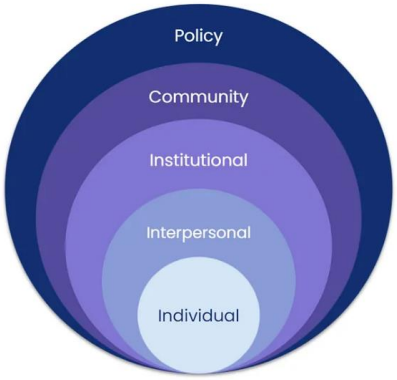


Figure 2: Illustration of the Socio-Ecological Model (Bronfenbrenner, 1994)

CONCEPTUAL FRAMEWORK

From the above analysis of the theories and models, I adapted a conceptual framework based on the SEM to inform this study given its benefits over others. The SEM was adapted to understand the

phenomena of pre-diagnosis LTFU and completion of the diagnostic process among people with presumed TB as seen in figure 3 (Bronfenbrenner, 1994).

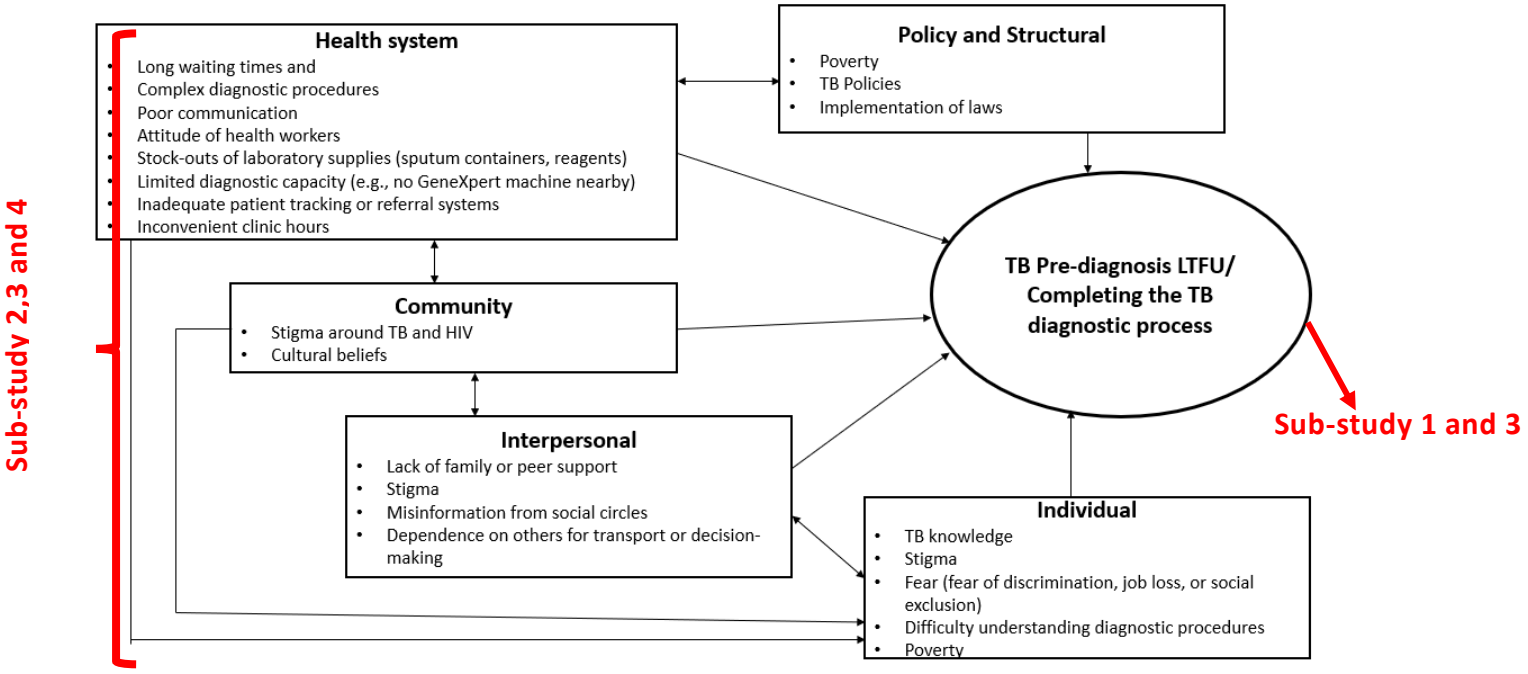


Figure 3: Conceptual framework-adapted from the socio-ecological model (bronfenbrenner, 1994)

Narrative

The SEM model provides a layered framework for understanding why many tuberculosis (TB) patients become lost to follow-up before diagnosis, highlighting how individual, interpersonal, community, organizational, and policy-level factors interact to create facilitators and barriers throughout the TB care cascade.

Individual Level Factors

On the individual level, patient awareness about TB symptoms is often limited, leading to delays or failure to seek care. Socioeconomic challenges also inhibit prompt health-seeking behaviour. These include fear of the disease, stigma, limited finances to visit health facilities

Interpersonal factors

At the interpersonal level, family relationships and social support play crucial roles. Poor family support, stigma, and discrimination within households and from community members may discourage patients from seeking healthcare. Conversely, when families are informed and supportive, patients are more likely to complete diagnostic procedures and engage with the health system.

Community factors

Community-level factors include prevailing cultural beliefs, local norms, and stigma, which can push patients toward not seeking care or resorting to traditional healers instead of health facilities. Widespread misconceptions such as who ever had TB has HIV create further delays and reduce community engagement with TB care.

Health System /Organizational factors

Organizational challenges include issues within health facilities or other organisations providing care, such as staff shortages, poor communication, lack of training, and logistical challenges in sample collection and processing. For example, few laboratory staff and shortages in logistics could lead to a long turnaround time for results causing patients to exit the health facilities without their results. Most patients who exit the health facilities without their results eventually get LTFU due to the difficulties associated with returning to collect results. Difficulties in accessing healthcare due to transportation, distance and cost also contribute to drop out of patients before diagnosis although these maybe also be regarded as personal factors.

Policy and Structural factors

Socioeconomic and policy factors, including poverty, policies and inadequate implementation of supportive laws, exacerbate pre-diagnostic LTFU. These factors shape the availability, accessibility,

affordability, and acceptability of TB services. For example, the current TB and HIV testing policy in Uganda creates perceived stigma and fear among people with presumed TB thus scaring them away from completing the TB diagnostic process.

CHAPTER THREE: GENERAL METHODOLOGY

3.1 DESIGN PHILOSOPHY AND PARADIGM

Pre-diagnosis LFTU of people with presumed TB is a complex phenomenon embedded in personal, community and health system factors (Garg et al., 2020, Feasey et al., 2021, Zawedde-Muyanja et al., 2022). Understanding these phenomena, therefore requires active participation of people with presumed TB and the health workers who offer the services through both deductive and inductive processes. This back-and-forth inquiry from different participants to enrich our understanding of these phenomena, hence pointed this study to pragmatism philosophy. Pragmatism is an approach that acknowledges the ontological perspective that truth about phenomenon exists and is ever changing based on experiences and perspectives that are socially constructed (Kaushik and Walsh, 2019, Hildebrand, 2011). Pragmatism therefore rejects the notion that a single method of inquiry can adequately explain complex phenomena and instead advocates for the dynamic use of methods that are most useful for answering the research question and solving practical problems (Shaw et al., 2010, Hall, 2013, Brierley, 2017). This study therefore employed a mixed methods for data collection.

A major strength of this pragmatism is its methodological flexibility, which enables researchers to draw on multiple forms of evidence and integrate quantitative and qualitative approaches to gain a more comprehensive understanding of a problem. It is particularly suited to complex health systems research where social, behavioural, and organisational factors interact to influence outcomes (Brierley, 2017, Long et al., 2018). Pragmatism also promotes the generation of actionable knowledge that can inform interventions, policies, and service delivery improvements (Allemang et al., 2022). However, there is criticism that integrating findings from diverse methods can be challenging, and there is a risk that different forms of evidence may not always align or provide a single coherent explanation of the phenomenon under study (Allemang et al., 2022, Gillespie, 2024). More so, pragmatism is highly context-sensitive, hence interventions found to be effective in one setting may not necessarily produce

similar outcomes in different contexts (Kaushik and Walsh, 2019). Despite these limitations, pragmatism provides a valuable framework for investigating pre-diagnosis LTFU by enabling the integration of diverse stakeholder perspectives and methodological approaches to develop contextually relevant and practical insights.

3.2 STUDY CONTEXT AND SETTING

3.2.1 Study context

This research was embedded in an ongoing study, MILEAGE4TB, hosted at Makerere University School of Public Health which sought to use SMS reminders, Phone call reminders and mobile money incentives to improve completion of the TB diagnostic process in Central Uganda. The study's aim was to contextually adapt the proposed intervention and evaluate its effectiveness using a randomized controlled trial (RCT) (Nuwematsiko et al., 2025). This PhD research supplemented the main study and evaluated the TB diagnostic process using a retrospective cohort analysis to identify the extent of pre-diagnosis and pre-treatment LTFU. Results from this analysis informed a qualitative inquiry into the facilitators and barriers for completion of the diagnostic process, which findings informed the contextual adaptation of the mHealth intervention to reduce LTFU in the main study. Further, a systematic review was conducted through this PhD study to synthesize existing evidence on what mHealth interventions have been used in the TB presumption phase in LMICs to further inform adaptation of the main study intervention. Together with the main study team, I coordinated the intervention adaptation process and implemented the interventions using an RCT. In this PhD study, I used data from the main RCT to evaluate the effect of an SMS and phone call only intervention to foster completion of the diagnostic process and qualitatively explored factors for use and implementation.

3.2.2 Study setting and rationale

This study was conducted in selected health facilities in Central Uganda *(Figure 4).*

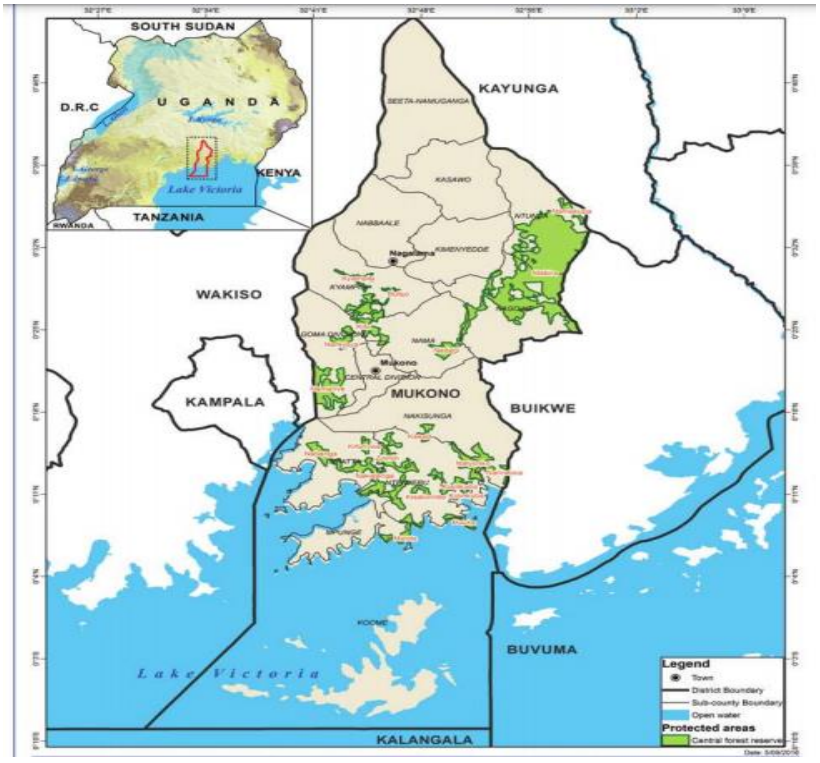


Figure 4: Map showing location of districts of the sampled study sites in Central Uganda

Central Uganda is one of the TB high burden regions in the country at 7.0% positivity rate for people with presumed TB screened with GeneXpert coupled with a high population and limited access to health care facilities (MOH, 2021a, NTLP, 2024, UBOS, 2017). Central region had the highest number, 46.7%, of confirmed TB patients lost to follow-up before treatment initiation in the 2021 catch up campaign (MOH, 2021a). All these factors place Central Uganda in a vulnerable position that requires urgent innovative solutions to reduce the TB burden while coping with the growing population and limited access to healthcare. According to the National Population and Housing Census (2024) results, Wakiso District has a total population of 3,411,177, Kampala, 1,797,722, Mukono, 929,224 people, and Luwero, 616,242 (UBOS, 2024).

Mukono district has a total of 3 hospitals, 3 health centres IV, 16 health centre III, 69 health centres II and 22 clinics; Wakiso a total of 15 hospitals, 19 health centre IV, 165 health centre III, 153 health

centre II and234 clinics; Kampala has 22 hospitals, 13 health centre IV, 48 health centre III, 585 health centre II and 781 clinics and Luwero 2 hospitals, 4 health centres IV, 25 health centre III, 50 health centres II and 4 clinics (MoH, 2018).

More than half of the households, 72.2% in Mukono, 79.7% in Wakiso, 81.9% in Kampala and 73.9% in Luwero are within 5 km radius the nearest health facility, whether public or private (UBOS, 2017). In terms of Information, communication and technology, more than half, 56.2% of the persons aged 10 years and above in Mukono district, 69.8% in Wakiso, 76.9% in Kampala and 49.6% in Luwero own at least one mobile phone(UBOS, 2017).

The health facilities in Central Uganda selected for this study included Entebbe Regional Referral hospital, Wakiso health centre (H/C) IV, Kojja H/C IV, Mukono General Hospital, St. Francis Hospital Nagalama, Mityana General Hospital, Luwero General Hospital and Kiruddu National Referral Hospital in Wakiso, Mukono, Mityana, Luwero and Kampala districts. Selection was based on study facilities of the main study, MILEAGE4TB, which based on high volume facilities (more than 10 people with presumed TB seen per day), level of facility (hospital or health centre) and ownership type that is whether public or private not for profit.

Diagnosis of TB in Uganda

In Uganda, the diagnosis of TB is usually carried out on patients who have symptoms suggestive of TB (people with presumed TB) such as a persistent cough of more than 2 weeks, night sweats, fever of more than 3 weeks, and previous contact with TB patient. Once people with presumed TB present themselves at the hospital, they get screened for TB, are registered in the presumptive TB register, examined clinically and sent for investigations either to the laboratory and or for chest X-ray. In the presumptive TB registers, health workers enter various information while asking the patients. Some of the information collected includes patient name, age, sex, telephone number, area of residence and

clinical factors like HIV status and previous history of TB. Patients who submit samples are then registered in the laboratory register and those who go for chest x-ray in the radiology register. TB is diagnosed following steps presented in the national algorithm for TB screening, diagnosis and management (figure 5). Diagnosis of TB is mainly by sputum microscopy, Xpert MTB/RIF, chest x-ray or urine TB LAM for HIV positive patients. Other investigations include tissue histology depending on how the patient presents and availability of the tests (NTLP, 2018). In 2017, Uganda adopted the policy recommendation to use Xpert MTB/RIF as the gold standard for diagnosis of TB whenever available with advantages of having a short turnaround time for results (NTLP, 2018). However, due to the cost and maintenance of the Xpert MTB/RIF, it is not available in some health facilities. But even those that have the Xpert MTB/RIF machine, stock out of cartridges often delays or limits diagnosis (Nalugwa et al., 2020, Hanrahan et al., 2016). Where the Gene Xpert machine is not available, samples are referred to high-level health facilities for testing through the hub system which implies a long turnaround time facilitating LTFU. In some instances, microscopy, chest X-ray and Urine TB LAM are used depending on the clinician's request and assessment.

Following the diagnosis, results are recorded in the relevant registers and notified to the National TB and Leprosy Program (NTLP). Patients who are diagnosed with TB either from the investigations or clinically are started on treatment immediately, their details written in the TB treatment register and reviewed after two weeks. There is limited follow-up on patients that turn out negative from the TB test for further investigations. There are also few efforts to support follow-up of both people with presumed TB and confirmed TB patients to complete care and the few that exist are majorly research or project driven (Musiimenta et al., 2020, Meyer et al., 2018, Sekandi et al., 2020a). Most on-going interventions are focused on supporting confirmed TB patients to start, adhere and complete treatment with little focus on patients in the presumptive phase (Babirye et al., 2019, Sekandi et al., 2020a, Hermans et al., 2017, Sekandi et al., 2020b). Whereas this TB care system was designed to ensure

prompt and complete diagnosis of people with presumed TB in Uganda, inherent gaps exist posing opportunities for LTFU along the cascade some of which can be addressed my mHealth interventions (Musiimenta et al., 2020, Babirye et al., 2019, Ggita et al., 2020, Meyer et al., 2020).

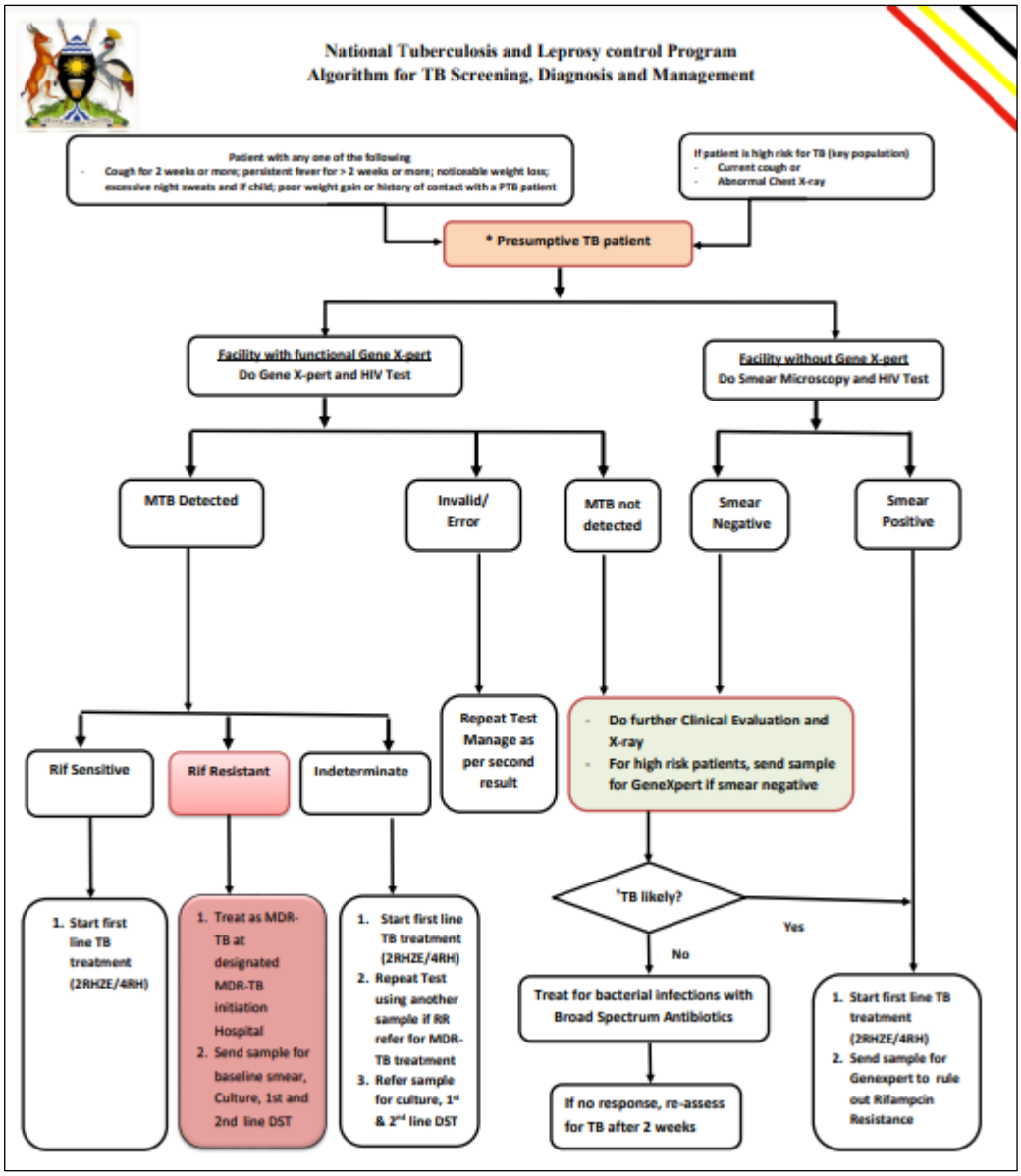


Figure 5: Uganda national algorithm for TB screening, diagnosis and management (GOU, 2017)

3.3 ETHICAL CONSIDERATIONS

This study was approved by the Research and Ethics Committee of Makerere University School of Public Health (#SPH-2023-427) and registration obtained from the Uganda National Council of

Science and technology (HS3000ES). The systematic review was registered with PROSPERO (Registration Number: CRD42025641651) and the main RCT where data was drawn for analysis registered with clinicaltrials.gov (#NCT05964842).

Written informed consent was obtained from all study participants in the surveys and qualitative studies before the start of data collection. No personal identifier information was collected from study participants. Research assistants were trained on ethics, confidentiality and data protection and security prior to the start of data collection. Further, data were collected using study tablets which were always retrieved at the end of the day to avoid breach of data privacy. Participants in sub-study 2 were invited to the study facilities for qualitative interviews through phone calls by facility health workers who had already interfaced with them at the time of healthcare seeking. All participants in the qualitative studies consented to be audio-recorded during the interviews and discussions. I maintained confidentiality of all data obtained by limiting access of the data to only the study investigator and data analysts. People with presumed TB who did not complete the diagnostic process, those who still had symptoms suggestive of TB and those diagnosed who had not started treatment were referred to the TB focal persons at the study sites for further management. Field researchers practiced infection prevention and control measures at all times during the data collection to protect themselves and the participant against COVID-19, which measures also doubled for protection against acquiring the TB infection. Some of these measures included masking, hand hygiene with an alcohol-based sanitizer and keeping a social distance of at least 2 meters.

3.4 OVERARCHING STUDY DESIGN

This study employed a mixed methods study design, sequential in nature using the quantitative approach first followed by qualitative to further explain the knowledge generated using quantitative methods.

3.5 METHODS PER SUB-STUDY

(Summary in appendix 1)

SUB-STUDY 1

Objective: To assess the proportion of pre-diagnosis LTFU among people with presumed TB and factors associated in Central Uganda.

Study design: This was a retrospective cohort study involving a review of routinely collected data of patients with presumed TB presenting to the study facilities.

Study population: The study included patients with presumed TB of all ages who presented to the study facilities from January 2019 to December 2022. Patients with presumed TB were defined as those presenting with any of the cardinal symptoms of TB: persistent cough of two weeks or more, night sweats, fever of more than two weeks, weight loss and if a child, poor weight gain and previous contact with a TB patient.

Inclusion and exclusion criteria

I included records of people with presumed TB of all ages who were identified in or referred to the study facilities for evaluation from January 2019 to December 2022. The four-year period was selected to allow comparison of the pre-diagnosis and pre-treatment LTFU; before and during the COVID-19 pandemic. I referred to 2019 as before the COVID-19 pandemic and 2020-2022 as during the pandemic based on WHO periods of declarations of COVID-19 as a public health emergency of international concern (WHO, 2023b, Cucinotta and Vanelli, 2020). I excluded patient records with missing variables of age, name, sex and date of registration when presumed for TB because these were identifiers for duplicates. Age was a key identifier for duplicates and the dates were to enable me determine if one completed diagnosis within the 30 days. I also excluded patients who were referred out to other health facilities because their dates and status of receiving results could not be ascertained. Patients who were

not presumed from the study facilities and just had samples for testing were also excluded because I could not ascertain their date of being presumed for TB. These referral cases are recorded mainly in the laboratory registers as the samples arrive for testing and very few of them go through the entry care points. Referred patients who go through the entry care points are entered in the presumptive TB registers and marked as "referral".

Sample size estimation

I used the Kish Leslie sample size estimation formula for proportion to obtain the minimum sample size required to determine the proportion of pre-diagnosis LTFU of people with presumed TB:

$$n_0 = \frac{Z^2 p(1-p)}{e^2}$$

Where*;* n_o = estimated sample size, p= anticipated proportion of pre-diagnostic drop out= 0.407 according to a previous study in Jinja by Ekuka et al (Ekuka et al., 2020), $(1 - p) = 0.593$, e = desired absolute level of precision = 0.05; no= (1.96^2* 0.407*0.593)/ (0.05^2) = 371 participants

Design effect of 2=742 participants

More so, sample size to account for the multivariable analysis of factors associated was also calculated using the formula of cross-sectional studies with two proportions:

$n = (Z\alpha/2+Z\beta)^2 * (p1(1-p1)+p2(1-p2)) / (p1-p2)^2$, where $Z\alpha/2=1.96$, $Z\beta=0.84$, $p1=0.385$, $P2=0.434$

P1 and P2 were obtained from a similar previous study by Ekuka et al, using the variable sex which has shown to be associated with pre-diagnosis LTFU from previous literature (Ekuka et al., 2020)**.**

N=1578 per group giving a total of 3156; considering a design effect of 2, the final sample size estimation =6312 participants.

Taking into account the largest sample size, 6312 was considered as the minimum number required.

Sampling procedures:

I used total enumerative sampling, where all records meeting the inclusion criteria were extracted from the registers. A post hoc power estimation was however performed to estimate whether I had the power to conduct the analysis, which gave a power estimation of 0.76 using Stata 14 software

Data collection procedures and tools:

Data were collected and cross-matched from paper-based TB registers (presumptive, laboratory, radiology and treatment). Four variables were used for cross-matching the data in the different registers: patient name, age, place of residence and date of presumption. The presumptive TB register was the starting point after which the patient with presumed TB was manually followed up by trained research assistants in the laboratory or radiology or treatment registers using the cross-matching variables. Data on patients with presumed TB who presented to the study health facilities were extracted from the presumptive TB registers at all screening points/units. These patients were then followed up in the laboratory and radiology registers for completion of TB diagnosis within 30 days from the date of being identified with presumed TB. Completion of TB diagnosis referred to undertaking the requested investigation and obtaining results from the test within 30 days. Patients with presumed TB who tested positive for TB were followed up in the facility treatment register for treatment initiation within 14 days from the date they were diagnosed. Patients appearing in the laboratory or radiology or treatment registers who were not recorded in the presumptive TB registers were not included in the study. This is because they were referrals from other health facilities and had a different pathway. All the facilities included in this study receive referred patients for both testing and treatment initiation from other health facilities. Patients who were missing any of the four cross-matching variables in the presumptive TB register were excluded. This was because they could not be

subsequently cross-matched in the other registers. Patient records which were not matching in the subsequent registers were treated as unique and cross-matched separately.

Data were collected using an extraction tool adapted from a similar study conducted in Zimbabwe (Murongazvombo et al., 2019). The data extraction tool was pre-tested, and the refined tool was uploaded to the *KoboCollect* mobile data collection app. The following variables were extracted: age, sex, place of residence recorded (Yes/No) and phone contact recorded (Yes/No), TB disease type, HIV status and dates of presumption, diagnosis and initiation of treatment for the patients with presumed TB and those who tested positive. Data on these variables were primarily extracted from the presumptive registers at the study facilities except for variables of diagnosis and treatment initiation. In case data on any of the variables were missing in the presumptive register, effort was made to retrieve it from other registers either laboratory, radiology or treatment at the point of cross-matching the data and entered. This is because all the health facility registers used for this study record patient's demographics and clinical data.

Variables and measurement

I defined pre-diagnosis LTFU as failure to test for TB and obtain results within 30 days of being identified with presumed TB. The 30-day follow-up period was selected based on previous studies for comparison (MacPherson et al., 2013, Pala et al., 2018). This referred to either dropping out before having the requested investigations done or after by not having results. Having results documented in the presumptive TB register was used as a proxy for receipt of results by the patient. The presumptive TB register was preferred for extracting data on receipt of results over the laboratory register because patients return to points of care where they were presumed for TB to obtain their results. At these points of care, patient's results are recorded and handed over to them. Pre-diagnosis LTFU was measured as the proportion of patients who were lost before testing for TB and receiving results within

30 days from being identified with presumed TB out of the total number of all patients with presumed TB registered in the study period.

Pre-treatment LTFU was defined as failure to initiate TB treatment within 14 days from the date of diagnosis based on previous studies (Zawedde-Muyanja et al., 2020a, Thomas et al., 2018, Mulaku et al., 2024b). This was measured as the proportion of diagnosed TB patients who were lost before initiating treatment within 14 days from when they were diagnosed out of the total number of diagnosed TB patients registered in the study period.

Independent variables

-Patient characteristics: age, sex, area of stay, nationality category, HIV status, TB disease and mobile phone recorded.

-Health facility characteristics: level, availability of supporting services and facility type

-Date of identification as presumptive TB, date of submitting the sample or undertaking the chest X-ray and data of receiving results. Dates will be extracted in the format (dd/mm/year).

-TB diagnostic test conducted which was either microscopy, Xpert MTB/RIF, TB Lam or chest X-ray.

Quality assurance and control

Research assistants with experience in TB care, research and extracting data from large databases were recruited and trained in a three-day workshop for data collection. Meetings were held at the end of each data collection day to check for adherence to the SOPs and operational definitions, consistency in data collection, and completeness of the data collected. Data submitted daily was checked for accuracy and any errors which was communicated to the research assistants to correct in the subsequent data extraction. The data extraction tool was pre-tested in Wakiso H/C IV located in Wakiso district which is a similar setting that is high volume and presents with characteristics of a

semi-urban facility. The data collection tools were pretested on 40 records to ensure reliability and consistency of the questions and also to get insights for preparations for the actual data collection. Sample size for pretesting the study tools was informed by previous studies that recommend a number between 30 and 75 to be able to capture about 75% of likely high impact problems (Blair and Conrad, 2011, Perneger et al., 2015).

Data management and analysis plan

Duplicate records were removed using identifiers of age, name initials, and registration date when the patient is presumed for TB. Patients with presumed TB who were missing dates of registration when presumed, sample collection and results date were also excluded because these were key variables for analysis. I dropped anyone with a duplicate registration date within 3 days which signified double registration. I used complete case analysis where entries with missing data were deleted.

Descriptive statistics such as frequency distributions, median and interquartile ranges (IQRs) were computed. The trends of pre-diagnosis LTFU over time were compared using a line graph. A multivariable modified Poisson regression model was fit via generalized linear models with family (Poisson) and a log link. The model estimated prevalence ratios of factors associated with pre-diagnosis LTFU (Zou, 2004). Modified Poisson regression was preferred over logistic regression because of higher proportions of pre-diagnosis and pre-treatment LTFU (i.e greater than 10%) hence, odds ratios would provide biased estimates of prevalence ratios (skove et al., 1998, Lee et al., 2009). Independent variables that were statistically significant at the bivariate analysis with p-value<0.2 and those known from the literature to be associated with pre-diagnosis LTFU were entered into a model to establish factors independently associated while controlling for known confounders. The level of statistical significance was set at a p-value ≤ 0.05. An exploratory logical model-building method following the conceptualization of the study outcome and literature review was used to generate the final model. Variables in a model that were found to be

consistently insignificant and did not add any value in terms of goodness of fit were eliminated. Selection of the final model was performed using likelihood ratio tests.

SUB-STUDY 2

Objective: To explore the facilitators and barriers to completion of the diagnostic process among people with presumed tuberculosis in Central Uganda

Design

This was an explanatory qualitative study using in- depth interviews (IDIs), focus group discussions (FGDs) and key informant interviews (KIIs) ensuring triangulation of data from the different categories of respondents.

Study population and sampling

I conducted 25 IDIs among patients identified with presumed TB in the study facilities. Participants were selected from the presumptive TB registers at each health facility by the research team supported by health workers. I included patients who were aged 18 years and above and were presumed for TB in the past one month. Purposive sampling was used to select participants for the IDIs based on their completion status of the TB diagnostic process (completed diagnostic process for TB within 30 days from when they were presumed for TB/not completed at all). Selection ensured representation of both males and females. Conducting IDIs among patients who had completed the diagnostic process and those who had not and with the different sexes was to ensure rich and diverse perspectives of the findings. People with presumed TB who reported being critically ill and those with no record of a phone number through which they could be contacted to invite them for interviews were excluded.

Data collection tools and procedures

The IDI interview guide was developed containing open-ended questions on facilitators and barriers to completion of the TB diagnostic process as well as suggestions on increasing completion. Some of the questions included understanding of the patients' knowledge on TB, experiences as they navigated

the TB diagnostic process, facilitators and barriers to submitting a sample for testing and collecting of results. The interview guide included probes to elicit more responses from participants but also to guide the interviewers on making checks for responses of previous participants to ensure credibility of the findings. The IDI guide was translated to Luganda, the most common language in the study area and pretested in one health facility in Wakiso district to ensure it yields the data needed. To limit bias in the study findings, the pre-test was conducted in one health facility in Wakiso district, which had similarities with the study sites in Mukono, Mityana and Buikwe districts such as being in Central Uganda and having both urban and semi-urban catchment populations. The tool was then revised based on the feedback obtained from the pre-test to improve on the clarity of questions and include more probes. Interviews were conducted in *Luganda* and lasted about 40-60 minutes.

Six FGDs were also conducted with TB patients aged 18 years and above who had been on treatment for one month to understand their experiences as they went through the diagnostic process after being identified with presumed TB. The selection of one month was to limit the recall bias from the participants. The FGDs were organised to be sex-specific groups. This is because TB is a highly stigmatised disease hence participants in the opposite sexes would not be comfortable inadvertently disclosing their TB status and sharing experiences leading to potential biased responses. Participants were purposively selected by the research team from the TB unit treatment registers at each health facility based on the inclusion criteria with the support of health workers. A focus group discussion guide was developed containing open-ended questions and probes on facilitators and barriers to completion of the TB diagnostic process as well as suggestions on increasing completion. The discussion was conducted in *Luganda* by a trained researcher and lasted between 50 minutes and 1 hour.

Names of eligible participants for both the IDIs and FGDs sampled from the presumptive and TB unit treatment registers were handed over to the TB facility linkage officers who contacted the patients

through phone calls using the contacts recorded in the registers at the health facilities. The TB facility linkage officers were introduced to the study and taken through the objectives and procedures for inviting participants for the interviews. During the phone conversation, they introduced the study to the potential participant as guided by the research team and invited the participant to come to the health facility for the interview if willing to participate. Selected patients whose phone contacts were unreachable at the time of data collection were contacted through the next of kin whose contacts are also recorded in the registers.

In addition, 20 KIIs with TB focal persons, heads of outpatients' departments (OPD), HIV/ART clinics, in-patient departments, laboratories and TB community linkage officers were conducted. The KIIs were selected purposively based on those who often interact and offer services to patients with presumed TB and those diagnosed in each study facility. That is, health workers who either provide TB screening or health education or counselling or testing or treatment to those diagnosed. Health workers who were on leave during the time of data collection were excluded from the study. I developed the KIIs interview guide containing open-ended questions with probes on experiences providing services to patients with presumed TB right from the point of screening to initiating treatment if diagnosed. I also explored their perspectives on likely facilitators and barriers to completing the TB diagnostic process and suggestions on increasing completion. Interviews with the health workers were conducted mainly in English.

The three methods of data collection that is; FGDs, KIIs and IDIs were used to enable triangulation of findings from the different methods and participants so as to obtain more rich data. All interviews were conducted between 18th April and 7th June 2023 by two trained qualitative researchers (RN and VK), male and female who hold a master's degree in Public Health and Sociology respectively. The two researchers were involved in the design of the study and drafting of the interview guides *(Supplementary file 2)*. A two-day training on data collection was conducted for the interviewers

together with the rest of the study team to ensure quality of the data to be collected. The training covered basic information on TB and the diagnostic process, ethics of conducting research, skills and procedures in conducting qualitative interviews and an overview of the interview guides. All interviews were conducted at the study health facilities in a place deemed safe, private and comfortable for both the research assistant and respondent and there were no non-participants during the interviews to ensure privacy. All interviews and discussions were audio recorded after obtaining written informed consent from the participant and notes taken by a trained note taker. Meetings were held at the end of each day between the qualitative researchers who were conducting interviews and other study investigators to check for adherence to the data collection standard operating procedures and to discuss emerging codes and themes about completion of the TB diagnostic process.

Data management and analysis

Audio recordings were transcribed verbatim in English by the researchers who conducted the interviews (VK and RN). The transcripts were not back translated to Luganda due to limited resources, however, the transcripts were cleaned and checked against the original audios by VK, a Luganda speaker, to ensure proper transcription and that complete data is available for analysis.

Thematic analysis was done following the steps suggested by Braun and Clarke (Braun and Clarke, 2006). Two researchers (VK and RN) experienced in qualitative research read through selected transcripts to familiarise themselves with the data. The researchers then read through the transcript the second time to develop codes independently using an abductive approach. For confirmability, the independent lists of codes from the two researchers were reviewed by other team members (EB, RN and LA) to assess agreement. Any discrepancies were clarified and resolved by comparing each coder's results with raw data until consensus was reached. The codes were then applied for line-by-line coding using ATLAS.ti software (version 6). The codes were analysed to formulate themes *(supplementary file 1)* which were further refined guided by the constructs of the socio-ecological

model and researcher's experiences during data collection. The socio-ecological model is based on the notion that behaviours are as a result of the complex interaction between humans and the environment where the two influence each other. The model conceptualizes this influence at different levels of; individual, interpersonal relationships, community and policy by Bronfenbrenner, 1994 (Bronfenbrenner, 1994). Findings from this study were shared back with participants during an insight workshop for their feedback which further guided the interpretation of the results. I triangulated data from all interviews at analysis to improve on the credibility of the findings. Relevant quotes were selected to represent the main themes. I conducted methods and data source triangulation where we used various data collection methods that is; IDIs, KIIs and FGDs. These methods further included varied participants to ensure collection of data from different sources. These included participants who had completed the TB diagnostic process, and those who had not completed at all or initiated TB treatment if diagnosed for the IDIs; TB patients who had recently initiated treatment for the FGDs and TB health care workers. Data from these different methods and participant categories were coded independently by the researchers and later harmonised in the analysis meetings with all study investigators.

SUB-STUDY 3

Objective: To Synthesize evidence on the mHealth interventions previously used to enhance completion of the TB diagnostic process and treatment initiation in LMICs.

Design

This was a systematic review synthesizing existing evidence on what mHealth interventions have been used to reduce pre-diagnosis and pre-treatment LTFU of people with presumed TB and those diagnosed. The Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols (PRISMA-P) 2015 guidelines were followed for conducting the review and reporting [20].

Inclusion criteria

1) Randomised controlled trials either individual level or cluster, quasi-experimental and cross-over studies (Higgins JPT, 2024) evaluating the use of mHealth in the TB pre-treatment phase. The interventions included text-messaging (SMS), voice based (e.g. phone calls, automated audios) and mobile phone applications.
2) No restriction regarding country, patient age, race, sex and publication language. We only restricted the publication date to between 2000 and 2024 because that is when mHealth gained popularity (Jusoh, 2017).
3) Studies whose population of focus for the intervention were people with presumed TB and those diagnosed of all ages. People with presumed TB were defined as anyone identified with symptoms suggestive of TB. That is; persistent cough of two weeks or more, night sweats, fever of more than two weeks and weight loss. Diagnosed TB patients were those who tested positive for TB bacteriologically by either Xpert MTB/RIF, smear microscopy or TB Lam or those detected by chest X-ray.

4) I focused on studies carried out within the hospital setting both outpatients and inpatients aimed at reducing pre-diagnosis and pre-treatment LTFU of people with presumed TB and those diagnosed or completion of TB diagnosis and treatment initiation. Interventions that started at the community and later linked to the health facilities were excluded.

No language restrictions were applied during the search.

Exclusion criteria

(1) Study of TB in non-human subjects or in vitro studies

(2) Duplicate publications or overlapping data

(3) Abstract-only papers as preceding papers, conference, editorial, and author response theses and books

(4) Articles whose full text was not available

(5) Case reports, case series, study protocols and systematic review studies.

Information Sources and Search Strategy

I searched for studies from seven electronic research databases; PubMed/ MEDLINE, Cochrane Central Register of Controlled Trials, EMBASE, Web of science, Scopus, IEEE Xplore and CINAHL. We also searched the two trials registries; ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP). Other sources of unpublished and grey literature including dissertations were also searched; Google Scholar, OpenGrey, ProQuest. We also hand-searched reference lists of included studies and similar systematic reviews for potential studies to include in the review. Additionally, i contacted authors of abstract papers for full-texts or their reports.

A comprehensive search strategy was designed for PubMed/MEDLINE and adjusted to suit other databases *(appendix 2).* I used the Population, Intervention, Comparator and Outcome (PICO) strategy while utilising MeSH terms, mTree and keywords, and boolean operators (AND, OR and AND NOT) to expand the search results. Key search terms included; presumptive TB, people with presumed TB, TB patients, mHealth, digital health, telemedicine pre-diagnosis, pre-treatment and treatment initiation. I brainstormed on the key search terms and searched relevant articles to benchmark together with the research assistants to identify more key words to include in the search terms. Different databases were searched for the corresponding MeSH and mTree terms which were later incorporated in the search strategy *(appendix 2)*. The search strategies were built and refined by two people (RN and DB) supported by a library information specialist to ensure accuracy. Articles from all databases and other sources were exported as EndNote files (including titles and abstracts) and then imported to rayyan.QCRI.org software for screening and inclusion in the study. Duplicate articles from the searches were verified and removed.

Screening and Data Extraction

Screening of the articles was conducted at two levels, title and abstract and full text independently in rayyan. QCRI by three reviewers (RN, TM and DB) based on the inclusion and exclusion criteria of the review while blinded to each other's decision. Once the reviewers finished the screening, blinding was removed to discuss conflicting decisions and reach consensus on inclusion or exclusion of the article. Where necessary, full texts were accessed for further clarification to guide consensus. In case of further disagreements on the articles, a third reviewer (RN2) was consulted and a final decision made. All excluded articles at each level and their reasons for exclusion were documented. The review process was summarized within the PRISMA flow chart (Liberati et al., 2009) see Figure 1.

A data extraction tool was designed and pre-tested to guide the collection of information from the included studies. Two review authors, (RN and DB) extracted data from the final articles. No blinding was done at the data extraction stage however, at the end the reviewers met and achieved consensus on the data extracted. Information was extracted on: study aim, design, location/ country, target population and sample size, type of mHealth intervention (text/voice messaging, one-way or two-way communication), mHealth function (educational, monitoring, reminder, communication and support), and the effects estimates. In case of key missing and unclear data, two attempts were made to contact the corresponding author or organization by e-mail to obtain the information. Multiple publications arising from the same study were used only once, based on the most comprehensive and recent publication. One review author (RN) entered all extracted data into Review Manager (RevMan) and a second review author (DB) checked entered data for accuracy and consistency against the data extraction sheets.

Risk of Bias Assessment

I assessed the risk of bias of included studies using two tools based on the study design of the article that is; the revised Cochrane tool for Risk of Bias (RoB2) for randomized studies and the Risk of Bias and Non-randomized Studies–of Interventions (ROBINS-I) for non-randomized studies. Two reviewers (RN and DB) conducted the assessment independently and resolved any differences through consensus. Where there were disagreements, a third reviewer (RN2) was consulted to reach a decision. In both tools, the risk of bias was assessed on the following domains; i) random sequence generation (selection bias) ii) allocation concealment (selection bias) iii) blinding of participants and personnel iv) blinding of outcome assessors v) incomplete outcome data vi) selective outcome reporting (reporting bias) and vii) other sources of bias (analysis bias).

Strategy for Data Synthesis and Analysis

Data were synthesized narratively while answering the aforementioned research questions. The primary outcomes were what mHealth interventions have been used and the purpose of use. Studies whose aim was not to prevent the LTFU of patients before being diagnosed and treatment initiation if diagnosed were excluded. Findings have been descriptively summarized in an evidence table and discussed while elaborating about the interventions, primary and secondary outcomes (*appendix 3*). Data were analysed in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions.* Studies were too heterogeneous based on the I^2 statistic hence we did not pool the effect estimate for the meta-analysis.

SUB-STUDY 4

This sub-study included objectives 4 and 5 conducted in two phases using mixed methods:

Objective 4 (phase 1): To assess the effect of an SMS or phone call intervention to foster completion of the TB diagnostic process in Central Uganda.

Objective 5 (phase 2): To explore factors that influence use of an SMS and phone call intervention to foster completion of the TB diagnostic process among people with presumed TB in Central Uganda.

Phase one: Assessing the effect of the SMS or Phone call intervention

Study design and population

Secondary data from an individual randomised controlled trial (RCT), MILEAGE4TB, were analyzed (Nuwematsiko et al., 2025). The trial aimed to use SMS, phone calls and transport incentives to enhance linkage to care of people with presumed TB in Uganda. We considered patients with presumed TB who were recruited in the trial between August 2023 and March 2024. Patient with presumed TB were defined as anyone who presented with symptoms or signs suggestive of TB. That is; cough, night sweats, fever of more than two weeks and weight loss. Patients who had key missing variables like dates of sample submission and receipt of results were excluded.

Description of the trial

The RCT was conducted in six health facilities in Central Uganda that is; Kiruddu National Referral Hospital, Entebbe Regional Referral Hospital, Mukono General Hospital, Luwero General Hospital, Kawoolo General Hospital and Wakiso H/C IV (Lower-level facility). Variation of the study health facilities was to allow for comparison of the effect of the intervention at different health facility levels,

ownership type and districts (semi urban and rural). Central Uganda is home to the capital city, Kampala and hosts the most populated districts, high-volume health facilities in the country including the five National Referral Hospitals.

Participants in the trial were randomized to the five study arms by research assistants using a ration of 2:2:2:1:1 that is; i) Standard of care (SOC – control group) ii) SMS only (up to three messages) iii) Phone call only (up to three phone calls) iv) SMS and transport incentive (3 messages and $3 upon collecting results) and v) Phone call and transport incentive (3 messages and $3 upon collecting results). Participants in each study arm were independent of the other with no overlaps. Recruitment of study participants in the different arms and health facilities was done in parallel. Each study facility independently randomised study participants to the different arms based on the target numbers they had per study arm. Randomisation was done using a pre-designed mobile App where the exact target numbers per study arm and health facility were pre-fed into the App. Upon each entry at recruitment, the App would keep randomly assigning participants to different study arms until it exhausted all of them per study arm. The inclusion criteria was patients who were; i) aged 18 years and above ii) presumed for TB within 12 hours iii) those sent for GeneXpert testing iv) current residents in the health facility catchment area v) owned a personal mobile phone (the patient had to be in possession of the phone at the time of screening) vi) able to read vii) willing to sign informed consent and viii)) speaks or reads Luganda (local language) or English. Excluded patients included those who; i) had plans to move out of the study area in the next 3 months ii) were participating in another related study e.g., SMS or phone call and iii) those presumed from the community outreach programs and referred to the health facility. More details on the methods of the MILEAGE4TB RCT are described elsewhere (Nuwematsiko et al., 2025).

Description of the relevant study arms

Standard of care (comparator arm)

Patients in the standard of care (control) arm continued to receive the routine TB care, according to the Uganda Ministry of Health guidelines which includes; i) screening for TB ii) identification of people with presumed TB and registration in the TB register iii) referral for testing iv) receipt of results v) notification of attending clinicians and patients through SMS when results from the Xpert MTB/RIF are ready vi) making phone calls to positive patients to return to the health facility and start treatment and vii) initiation of treatment for positive TB patients.

SMS only arm: Participants in this arm received up to three SMS reminders. The first SMS was sent on day zero, which is the day of enrolment into the study. The second SMS was sent once the participant results were ready. If the patient did not return to complete the TB diagnostic process (i.e testing and receiving their results) within one day of the second SMS, a third SMS was sent. The 3rd SMS was a re-enforcement to remind the participants to return and complete diagnosis or initiate treatment if they did not return with the 2nd SMS. The SMS script is indicated below:

"Good day, you are reminded to come back to Entebbe Hospital".

"Olunaku olulungi, ojjukizibwa okukomawo ku Entebbe Hospital"

Standard SMS reminders were designed and manually sent by the research team using the telecom service providers MTN and Airtel in either Luganda (the local language) or English based on the preferred language of the participant as determined at enrolment. The SMS was one-way and the content neutral ensuring no mention of the word TB or even patient name. Transmission of the message sent was used as a proxy for the receipt of the SMS by the participant.

Phone call only arm: In this arm, participants received up to three phone call reminders in addition to the usual standard of care. The first phone call was made on the day of enrolment into the study

(day zero). The second phone call was made once the participant results were ready. If one day after the second phone call the patient has not returned to complete the TB diagnostic process, a third phone was made. The 3rd phone call was a re-enforcement to remind the participants to return and complete diagnosis or initiate treatment if they did not return with the 2nd phone call. Phone calls were made in either Luganda (the local language) or English based on the preferred language of the participant as determined at enrolment. The phone script is included as appendix 16.

Study hypothesis:

SMS or phone call intervention will reduce the proportion of pre-diagnosis LTFU among people with presumed TB in the intervention arm compared to the standard of care (SOC).

Alternative hypothesis:

-SMS reminders reduce the proportion of pre-diagnosis LTFU among people with presumed TB in the intervention arm 1 by 25% compared to the SOC.

-Phone call reminders reduce the proportion of pre-diagnosis LTFU among people with presumed TB in the intervention arm 2 by 30% compared to the SOC.

Null hypothesis:

-There is no difference in the proportion of pre-diagnosis LTFU among people with presumed TB in the SMS only arm and the control arm (SOC).

-There is no difference in the proportion of pre-diagnosis LTFU among people with presumed TB in the phone call only arm and the control arm (SOC).

Blinding

Due to the nature of the intervention, participants and research assistants were not be blinded to the study arms. It was not possible to blind the participants because they were the ones delivering the SMS and phone call intervention hence, they had to know which participant belonged which study arm. However, the data analysts was blinded of the study arms. Eligible patients were recruited and randomised to the five study arms. Follow-up interviews were conducted at 30 days after baseline survey for all study participants at the health facilities. In cases where participants were not able to return to their respective health facilities, phone calls were made by the Research Assistants to interview them and home visits conducted for those who could not be reached at all either by coming to the health facility or by phone call. At follow-up interviews, each participant was asked if they read the SMS or received the phone call to ascertain receipt of the intervention. We further obtained monthly statements from the telecom companies to verify if the SMS and phone calls had been made to the participants.

More detailed methods on the main trial are included in the supplementary paper (Nuwematsiko et al., 2025).

Sample size and sampling for the data extraction

I calculated sample size to estimate the minimum sample required for the analysis.

The sample size was estimated using the sample size formula for comparative proportions based on the pre-diagnosis LTFU of 40% (Ekuka et al., 2020), an alpha of 0.05, power of 0.8, and the assumptions that relative to the control (SOC), SMS reminders would likely reduce the pre-diagnosis LTFU by 25% (from 40% to 30%) and phone calls by 30% compared to the SOC. Adjusting for a post-enrolment attrition rate of 20% and design effect of 1.5, the study needed a total of 1410 participants (470 per arm). Total enumerative

$$2n = \frac{4(z_\alpha + z_\beta)^2 \bar{p}(1-\bar{p})}{(p_c - p_I)^2}$$

sampling was utilised, where all records meeting the inclusion criteria were considered from the database.

Data collection procedures

A data extraction tool was designed to extract data on the key variables required for the analysis. Data on age, sex, study arm, intervention received, occupation, distance to the health facility where TB diagnosis was made, date when identified as a presumptive TB, date when patient received the and other background characteristics were extracted.

Outcomes

Primary outcomes:

i) Completion of the TB diagnostic process (yes/no) 30 days after one is presumed to have TB. We defined completion of diagnosis as undertaking the requested TB investigation and obtaining results from the test within 30 days from the date of being identified with presumed TB. The 30-day completion period was selected based on previous studies for comparison (Pala et al., 2018).

Secondary outcome:

i) Median time to completing TB diagnosis. This was defined as the time from being presumed to have TB to the time of receiving results.

Data management and analysis

Data were extracted directly into Excel and cleaned in Stata software version 14. Descriptive statistics such as frequency distributions, median and interquartile ranges (IQRs) were computed. Chi-square

tests were performed for categorical outcomes. Intention-to-treat analysis was conducted with participants in the intervention arm considered exposed to the intervention regardless of whether or not they actually received specific intervention services. Modified Poisson regression was used to assess the association between each intervention and the SOC. No multiple hypotheses comparisons were done. A p-value <0.05 was considered statistically significant. There was no sub-group analysis between the study arms as the sample size had not been powered to achieve this. For time to completion of TB diagnosis, survival analysis method was used. Completion of TB diagnosis was based on 30 days after being presumed for TB using the Kaplan-Meir methods and survival functions assessed over the 30-day period based on our operational definition. A patient was considered to have completed TB diagnosis if they collected their TB test results within 30 days from being presumed for TB. Bivariate analysis was used to examine the relationships and Modified Poisson regression analysis used to analyse all the variables associated with completion of TB diagnosis, with a p-value of 0.05.

Phase two: Exploring influencing factors for the use of an SMS or phone call intervention to foster completion of the diagnostic process among people with presumed TB in Central Uganda

Study population: Qualitative interviews were conducted among people with presumed TB aged 18 years and above who participated in the RCT to explore what factors influenced their use or non-use of an SMS and phone call intervention. We also interviewed the primary study staff who delivered the SMS and phone call intervention for more insights.

Sample size estimation

Twenty-one IDIs with people with presumed TB and those diagnosed who participated in the RCT were conducted to explore what factors enabled the use of an SMS and phone call intervention to reduce LTFU in the TB presumption phase. In addition, nine KIIs with the study implementing staff

were conducted to further explore factors that enabled the use of an SMS and phone call intervention to reduce LTFU in the TB presumption phase.

Sampling procedure

Purposive sampling was used to select participants for the IDIs. Participants were selected based on their completion status of the diagnosis process and time to completion. Sampling ensured representation of both males and females.

Data Collection Procedures:

An interview guide was developed following the constructs of the SEM. The interviews were audio recorded after obtaining written informed consent from the participant and notes taken where necessary. Each interview was conducted in a place deemed safe, private and comfortable for both the research assistant and respondent lasting about 40-60 minutes.

Data Management and Analysis Plan

Audio recordings were transcribed verbatim and thematic analysis conducted. In the initial coding, two researchers experienced in qualitative research read through selected transcripts to familiarise themselves with the data and generate codes and theories. The codes and theories were compared by the two researchers until consensus is reached. The codes were then applied for line-by-line coding using ATLAS.ti (version 7). Analysis was concurrently done as the data was being collected to ensure generation of theories and testing them as the interviews were on-going.

3.6 OVERALL DATA STORAGE AND SECURITY

All quantitative data from the *Kobocollect* mobile app were submitted daily to the server and checked for accuracy and any errors which were communicated to the research assistants for correction during subsequent data extraction. The data collection phones and server were password protected. The server

was only accessed by the Biostatistician and study investigators. The final datasets were downloaded from the *Kobocollect* mobile app into an Excel spreadsheet and exported to Stata software version 14 for cleaning and analysis.

CHAPTER FOUR: RESULTS

Introduction

The study results are presented as per the sub-studies that constitute this thesis following the Makerere University directorate of research and graduate training guidelines for research proposals, research reports, thesis and dissertations (Makerere University, 2011).

4.1 PROPORTION OF PRE-DIAGNOSIS LTFU AND FACTORS ASSOCIATED AMONG PEOPLE WITH PRESUMED TB IN CENTRAL UGANDA (SUB-STUDY 1)

From this cohort analysis, a total of 13,496 records of people with presumed TB were abstracted from the facility records. Of these, 432 records were excluded from the analysis (Figure 6).

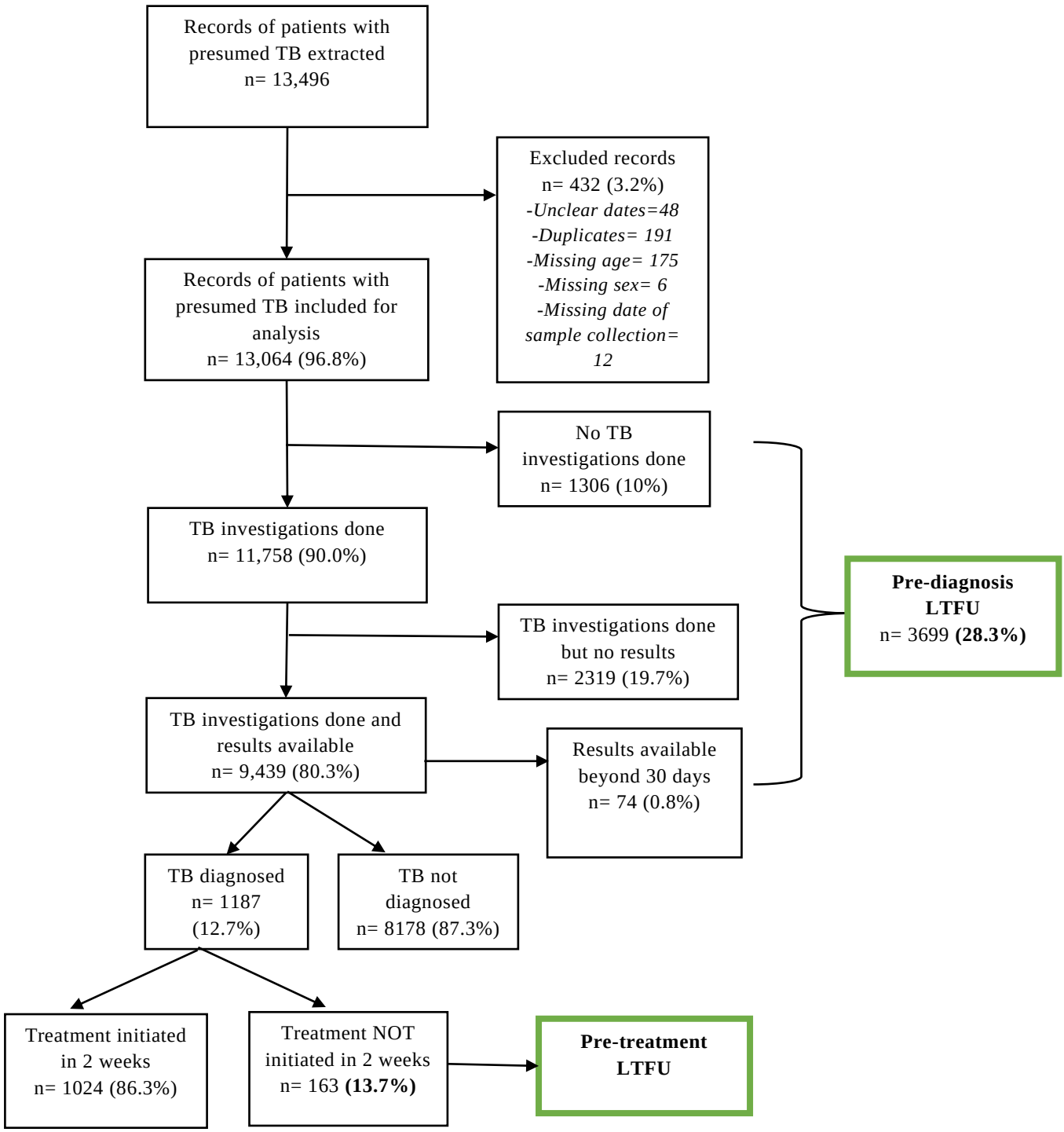


Figure 6: Flow diagram of the data extracted and analysed

Socio-demographic and clinical characteristics of study participants in the cohort analysis

Thirty-nine percent (5,213/13,064) of the patients were aged 25 to 44 years, with a median age of 35 years (IQR, 24-50). Over half of the patients 57.1% (7,462/13,064) were female. The percentage of patients with presumed TB was highest in the year 2022 at 34.2% (4,464/13,064) and lowest in 2020 at 14.9% (1956/13,064) see Table 2. Forty-two percent of the patients were living with HIV, 42.9% (5,605/13,064) see Table 2.0.

Table 2.0: Socio-demographic and clinical characteristics of people presumed with TB between 2019 and 2022 in the study facilities in central Uganda

Variable	N = 13,064 (%)
Age (median =35, IQR; 24, 50)	
0 to 14	1603 (12.3)
15 to 24	1907 (14.6)
25 to 44	5213 (39.9)
45+	4341 (33.2)
Sex	
Male	5,602 (42.9)
Female	7,462 (57.1)
Record of place of residence available	
Yes	11,002 (84.2)
No	2,062 (15.8)
Record of phone contact available	
Yes	8,679 (66.4)
No	4,385 (33.6)
Facility unit of screening for patients with presumed TB	
Outpatient department	4302 (32.9)
TB Unit	2,995 (22.9)
Maternity	398 (3.1)
HIV clinic	3,506 (26.8)
*Pediatric clinic	1,284 (9.8)
**Community outreach programs	579 (4.4)
Year of presumption	
2019	3,760 (28.8)
2020	1,956 (14.9)
2021	2,884 (22.1)
2022	4,464 (34.2)
Facility ownership	
Public (Government funded)	10,220 (78.2)
Private not for Profit (PNFP)	2,844 (21.8)
Facility level	
Health centre IV	1,668 (12.8)
Hospital	11,396 (87.2)
Accessibility to TB testing services at the health facility	
Multiple services (Gene Xpert, microscopy, TB LAM, Chest Xray)	11,396 (87.2)
Only microscopy	1,668 (12.8)
District of presumption	
Buikwe	4615 (35.3)
Mityana	3937 (30.1)
Mukono	4512 (34.6)
HIV status	
Negative	5,936 (45.4)
Positive	5,605 (42.9)
Unknown	1,523 (11.7)

** These numbers were from the hospitals; the health centre IV does not have a pediatric clinic.*

***Patients with presumed TB from the community outreach programs were documented in the health centre IV only in a presumptive TB register at the outpatient department*

Pre-diagnosis LTFU and factors associated among people with presumed TB

Out of the 13,064 participants, 10.0% (1306) were LTFU before undertaking the requested TB tests and 19.7% (2319/11758) before results collection. Overall, 28.3% (3699/13064) experienced pre-diagnosis LTFU (Figure 6). Over half of those who conducted the TB investigations required, did not have their test results documented in the laboratory or chest x-ray register on the same day of being presumed, 52.8% (4983/9439). TB was diagnosed among 12.7% (1187/9365) patients (Figure 7). Pre-diagnosis LTFU among the study participants was highest in 2019 at 48.7% (1,832/3760) and 42.9% (840/1956) in 2020. This was followed by a sharp decline in 2021 to 14.3% (413/2884) and 13.8% (614/4464) in 2022 (Figure 7).

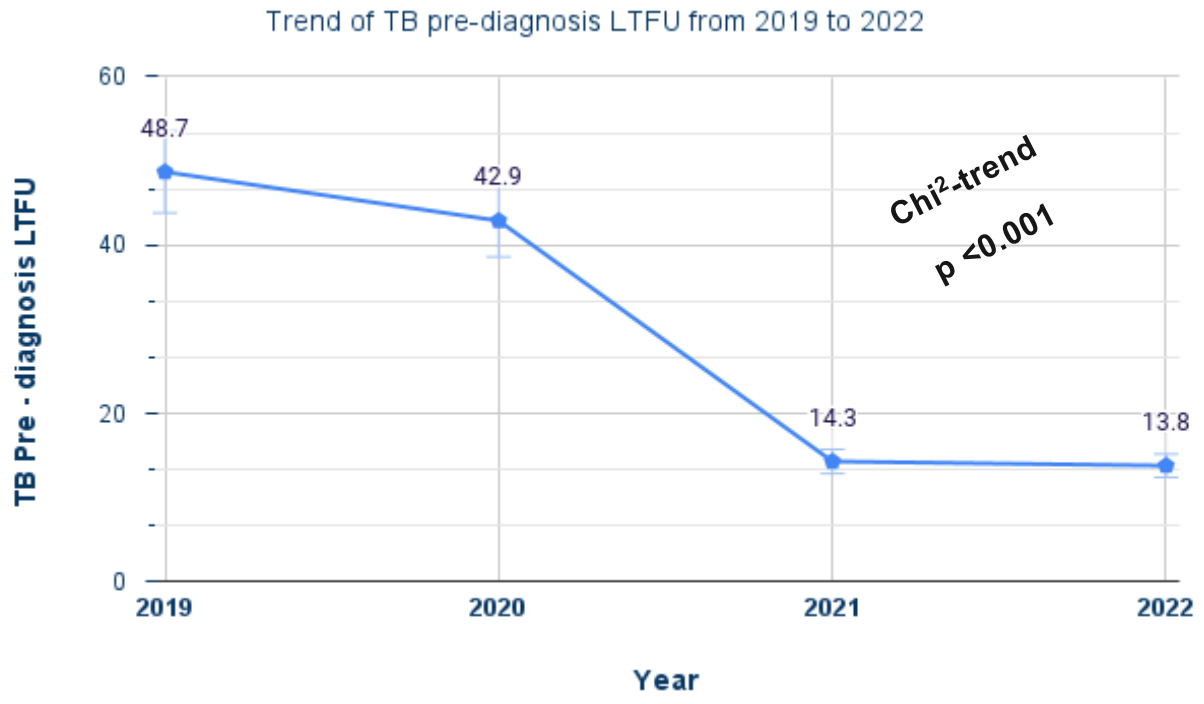


Figure 7: Trend of pre-diagnosis LTFU of participants from 2019 to 2022

Time to completing TB diagnosis among people with presumed TB

Completion of TB diagnosis was highest in the first two days with a median of 2 days (Figure 8). There was no significant difference between the time to completion of TB diagnosis between males and females (figure 9). Time to completing TB diagnosis was significantly higher among participants in H/C IVs than those presumed in hospitals at p = < 0.001 (figure 10).

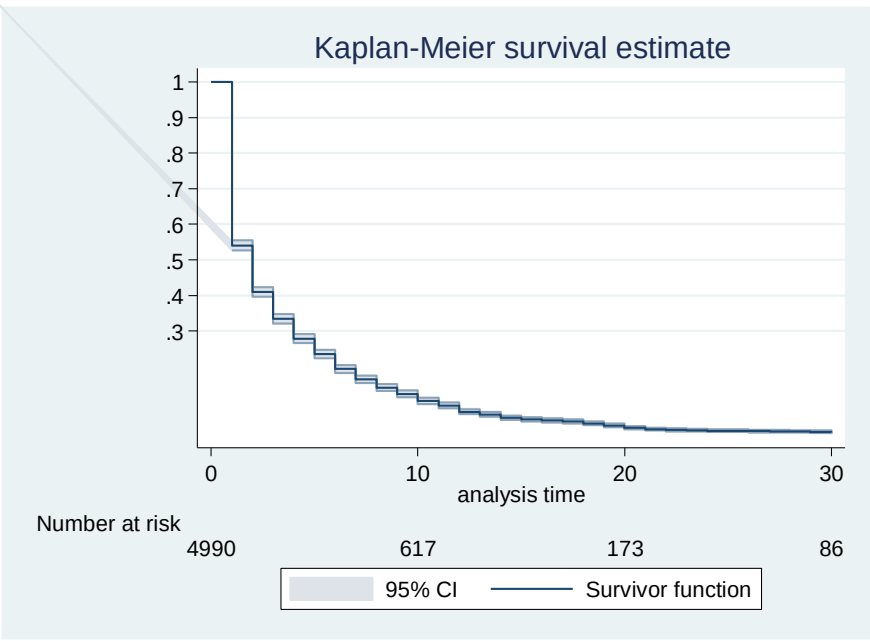


Figure 8: Kaplan Meier curve showing the time to completion of the TB diagnostic process

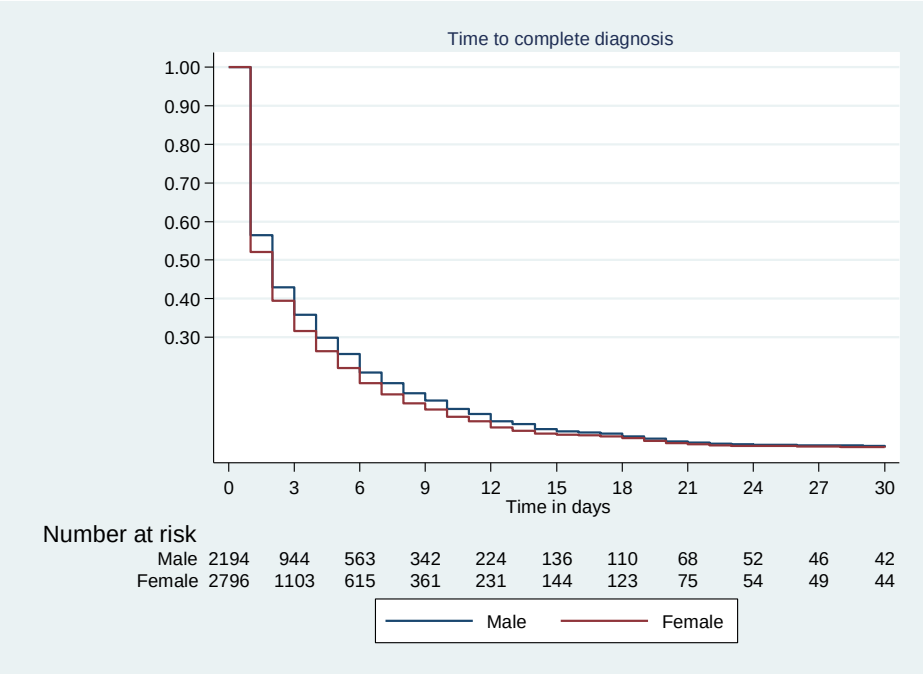


Figure 9: Kaplan Meier of completion of the TB diagnostic process by sex of participants

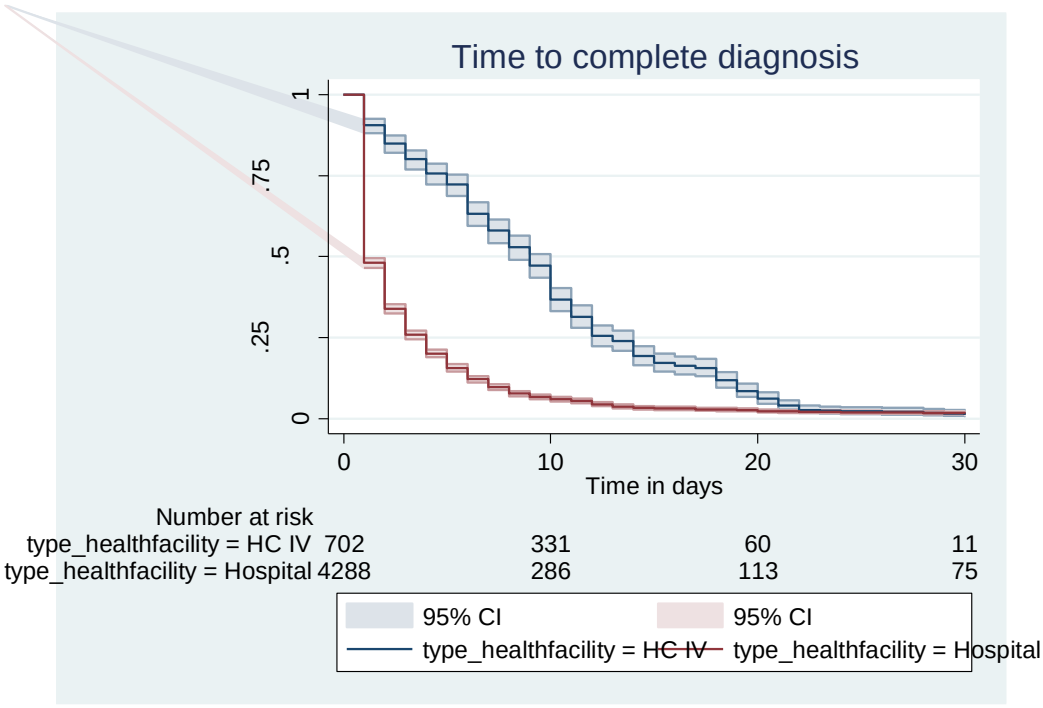


Figure 10: Kaplan Meier showing completion of the TB diagnostic process by type of health facility

Factors associated with LTFU before undertaking the requested TB tests among people with presumed TB in Central Uganda

At multivariate analysis, those aged 0-14 years (adj PR=1.35, 95% CI: 1.17, 1.54), patients with no record of place of residence (adj PR=4.46, 95% CI: 3.96, 5.01) and no record of phone contact (adj PR=1.27, 95% CI: 1.15, 1.40) and patients presumed from the maternity clinic (adj PR=1.50, 95% CI: 1.19, 1.89) were more likely to experience LTFU before undertaking the requested TB tests. In addition, patients with an unknown HIV status (adj PR=2.13, 95% CI: 1.86, 2.43) were also more likely to experience LTFU before undertaking the requested TB tests compared to those were HIV negative. On the other hand, patients presumed from the TB, Peadiatric clinics and community outreach program and those presumed from Hospitals (adj PR=0.46, 95% CI: 0.41, 0.52) and PNFPs (adj PR=0.79, 95% CI: 0.67, 0.95) were less likely to be LTFU before undertaking the requested TB tests (Table 3.0).

Table 3.0: Factors associated with LTFU before undertaking the requested TB tests from 2019 to 2022 in study health facilities in Central Uganda

Characteristic	LTFU before sample collection% (n/N)	Crude PR (95% CI)	Adjusted PR (95% CI)	P-value
Age				
45+	9.7 (422/4341)	1 (Ref)	1 (Ref)	
0 to 14	17.0 (273/1603)	1.75 (1.52-2.01)	**1.35 (1.17-1.55)**	**<0.001***
15 to 24	8.4 (161/1907)	0.87 (0.73-1.03)	**0.81 (0.69-0.96)**	**0.013***
25 to 44	8.6 (450/5213)	0.89 (0.78-1.01)	**0.86 (0.76-0.97)**	**0.014***
Sex				
Male	9.7 (542/5602)	1 (Ref)	1 (Ref)	
Female	10.2 (764/7462)	1.06 (0.95-1.17)	1.05 (0.95-1.16)	0.338
Record of place of residence available				
Yes	6.5 (719/11002)	1 (Ref)	1 (Ref)	
No	28.5 (587/2062)	4.36 (3.95-4.81)	**4.46 (3.96-5.01)**	**<0.001***
Record of phone contact available				
Yes	9.0 (784/8679)	1 (Ref)	1 (Ref)	
No	11.9 (522/4385)	1.32 (1.19-1.46)	**1.27 (1.15-1.40)**	**<0.001***
Facility unit of screening for patients with presumed TB				
Outpatient department	15.7 (675/4302)	1 (Ref)	1 (Ref)	
TB Unit	7.7 (231/2995)	0.49 (0.43-0.57)	**0.68 (0.59-0.79)**	**<0.001***
Maternity	18.1 (72/398)	1.15 (0.93-1.44)	**1.50 (1.19-1.89)**	**<0.001***
HIV clinic	6.7 (234/3506)	0.43 (0.37-0.49)	**0.53 (0.44-0.63)**	**<0.001***
Pediatric clinic	5.8 (74/1284)	0.37 (0.29-0.46)	**0.65 (0.52-0.82)**	**<0.001***
Community outreach programs	3.5 (20/579)	0.22 (0.14-0.34)	**0.14 (0.09-0.22)**	**<0.001***
HIV status				
Negative	8.2 (487/5936)	1 (Ref)	1 (Ref)	
Positive	7.7 (430/5605)	0.94 (0.83-1.06)	1.15 (0.99-1.32)	0.060
Unknown	25.5 (389/1523)	3.11 (2.76-3.51)	**2.13 (1.86-2.43)**	**<0.001***

Continued Table 3.0: Factors associated with LTFU before undertaking the requested TB tests from 2019 to 2022 in study health facilities in Central Uganda

Characteristic	LTFU before sample submission % (n/N)	Crude PR (95% CI)	Adjusted PR (95% CI)	P-value
Year of presumption				
2019	12.3 (461/3760)	1 (Ref)	1 (Ref)	
2020	10.1 (197/1956)	0.82 (0.70-0.96)	0.91 (0.78-1.05)	0.201
2021	7.6 (218/2884)	0.62 (0.53-0.72)	**0.41 (0.35-0.47)**	**<0.001***
2022	9.6 (430/4464)	0.79 (0.69-0.89)	**0.50 (0.44-0.57)**	**<0.001***
Facility level				
Health centre IV	18.2 (304/1668)	1 (Ref)	1 (Ref)	
Hospital	8.8 (1002/11396)	0.48 (0.43-0.54)	**0.46 (0.41-0.52)**	**<0.001***
Facility ownership				
Public (Government funded)	11.4 (1166/10220)	1 (Ref)	1 (Ref)	
Private not for Profit (PNFP)	4.9 (140/2844)	0.43 (0.36-0.51)	**0.79 (0.67-0.95)**	**0.013***
Accessibility to TB testing services at the health facility				
Only microscopy	18.2 (304/1668)	1 (Ref)		
Multiple services (Gene Xpert, microscopy, TB LAM, Chest Xray)	8.8 (1002/11396)	0.48 (0.43-0.54)		
District of presumption				
Buikwe	6.7 (309/4615)	1 (Ref)		
Mityana	14.1 (553/3937)	2.09 (1.84-2.39)		
Mukono	9.8 (444/4512)	1.47 (1.28-1.69)		

** Statistically significant at <0.05*

Factors associated with LTFU before collection of results among people with presumed TB in Central Uganda

At multivariate analysis, females (adj PR=1.07, 95% CI: 1.00, 1.15), those whose details of residence were not recorded in the registers (adj PR=1.82, 95% CI: 1.59, 2.09) and patients presumed from the TB unit (adj PR=1.11, 95% CI: 1.03, 1.21) were more likely to be LTFU before collection of results. In addition, patients with an unknown HIV status (adj PR=1.33, 95% CI: 1.19, 1.49), those presumed from hospitals (adj PR=1.51, 95% CI: 1.27, 1.78) and those presumed from PNFPs (adj PR=1.26, 95% CI: 1.16, 1.37) were also more likely to be LTFU before collection of results. On the other hand,

patients presumed from the ART clinic (adj PR=0.88, 95% CI: 0.79, 0.98), Peadiatric clinic (adj PR=0.86, 95% CI: 0.75, 0.99) and the community (adj PR=0.17, 95% CI: 0.06, 0.45) were less likely to be lost before completing TB diagnosis compared to those presumed from the OPD (Table 4.0).

Table 4.0: Factors associated with LTFU before collection of results from 2019 to 2022 in study health facilities in Central Uganda

Characteristic	LTFU before collection of results % (n/N)	Crude PR (95% CI)	Adjusted PR (95% CI)	P-value
Age				
45+	20.3 (796/3919)	1 (Ref)	1 (Ref)	
0 to 14	19.9 (264/1330)	0.98 (10.86-1.11)	1.11 (0.99-1.24)	0.063
15 to 24	20.6 (359/1746)	1.01 (0.91-1.13)	1.01 (0.91-1.13)	0.800
25 to 44	18.9 (900/4763)	0.93 (0.85-1.01)	0.98 (0.91-1.06)	0.604
Sex				
Male	18.9 (960/5060)	1 (Ref)	1 (Ref)	
Female	20.3 (1359/6698)	1.07 (0.99-1.15)	**1.07 (1.00-1.15)**	**0.046***
Record of place of residence available				
Yes	20.8 (2138/10283)	1 (Ref)	1 (Ref)	
No	12.3 (181/1475)	0.59 (0.51-0.68)	**1.82 (1.59-2.09)**	**<0.001***
Record of phone contact available				
Yes	19.3 (1521/7895)	1 (Ref)	1 (Ref)	
No	20.7 (798/3863)	1.07 (0.99-1.16)	1.05 (0.98-1.13)	0.179
Facility unit of screening for patients with presumed TB				
Outpatient department	20.7 (751/3627)	1 (Ref)	1 (Ref)	
TB Unit	29.1 (804/2764)	1.40 (1.29-1.53)	**1.11 (1.03-1.21)**	**0.011***
Maternity	20.6 (67/326)	0.99 (0.79-1.24)	0.88 (0.71-1.09)	0.231
HIV clinic	15.3 (500/3272)	0.74 (0.67-0.82)	**0.88 (0.79-0.98)**	**0.024***
Pediatric clinic	15.9 (193/1210)	0.77 (0.67-0.89)	**0.86 (0.75-0.99)**	**0.034***
Community outreach programs	0.7 (4/559)	0.03 (0.01-0.09)	**0.17 (0.06-0.45)**	**<0.001***
HIV status				
Negative	21.0 (1145/5449)	1 (Ref)	1 (Ref)	
Positive	18.1 (934/5175)	0.86 (0.79-0.93)	0.97 (0.89-1.05)	0.483
Unknown	21.2 (240/1134)	1.01 (0.89-1.14)	**1.33 (1.19-1.49)**	**<0.001***

Continued Table 4.0: Factors associated with LTFU before collection of results from 2019 to 2022 in study health facilities in Central Uganda

Characteristic	LTFU before results collection % (n/N)	Crude PR (95% CI)	Adjusted PR (95% CI)	P-value
Year of presumption				
2019	41.1 (1357/3299)	1 (Ref)	1 (Ref)	
2020	35.8 (629/1759)	0.87 (0.81-0.94)	**0.87 (0.81-0.94)**	**<0.001***
2021	6.3 (169/2666)	0.15 (0.13-0.18)	**0.14 (0.12-0.16)**	**<0.001***
2022	4.1 (164/4034)	0.09 (0.08-0.12)	**0.09 (0.08-0.11)**	**<0.001***
Facility level				
Health centre IV	8.7 (118/1364)	1 (Ref)	1 (Ref)	
Hospital	21.2 (2201/10394)	2.45 (2.05-2.92)	**1.51 (1.27-1.78)**	**<0.001***
Facility ownership				
Public (Government funded)	20.0 (1811/9054)	1 (Ref)	1 (Ref)	
Private not for Profit (PNFP)	18.8 (508/2704)	0.94 (0.86-1.03)	**1.26 (1.16-1.37)**	**<0.001***
Accessibility to TB testing services at the health facility				
Only microscopy	8.7 (118/1364)	1 (Ref)		
Multiple services (Gene Xpert, microscopy, TB LAM, Chest Xray)	21.2 (2201/10394)	2.45 (2.05-2.92)		
District of presumption				
Buikwe	26.3 (1132/4306)	1 (Ref)		
Mityana	16.6 (561/3384)	0.63 (0.58-0.69)		
Mukono	15.4 (626/4068)	0.59 (0.54-0.64)		

** Statistically significant at <0.05*

More details of this paper are presented in Paper 1 [Pre-diagnosis and pre-treatment loss to follow-up and associated factors among patients with presumed tuberculosis and those diagnosed in Uganda. *BMC Health Serv Res. 2024 Dec 23;24(1):1638. doi: 10.1186/s12913-024-12115-4. PMID: 39710664; PMCID: PMC11665076.* **Nuwematsiko R,** Kiwanuka N, Wafula ST, Nakafeero M, Nakanjako L, Luzze H, Turyahabwe S, Sekandi JN, Atuyambe L, Buregyeya E (2024)] (Nuwematsiko et al., 2024).

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RESEARCH Open Access

Pre-diagnosis and pre-treatment loss to follow-up and associated factors among patients with presumed tuberculosis and those diagnosed in Uganda

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Abstract

Background Loss to follow-up (LTFU) of patients with presumed tuberculosis (TB) before completing the diagnostic process (pre-diagnosis LTFU) and before initiating treatment for those diagnosed (pre-treatment LTFU) is a challenge in the realization of the End TB Strategy. We assessed the proportion of pre-diagnosis and pre-treatment LTFU and associated factors among patients with presumed TB and those diagnosed in the selected health facilities.

Methods This was a retrospective cohort study involving a review of routinely collected data from presumptive, laboratory and TB treatment registers from January 2019 to December 2022. The study was conducted in three general hospitals and one lower-level health center IV in Central Uganda. We defined pre-diagnosis LTFU as failure to test for TB and obtain results within 30 days from the date of being presumed and pre-treatment LTFU as failure to initiate TB treatment within 14 days from the date of diagnosis. Modified Poisson regression was used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) of factors associated with pre-diagnosis and pre-treatment LTFU.

Results Of the 13,064 patients with presumed TB, 39.9% were aged 25 to 44 years, and 57.1% were females. Almost a third, 28.3% (3,699/13.064) experienced pre-diagnosis LTFU and 13.7% (163/1187) did not initiate treatment within 14 days from being diagnosed. Pre-diagnosis LTFU was more likely to occur among patients aged 0-14 years (adj PR 1.1, 95% CI: 1.06,1.24), females (adj.PR=1.06, 95% CI: 1.01, 1.12) and those with no record of place of residence (adj. PR=2.7, 95% CI: 2.54, 2.93). In addition, patients with no record of phone contact were more likely to be LTFU, (adj. PR=1.1, 95% CI: 1.05, 1.17). Pre-treatment LTFU was also more likely among patients with no record of place of residence (adj PR 7.1, 95% CI: 5.13,9.85) and those with no record of phone contact (adj PR 2.2, 95% CI: 1.63,2.86). Patients presumed from the HIV clinics were 40% less likely to experience pre-treatment LTFU compared to those in the outpatient departments (adj PR 0.6, 95% CI: 0.41,0.88).

Conclusion High proportions of pre-diagnosis and pre-treatment LTFU were observed in this study. This calls for urgent interventions at these time points in the TB care cascade to be able to realise the End TB Strategy.

Keywords Tuberculosis, loss to follow, Up, pre, Diagnosis loss to follow, Up, pre, Treatment loss to follow, Up, Uganda

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4.2 FACILITATORS AND BARRIERS FOR COMPLETION OF THE TB DIAGNOSTIC PROCESS IN CENTRAL UGANDA (SUB-STUDY 2)

Characteristics of study participants

Out of 25 in-depth interview participants interviewed, 15 were female and almost a third aged between 45 years and above. Almost half (11/25) were farmers by occupation. We conducted six focus group discussions with 42 participants ranging between 6-8 per group, an average of seven participants. Most participants of the focus group (14), were aged 31-39 years of age and more than half (23), were females. Of the 20 key informants; three-quarters of them were female and most aged between 20-30 years (6) and 31-40 years (6).

Interviews from the patients (IDIs and FGDs) and health workers (KIIs) showed related views on the facilitators and barriers to completing the TB diagnostic process, therefore the presentation of the results is integrated. Where necessary the similarities or differences across participant categories are highlighted. The findings are presented according to the categories of individual, health system and community factors. Six themes were obtained that is; i) individual level facilitators ii) individual level barriers, iii) health system facilitators iv) health system barriers v) interpersonal and community facilitators and vi) interpersonal and community barriers. Findings are summarized in Figure 11.

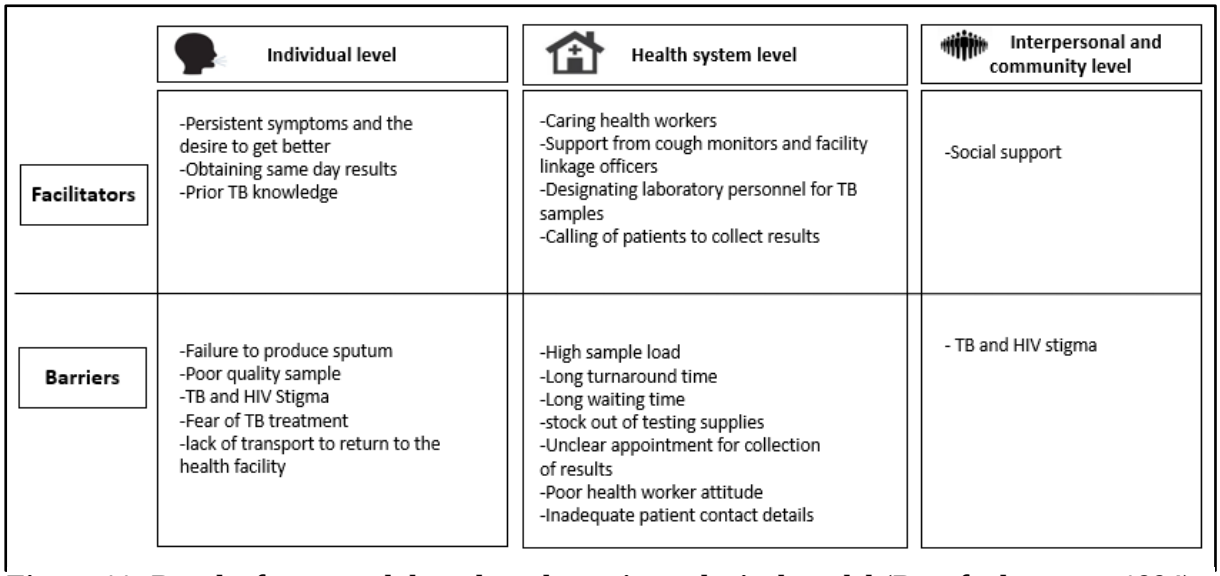


Figure 11: Results framework based on the socio-ecological model (Bronfenbrenner, 1994)

FACILITATORS FOR COMPLETION OF THE TB DIAGNOSTIC PROCESS

Three themes with corresponding sub-themes emerged under facilitators for completion of the TB diagnostic process: i) individual facilitators (persistent symptoms and the desire to get better, obtaining same day results and prior TB knowledge) ii) health system facilitators (caring health workers, support from cough monitors and facility linkage officers, designated TB laboratory personnel and calling of diagnosed patients to collect results) and interpersonal and community facilitators (social support).

Individual level facilitators

Almost all IDI participants, 92%, who completed the TB diagnostic process and those in all FGDs, mentioned that experiencing persistent TB symptoms and the desire to get better was a facilitator for completing the diagnostic process. Participants stated that the pain alone from the persistent symptoms was a motivation to go through the whole process of getting a diagnosis and initiating treatment if diagnosed with TB in order to get better. In some instances, participants mentioned taking medication either from private clinics or pharmacies to get relieved of the symptoms which still persisted thus prompting them to get tested for TB. Persistent cough with chest pain was the commonly mentioned symptom mentioned by most participants, cutting across females and males. Relatedly, compared to females, more males expressed coming to the health facilities when already in too much pain hence motivated to complete the diagnostic process.

> *"It was the pain that I was going through that motivated me to do everything that the health workers asked me to do. I always had fevers, would cough a lot and had been on treatment for a long time with no change…."* **39-year-old female IDI participant, completed the diagnostic process**

Obtaining same day results: close to a quarter of the participants mentioned receiving results on the same day of being presumed for TB and attributed their completion of the diagnostic process to that.

They said it was because they were able to wait and get their results without the need to return to the health facility, which was associated with more transport costs, need for time off work and potential stigma from repeat visits to the health facility. Obtaining same day results was commonly mentioned by participants in the private not-for profit health facility. One participant in a female FGD affirmed that if she had not received results that very day, she would never have come back to complete the TB diagnostic process for fear of being stigmatized by her family.

> *"I feared people at home to know that I have TB…if I was not told that I have TB on that same day and also given drugs, I do not think I would have come back to the hospital"* **25-year-old female FGD participant, Hospital**

Having prior knowledge on TB was mentioned as another key facilitator to completing the TB diagnostic process. This was because the patients already knew about TB, the benefits of testing and wanted to know the results. This was commonly mentioned by IDI and KII participants. The knowledge was obtained through previous experience with people with TB either by nursing or living with them, having a history of TB and interaction with people with TB in the community. Compared to females, males were less knowledgeable on TB. Additionally, sensitization from health workers in previous health facility visits was mentioned as a source of TB knowledge for some participants. In one of the KII, a participant explains how prior knowledge motivates the patients:

> *"There are clients that we get who come straight to be tested for TB. They do not wait to be screened. They see the signs and symptoms and come. We get those too a lot. So, someone like that easily complies with the processes…Sometimes the client has a TB patient at home, so when they start to cough, they turn up to be tested too."* **47-year-old female KII_TB unit, Hospital**

On the other hand, in all FGDs, it was mentioned that some patients don't submit the sputum samples and return to collect results because they have limited knowledge on TB. The knowledge gap was specifically on the benefits of testing, not knowing that TB can be cured and consequences of not getting treatment if one has TB.

Health system facilitators

Caring health workers: The positive interaction with healthcare workers motivated patients to get tested for TB. This was mentioned by over a half (56%) of the IDI participants who completed the TB diagnostic process and in most FGDs. The care was reported in the form of counselling, talking to them politely, guidance on the next steps in the diagnostic process and giving them extra information on TB. The care from health workers was also described to motivate patients who were diagnosed with TB to proceed further and start treatment. This was pointed out mainly by males and adults above 30 years across all the health facilities.

> *"According to what you have gone through while suffering from what you don't know, you can come here and ask for the tests yourself. The health workers are caring in a way that when you come, they immediately attend to you. The health worker's attitude and how they talk to us motivates us. These health workers always help to show us what to do and where to go."* **51-year-old male FGD participant, Hospital**

From the health system perspective, the care and support from cough monitors (health workers designated to assist in cough monitoring for a sputum sample from people with presumed TB) and TB facility linkage officers enables sensitization, symptomatic screening of patients and patient follow-up for samples and treatment initiation as mentioned by most KIIs (12/20). In the KIIs, it was noted that patient screening and follow-up would have been challenging with the heavy workload and low staffing especially in the hospitals. Having these support staff was therefore viewed as a strong pillar

for supporting patients to complete the diagnostic process since they are mainly designated to do that with limited competing work. Furthermore, staff from the TB departments were described by all laboratory personnel as caring, supportive and responsible. They described their support in; sample collection, following up submitted samples for results, calling back patients (those with poor quality samples or whose samples were lost) and sometimes collecting the printed results and dispatching them to the requesting departments. This was mentioned to reduce the work load of the laboratory staff thus reducing the turnaround time of the results. In one health facility, staff from the TB departments were mentioned to support in sample collection from patients at the different service delivery points to reduce on the waiting time at the laboratory. One key informant mentioned how the support from the TB focal person helps them not to miss out on testing any patient;

> *"There is a close link with the TB personnel who really support us a lot...The good thing is that the TB focal person for the facility is really active. So, he always comes in and then checks on how many patients were worked on, what are the details, what could be the results."* **36-year-old female KII_laboratory, Health centre IV**

Having designated laboratory personnel to run TB samples was mentioned by three quarters of participants in the KIIs as a strong facilitator for having a diagnosis for patients. These designated personnel prioritize the TB samples in addition to the other laboratory workload and ensure that all samples received are run on time and sends back results to the requesting departments. It was noted that these personnel also take the initiative to alert the requesting unit and TB focal person once a patient's result comes out positive. This is to ensure that the patient is called back to the health facility to initiate treatment. In two health facilities, it was mentioned that this laboratory person prioritizes patients with presumed TB for sample collection to reduce their waiting as a way to motivate them to

complete the diagnostic process. Additionally, one key informant, a laboratory manager, mentioned that not all staff want to process and analyse TB sputum samples because they find them unpleasant. She explained that previously, most of the laboratory staff would leave the sputum samples unanalysed for her to process when on duty. This prompted her to designate specific personnel to analyse these samples so that patient's results are not delayed.

Calling of patients diagnosed with TB to collect results also facilitated almost all participants who were diagnosed to collect results and start treatment. In the majority of the KIIs (17/20), participants said they always call back patients who are diagnosed with TB to return to the health facilities and initiate treatment immediately. This happens in cases where the patient had left the health facility without collecting their results. Health workers contact patients by telephone using the contact details recorded in the health facility registers or those of the next of kin if the patient is unreachable on their personal telephone. Participants in some of the IDIs and all FGDs also said the same, that the phone call helped them to come back to the facility, collect results and initiate treatment.

> *"The health worker called me directly and told me that the results from my sputum show that I have TB and also asked me if I can go there on Monday and start taking drugs. I was going through a lot of pain. I had coughed for weeks… I was looking forward to Monday to go to hospital and start my medications."* **39-year-old female FGD participant, Hospital**

However, some KIIs (35%), stated that calling of patients was sometimes challenged by no airtime to make the phone calls and poor record taking of the patient contact details. It was noted that some health workers do not record the contact numbers of the patients or record incomplete numbers. On the other hand, other KIIs pointed out that patients submit wrong or incorrect contact numbers when they feel they don't want to be contacted. This was mentioned to be common among young people and those who stay in distant places.

"The other problem I have seen is amongst the youth and the people on islands, some of them forge numbers (telephone contacts). They give us forged telephone numbers. There is a client that we received I think in 2021 from Buvuma (an island). The lady turned TB positive, we tried to call and the phone was not available. It was not available on the network. So that is a problem too." **23-year-old male KII_TB Unit, Hospital**

Interpersonal and community facilitators

Receiving social support was mentioned by most IDI participants (14/25) and few FGDs (2) as a key factor that encouraged them to get tested for TB, collect results and initiate treatment when diagnosed. The support came mostly from parents, spouses and close relatives in the form of accompanying them to the health facility, advising and counselling them to get tested, and giving them money for transport and food while visiting the health facility. The social support was more pronounced among females and the young people under 35 years of age as narrated below;

"My mother encouraged me to come for testing to see what is wrong with them. She also counselled me and told me whatever the results I will not be the first." **23-year-old female IDI participant, completed diagnosis**

BARRIERS FOR COMPLETION OF THE TB DIAGNOSTIC PROCESS

We identified three themes under barriers for completion of the TB diagnostic process: i) individual-level barriers (inability to produce sputum, TB and HIV stigma, lack of transport to return to the health facility, fear of TB treatment) ii) health system barriers (long turnaround time for results, high sample load, stock out of testing supplies, unclear appointment for collection of results, poor health worker attitude, inadequate patient contact details) and interpersonal and community barriers (TB and HIV stigma).

Individual-level barriers

A few IDI participants (5/13), who did not complete the TB diagnostic process mentioned that they were unable to provide a sputum sample into the laboratory specimen container for testing. They mentioned trying all they could to produce the sputum but were unable and eventually went home. Three out of the five participants mentioned that they returned to the health workers for advice when they were unable to produce the sputum. These were advised to get an early morning sample while other participants said they simply left the health facility without consulting. For some participants, they were still unable to produce the early morning sputum sample and others were successful. Those who were unable to produce the sputum completely mentioned not returning to the health facility for fear of being reprimanded by the health workers if they came back without a sample. Because of the fear to go back to the health workers, patients ended up either submitting a poor-quality sample or disappearing from the health facility.

> *"I wanted to know the results truthfully but I did not have sputum. I do not know what I put in there. I coughed, coughed, and coughed…but I did not have it. When they asked for it (sputum), I did what I did and spat in the container but it was not sputum."* **39-year-old female IDI participant, lost to follow-up (LTFU)**

A few KIIs explained that some patients are unable to produce sputum because health workers rarely tell patients the techniques of sputum production during sensitization and counselling sessions. It was noted that patients are also not informed of other available tests in instances where one is unable to produce sputum which causes patients to disappear from the health facilities. It was further mentioned that limited sensitization also leads to poor quality samples from patients with some submitting either saliva or an insufficient sample. A key informant narrates below how patients do not return to the health workers once they are unable to produce sputum.

"There are some patients when they are told to collect sputum, they find it difficult to get that sputum, so when they fail, they just give up. When they are asked to collect sputum, they go in that area where they are supposed to collect the sputum from and when they fail, they just lose hope and sometimes they are not explained to the other options. So, they just give up and go away." **34-year-old male KII_TB Unit, Hospital**

TB and HIV related stigma was reported to lead to LTFU from the TB diagnostic process. The drivers of the stigma were; i) fear of association with HIV/AIDS, ii) fear of social exclusion and iii) fear of spreading TB to the rest of the family members. Participants in the IDIs and FGDs feared being labelled as people living with HIV because of the community understanding that whoever has TB also have HIV. They also expressed the fear of being stigmatized and socially excluded in the community by family members if they found out that they were being presumed for TB. Hence, they feared to be isolated, gossiped about, being seen using TB services and taking medication. The stigma was reported across all ages and sexes, and by participants in all IDIs and in all FGDs.

"It is because of fear. Personally, I was initially afraid as well. I imagined what it would be like if I were seen taking TB drugs, and my mom telling me not to take them from here. I also thought about how people would gossip about me if they saw me taking those drugs. So, I decided to leave it up to them and not take the drugs because I was worried about how people would perceive me." **27-year-old female FGD participant, Hospital**

The barrier of TB and HIV stigma was also attested to by key informants who mentioned that the community associates TB to HIV/AIDS which discourages people with presumed TB from testing for fear of being labelled by the community as people living with HIV. A key informant in one of the hospitals explained how stigma makes patients not to test for TB:

"Stigma makes them disappear because most people think that when you have TB you are HIV positive…So these patients fear seeing them in the line of people testing for TB and HIV…that kind of fear causes the patients to get lost and fail to complete the diagnostic process. The person is asked to produce the sample and they instead choose to leave the facility" **43-year-old male KII TB Unit, Hospital**

The TB/HIV testing policy being implemented in the study facilities was mentioned to further increase the stigma which deters away some patients when presumed for TB. Majority of the participants in KIIs (70%) and IDIs (56%) and in few FGDs (3) said patients know that they will not only be tested for TB but also for HIV and this scares them so much. The main fear was getting HIV positive results once tested followed by daily swallowing of drugs for the rest of their lives which scared them away. Participants stated that some community members thus prefer to live in ignorance of their HIV status than face this reality of swallowing drugs daily. The fear of being tested for HIV was commonly mentioned among males and participants under 40 years of age.

"Some people are told to go and test but they refuse because they fear and they know they are not only going to be tested for TB but they also have to be tested for HIV and this thing scares them so much" **36-year-old male FGD participant, Hospital**

Lack of transport to return to the health facility either to submit a sample or collect results from the test was also reported as a barrier for completion of the TB diagnostic process. This was mentioned by participants who did not get a spot sputum sample and needed to take back the sample the next day and by those who did not collect results or initiate treatment on the day of the health facility visit. Participants reported that they do not receive results on the same day they are presumed for TB hence the need to return to collect results or initiate treatment which requires money for transport. This was commonly mentioned by females and those who reside in areas far away from the health facilities.

Participants who stay far said it is worse for them compared to those who stay in nearby places. Close to half of the participants across IDIs, KIIs and in all FGDs mentioned the lack of transport as a major barrier.

> *"The distance and the transport fees made it difficult for me. If it were nearby, I would have returned even that very day…. But the distance is long and you have to first gather some money before you can be able to come back to the facility."."* **50-year-old male IDI participant LTFU**

The fear of TB results and treatment was mentioned in all FGDs and by most IDI (40%) and KII participants (25%) as a key contributor to LTFU before completing the TB diagnostic process. It was noted that generally some people fear taking drugs hence they will disappear from the health facilities before knowing the results. The fear of taking TB drugs is further amplified by the TB and HIV stigma with participants fearing to be seen taking TB drugs and be mistaken for swallowing HIV drugs. Other participants mentioned knowing that TB treatment is for six months hence see it as a long time, which makes them not to proceed to test for TB preferring to live in ignorance of their status. Other participants who had seen the drugs perceived them as big tablets hence feared swallowing them. All these perceptions on the TB drugs and duration were reported to discourage patients from testing for TB.

> *"Some people fear to know the results and also fear taking the drugs. Some people have fear within themselves and also do not imagine themselves taking the TB drugs especially when they have seen the drugs. Tablets are too big and are taken for a long time. Some people feel sorry for themselves and say that they do not want to take drugs. This makes them not to come back."* **52-year-old male FGD participant, Hospital**

More so, people living with HIV were cited to fear the potential pill burden in case the results come back positive for TB. This is because they are already swallowing ARVs daily and perceive the addition of other daily TB drugs as cumbersome hence they shy away from the diagnosis. This causes them to not test for TB or even collect their results.

> *"Another thing that makes people to not want to complete the process (TB Diagnosis) is the fact they are already taking HIV drugs. They imagine how they will be able to take both drugs concurrently and so they will decide to stay on the HIV drug only…The fact that the TB drugs are also taken for a long period of six months and yet the HIV drugs are already for a lifetime makes them to stay away from completing TB diagnosis. They just have hope that they will somehow recover from the TB without drugs yet that is not possible".* **40-year-old male FGD participant, Health centre IV**

Health system barriers

High sample load from lower-level health facilities was mentioned in the two public hospitals as a barrier for same day analysis of samples. These hospitals receive many samples from different referring facilities in addition to those collected from the patients seen in their facility departments. This was further complicated by the type of Xpert MTB/RIF machines available in the facilities which can only analyse few samples at a time. This led to a long turnaround time for results and consequently long waiting time for the patients. In most cases, they asked the patients to return and collect results either the next day or after some days which led to some of them getting lost from the diagnostic process.

"We work on samples from lower facilities and in a day, we can work on thirty (30) or more than that throughout the district. This gene expert takes one hour to run, just running and when it comes to sample collection, we can give it like three (3) hours in total. You find that time for patients to wait is long. It is too hard for them to wait...As I have told you, when they go back to the village, coming back is a problem." **30-year-old male KII_laboratory, Hospital**

Relatedly, long waiting time for results was mentioned by over half of the participants in IDIs, KIIs and all FGDs. Patients reported a long waiting time either on the day of sample submission when told to wait for results that very day or long waiting in days when one is told to return because the results will not ready on the same day of sputum submission. The long waiting time was said to lead to frustration and one making a decision to either return or not return to collect the results. For patients who are told to return on another day and collect results, it was mentioned that some health workers attempt to give them a date to return with the hope that results will be ready then. However, it was not always guaranteed that the patients will find results on the given date. Some participants mentioned the possibility of not finding results on that day they are told to return and collect them. This therefore meant more waiting time and the need for another return visit to the health facility. Participants narrated that every return to the health facility necessitated time off work and more transport money beyond that which was originally planned at the first visit. This was therefore seen to make completion of the TB diagnostic process tedious and costly.

"The long waiting time for results also makes them disappear. For example, those who have given in their sample on Tuesday are told to come for their results on Friday. But remember he may come on Friday and be told to come back on Monday. All that is money wasted on transport." **44-year-old female KII_TB Unit, Hospital**

On the other hand, some participants mentioned not being given clear appointment dates when to collect the results which left them in uncertainty causing them to make random visits to the health facilities before obtaining results. Unclear appointments for collection of results coupled with poor communication was reported by majority of the IDIs (19/25) and in three FGDs as a barrier. This meant patients making several back-and-forth trips to the health facility checking for readiness of results which was mentioned by some participants to expose them to stigma and doubt by the people around them.

> *"They did not call me and they also did not give me a date so that when the date reaches, I go back. But they did not tell me so I didn't know. When they did not give me a return date or call me, I went silent…what scared me was frequenting the hospital and what people would say and think about it, especially my mother. Had they called me, I would have come back.* **" 37-year-old female IDI participant_LTFU**

> *"I thought that they would give me the results on that day, but they told me that they would call me and tell me when to return…They did not call me and they also did not give me a date. When they did not give me a return date or call me, I went silent."* **52-year-old female IDI participant_LTFU**

Stock out of testing supplies at the health facilities also hindered patients from completing the diagnostic process. Laboratory staff in the hospitals mentioned a common stock out of Xpert MTB/RIF cartridges which forces them to halt sample collection and processing. More so, a few participants (20%) said that some tests not being available at the health facility increases the likelihood of patients being lost from the process. In such cases, patients are sent for testing outside of the health facility, which was often associated with costs. In that process, the patients do not return to the health facilities either because of the cost or they are unable to get time and transport to return to the health facility.

Chest x-ray was the commonly missing test in the public facilities and patients were often referred to the private facilities with the machine which came at a cost.

> *"It (Chest x-ray) is not so common because it has got a cost and it's not within our health facility and area, so one has to travel to Mukono town for x-ray. So then coming back with results is not common. It may be a handful of them who come back."* **29-year-old male KII_TB unit, Health centre IV**

Poor health worker attitude towards TB was also reported as a barrier when screening and handling patients with presumed TB in all FGDs and in a quarter of the IDIs. Some KIIs (20%) especially in hospitals reported that health workers handle these patients with a negative attitude in terms of the way they screen them, send them for sputum samples and respond to them when they ask questions or have made an error in any of the health facility processes. Relatedly, some patients mentioned being stigmatized by health workers who shout at them to wear masks when coughing and to extend far when talking to them. This attitude made the patients feel unwanted hence feared to return to the health worker when asked to submit the sputum sample.

> *"TB is so painful. The health worker was asking me questions and I could not answer the questions. She asked me if I did not have a mouth to speak. I had the mouth, but was unable to speak. I did not know what to tell the health worker."* **41-year-old female IDI participant, completed diagnosis**

Health workers also acknowledged the fact that the negative attitude of their fellow staff demotivates patients to complete the diagnostic process. Patients were mentioned to seek care when in pain and after trying many different options to get healed but in vain, including going to the traditional healers. This was mentioned as costly and frustrating for patients which requires handling them with care when they finally come to the health facilities.

"The health workers bad and negative attitude towards the patient scares them away. At times these patients come here when they no longer love themselves because of the pain. Actually, some sacrifice their stuff to witch doctors to get healed so they need to be handled well." **55-year-old male KII_TB Unit, Hospital**

Inadequate patient contact details: **s**ome of the key informants (15%) noted poor documentation of patient tracer information such as telephone contact and home address as a key barrier for receiving results and initiating treatment. Participants described this as either contacts not being collected at all or contacts available but incorrect. This tracer information was mentioned to aid health workers with patient follow-up especially when a patient's results are positive for TB and contact tracing as below;

"One of the reasons (for the loss of patients) is poor documentation. So, you presume someone and you don't write their phone numbers and not even their next of kin phone number. Those people you can hardly find them… You find that all you know about that person is where they live and the area is very big. Even people have the same names, so some people are lost in that way." **38-year-old male KII_ OPD, Health centre IV**

More details of this paper are presented in Paper 2 [Facilitators and barriers for completion of the diagnostic process among people with presumed tuberculosis in Central Uganda. *PLOS Glob Public Health. 2025 Sep 19;5(9):e0004808. doi: 10.1371/journal.pgph.0004808. PMID: 40971693; PMCID: PMC12449001.* **Nuwematsiko R,** Atuyambe L, Kasiita V, Kiwanuka N, Musiimenta A, Rutebemberwa E, Buregyeya E **(2025)] (Nuwematsiko, 2025).**

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RESEARCH ARTICLE

Facilitators and barriers for completion of the diagnostic process among people with presumed tuberculosis in Central Uganda

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Abstract

Uganda has improved its tuberculosis (TB) diagnostic processes over the years since the scale up of the Xpert MTB/RIF testing in 2012. However, there are continued delays in diagnosis and missing people with TB who are either not diagnosed or notified. We explored facilitators and barriers for completion of the TB diagnostic process among people with presumed TB in selected health facilities in Central Uganda. This was a qualitative exploration involving 25 in-depth interviews with people with presumed TB and six sex stratified focus group discussions with people with TB who had recently initiated treatment. We also conducted 20 key informant interviews with health workers providing TB services. All interviews and discussions were audio recorded and transcribed verbatim. Thematic analysis was carried out using Atlas.ti software version 6.0 guided by the constructs of the socio-ecological model. Key facilitators for completion of the TB diagnostic process included; individual factors (persistent symptoms and the desire to get better, obtaining same day results and

4.3 EVIDENCE ON THE USE OF MOBILE HEALTH INTERVENTIONS TO ENHANCE COMPLETION OF THE TUBERCULOSIS DIAGNOSTIC PROCESS AND TREATMENT INITIATION AMONG THOSE DIAGNOSED IN LMICs (SUB-STUDY 3)

The search yielded 1,296 records; 761 identified from electronic database searches and 535 from other sources. After deduplication, we screened 837 reports by title and abstract. Of these, 811 were not relevant hence we obtained full texts for 26 reports. After reading the full texts, we excluded 14 reports some of which were duplicates, had different outcomes, those whose main results were reported in another study and those which were conference abstracts and letters to editor. I identified 12 studies that met our inclusion criteria (Bassett et al., 2019, Chadha et al., 2017, Choun et al., 2017, Farley et al., 2019, Majella et al., 2021, Maraba et al., 2018a, Maraba et al., 2018b, Marx et al., 2022, Meehan et al., 2023, Mwansa-Kambafwile et al., 2022, Stalin et al., 2020, Wagstaff et al., 2019) see Figure 12.

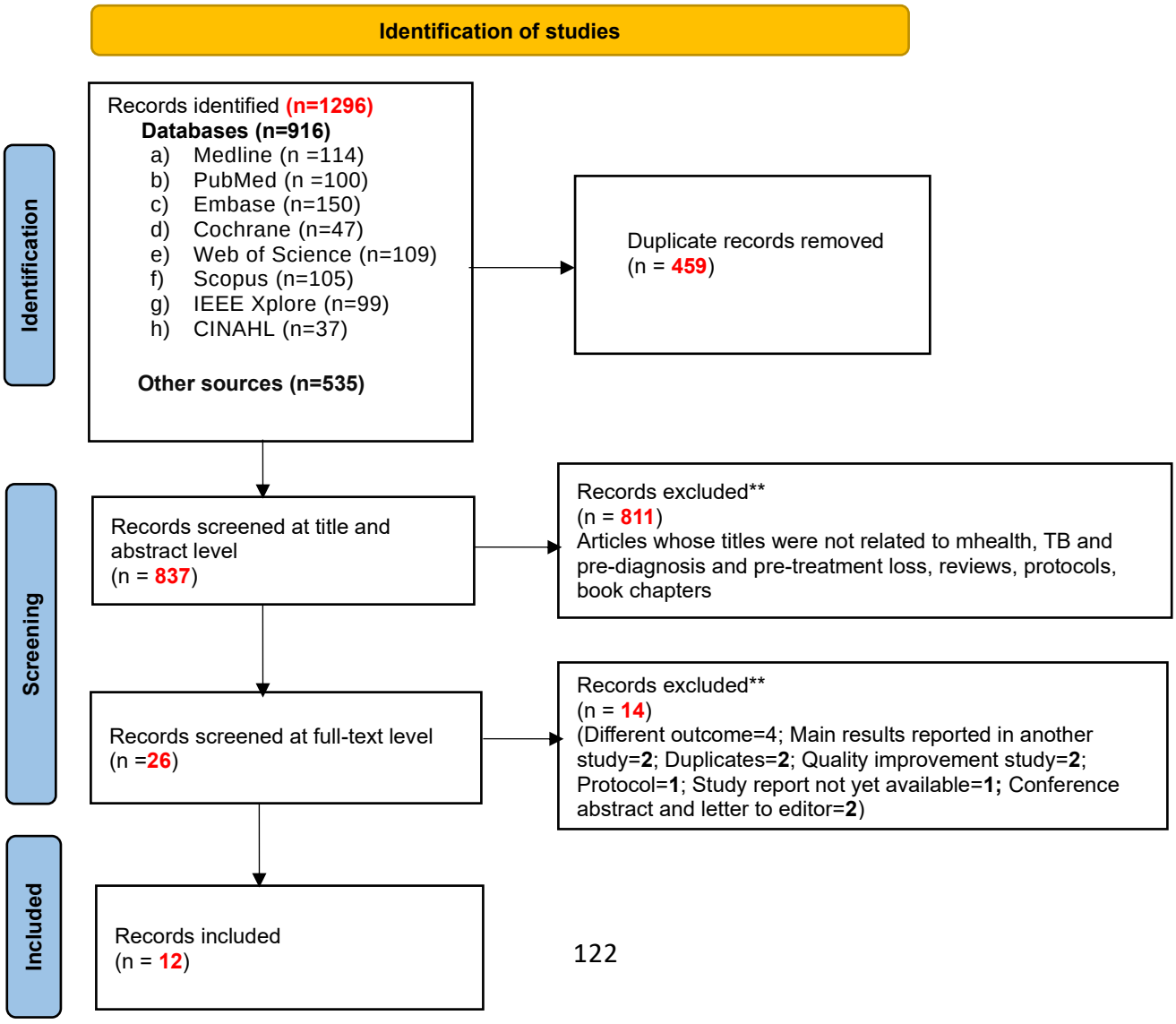


Figure 12: Flow diagram showing records selection and included studies

Study setting and context

The studies were published between 2017 and 2023 from South Africa (Meehan et al., 2023, Wagstaff et al., 2019, Maraba et al., 2018a, Maraba et al., 2018b, Mwansa-Kambafwile et al., 2022, Marx et al., 2022, Bassett et al., 2019, Farley et al., 2019), India (Chadha et al., 2017, Majella et al., 2021, Stalin et al., 2020), and Cambodia (Choun et al., 2017). All studies were conducted in public health facilities.

Study designs and context

Of the 12 studies included; four were RCTs (Wagstaff et al., 2019, Mwansa-Kambafwile et al., 2022, Majella et al., 2021, Bassett et al., 2019), and the rest, eight, quasi-experimental studies (Maraba et al., 2018a, Marx et al., 2022, Stalin et al., 2020, Choun et al., 2017, Farley et al., 2019, Maraba et al., 2018b, Chadha et al., 2017, Meehan et al., 2023) see *supplementary file 2.*

Description of study participants

The studies included people with presumed TB alone (Marx et al., 2022), diagnosed TB patients alone (Bassett et al., 2019, Chadha et al., 2017, Choun et al., 2017, Majella et al., 2021, Maraba et al., 2018a, Meehan et al., 2023, Mwansa-Kambafwile et al., 2022, Stalin et al., 2020) and both people with presumed TB and diagnosed patients (Farley et al., 2019, Maraba et al., 2018b, Wagstaff et al., 2019).

mHealth interventions used in the TB pre-diagnosis and pre-treatment phase

The mHealth interventions used to reduce pre-diagnosis and pre-treatment LTFU included SMS, phone calls, WhatsApp messages, and mobile applications (apps). Three studies used SMS alone (Wagstaff et al., 2019, Bassett et al., 2019, Mwansa-Kambafwile et al., 2022) and four studies used phone calls alone (Majella et al., 2021, Stalin et al., 2020, Maraba et al., 2018a, Choun et al., 2017). Three studies used a combination of custom designed mobile application and SMS (Farley et al., 2019, Chadha et

al., 2017, Maraba et al., 2018b), one with WhatsApp messages and phone call (Marx et al., 2022) and one a combination of phone call and SMS (Meehan et al., 2023). One study compared the mHealth intervention to a paper-based recording intervention (Majella et al., 2021) while the rest compared to the usual standard care or nothing (Supplementary file 2). The follow-up time for patients ranged from 7 days (Chadha et al., 2017) to 1 year (Farley et al., 2019).

Most studies, three quarters (9/12), aimed at using mHealth interventions to reduce pre-treatment loss to follow-up only (Bassett et al., 2019, Majella et al., 2021, Choun et al., 2017, Mwansa-Kambafwile et al., 2022, Maraba et al., 2018a, Meehan et al., 2023, Maraba et al., 2018b, Farley et al., 2019, Stalin et al., 2020) while two focused on pre-diagnosis loss to follow-up alone (Marx et al., 2022, Wagstaff et al., 2019) and one study by Chadha at al., focused the intervention on both pre-diagnosis and pre-treatment loss (Chadha et al., 2017).

Functions and implementation considerations of the mHealth interventions

Messages both SMS and WhatsApp were mainly used as reminders to collect results, appointments and to deliver test results (Wagstaff et al., 2019, Bassett et al., 2019, Mwansa-Kambafwile et al., 2022). SMS messages were sent to patients either via a bulk SMS service (Wagstaff et al., 2019) or automatically generated by the mobile app or system (Farley et al., 2019, Chadha et al., 2017). SMS were sent in evening hours (Wagstaff et al., 2019), majorly a day before the expected clinic visit (Wagstaff et al., 2019). All messages were sent in both English and the local language (Wagstaff et al., 2019, Mwansa-Kambafwile et al., 2022, Stalin et al., 2020).

Phone calls were used mainly for tracking patients to ensure they either got diagnosed or initiated treatment if positive (Majella et al., 2021, Stalin et al., 2020, Maraba et al., 2018a, Choun et al., 2017, Meehan et al., 2023, Marx et al., 2022). Phone calls were made by the study staff using standardised scripts (Majella et al., 2021). Due to phone challenges such as network and spoilage, studies made

several call attempts to the patient to deliver the intervention before labelling them lost. The frequency of call attempts and for how long varied across studies. For example, Majella et al., made six phone call attempts over three days with an interval of at least six hours (Majella et al., 2021). Patient telephone numbers were often verified with a missed call to ensure correctness of the number recorded (Stalin et al., 2020).

Most interventions with mobile Apps were used for referrals/linkages and for recording patient information (Farley et al., 2019, Chadha et al., 2017, Maraba et al., 2018b) primary targeted at health workers as the primary users. Patients were beneficiaries of either an SMS or phone call prompted by the mobile App (Farley et al., 2019, Chadha et al., 2017, Maraba et al., 2018b). Only one study which used WhatsApp messages targeted patients (Marx et al., 2022). Mobile Apps required users who possessed smart phones and these had to undergo training to use the Apps versus those who used SMS and phone calls.

For all interventions, the follow-up time for patients ranged from 7 days (Chadha et al., 2017) to 1 year (Farley et al., 2019).

Effect of mHealth interventions on relevant outcomes

SMS-based interventions

Among studies that used SMS alone, all in South Africa, there was mixed evidence of their effect on TB treatment initiation. Mwansa-Kambafwile et al., used SMS and Ward Based Outreach Teams (WBOTs) independently in comparison to the standard of care (SOC). Although more patients in the SMS group (92/105; 88%) initiated treatment than in the SOC group (81/104; 78%), this difference did not reach statistical significance ($P = 0.062$). However, the median time to treatment initiation was significantly shorter in the SMS group than in the SOC group ($P < 0.001$) (Mwansa-Kambafwile et al., 2022). Another study by Wagstaff and colleagues also saw a small effect of 62.0% vs 51.5% in the

control arm, p = 0.05 for treatment initiation within 2 days which effect later diminished as the follow-up interval increased (Wagstaff et al., 2019). Although Basset et al., reported a statistically significant finding of 50% (95% CI 36%, 88%) for those in the intervention arm linking to TB clinic within three weeks, this study had a high risk of bias mainly stemming from randomisation where and outcome measurement (Bassett et al., 2019).

Phone call-based interventions

Phone call interventions in the included studies showed statistical significance, with Majella et all reporting a significant absolute risk difference of 9% (95% CI [1.5, 16.6], P = 0.01) in the phone call arm compared to the control arm (Majella et al., 2021). In another study, following a phone call and home visit intervention in India to increase treatment initiation after referrals from medical colleges to peripheral health institutions, there was a significant increase in the proportion of feedback on TB patients initiating treatment which increased from 61% to 66% in the first and second quarters during implementation (P < 0.05) (Stalin et al., 2020). In another study by Maraba et al., there was no statistical significance between time to TB treatment initiation in the pre-implementation period [4 days (IQR 2–6)] compared to the implementation period [3 days (IQR 2–5); (p = 0.5)] (Maraba et al., 2018a). One study by Choun and colleagues (Choun et al., 2017) did not analyse for statistical significance of the intervention.

Mobile apps-based interventions

Mobile apps were mainly used for referrals/linkages and for recording patient information (Farley et al., 2019, Chadha et al., 2017, Maraba et al., 2018b). Most interventions with mobile phone apps were primary targeted at health workers as the primary users with patients as beneficiaries of either an SMS or phone call prompted by the mobile apps (Farley et al., 2019, Chadha et al., 2017, Maraba et al., 2018b). Only one study which used WhatsApp messages targeted patients (Marx et al., 2022). Mobile

apps required participants who possessed smart phones and these had to undergo training to use the apps versus those who used SMS and phone calls.

Combined mHealth interventions

There was mixed evidence on the effect of combined mHealth interventions. Meehan et al., used SMS and phone calls to improve treatment initiation, an intervention labelled "alert-and-response patient management" compared to a hospital-recording intervention in three sub-districts in South Africa (Meehan et al., 2023). Eighty three percent (5598/6773) of the diagnosed TB patients-initiated treatment within the 30 days. There was a significant reduction in pre-treatment LTFU in sub-districts where the alert-and-response patient management intervention was implemented compared with subdistricts where only the hospital-recording intervention was implemented. In one sub-district, it was 49.3% (95% CI, 32.4%–62.0%) vs 32.2% (95% CI, 5.4%–51.4%), and in another, 34.2% (95% CI, 20.9%–45.3%) vs 13.4% (95% CI, 0.7%–24.4%). However, there was no relative reduction in initial LTFU in the third sub-district.

Maraba and colleagues used a mobile application and SMS to reduce TB pre-treatment LTFU versus the usual paper-based system in health facilities in South Africa (Maraba et al., 2018b). Although the proportion of patients who initiated treatment within 28 days increased during intervention implementation (Mobile app and SMS at 28/33 (84.8%) versus paper register 30/44 (68.2%), this was not statistically significant (p = 0.08)]. In another study (Marx et al., 2022) using WhatsApp messaging and phone calls, there was no association between failure to respond to WhatsApp and pre-diagnosis LTFU of patients. Two studies did not evaluate the association between their intervention and the outcome (Chadha et al., 2017, Farley et al., 2019).

Risk of bias in included studies

The risk of bias judgements for all included studies is summarised in Figure 13 for the randomised controlled studies and Figure 14 for the non-randomised. For randomised studies, the sources of bias were i) the randomisation process where the allocation sequence was not concealed to the field staff (Bassett et al., 2019, Wagstaff et al., 2019) ii) measurement of the outcome where outcome assessors were not blinded (Majella et al., 2021, Bassett et al., 2019) iii) deviation from the intended intervention where in most studies it was not possible to blind the participants and field staff to the interventions because of the nature of the interventions (Majella et al., 2021, Bassett et al., 2019, Mwansa-Kambafwile et al., 2022, Wagstaff et al., 2019) and iv) reporting bias where in one of the studies, the focus shifted post intervention from the primary to the secondary outcome due to lower than anticipated case finding (Bassett et al., 2019) see Figure 13.

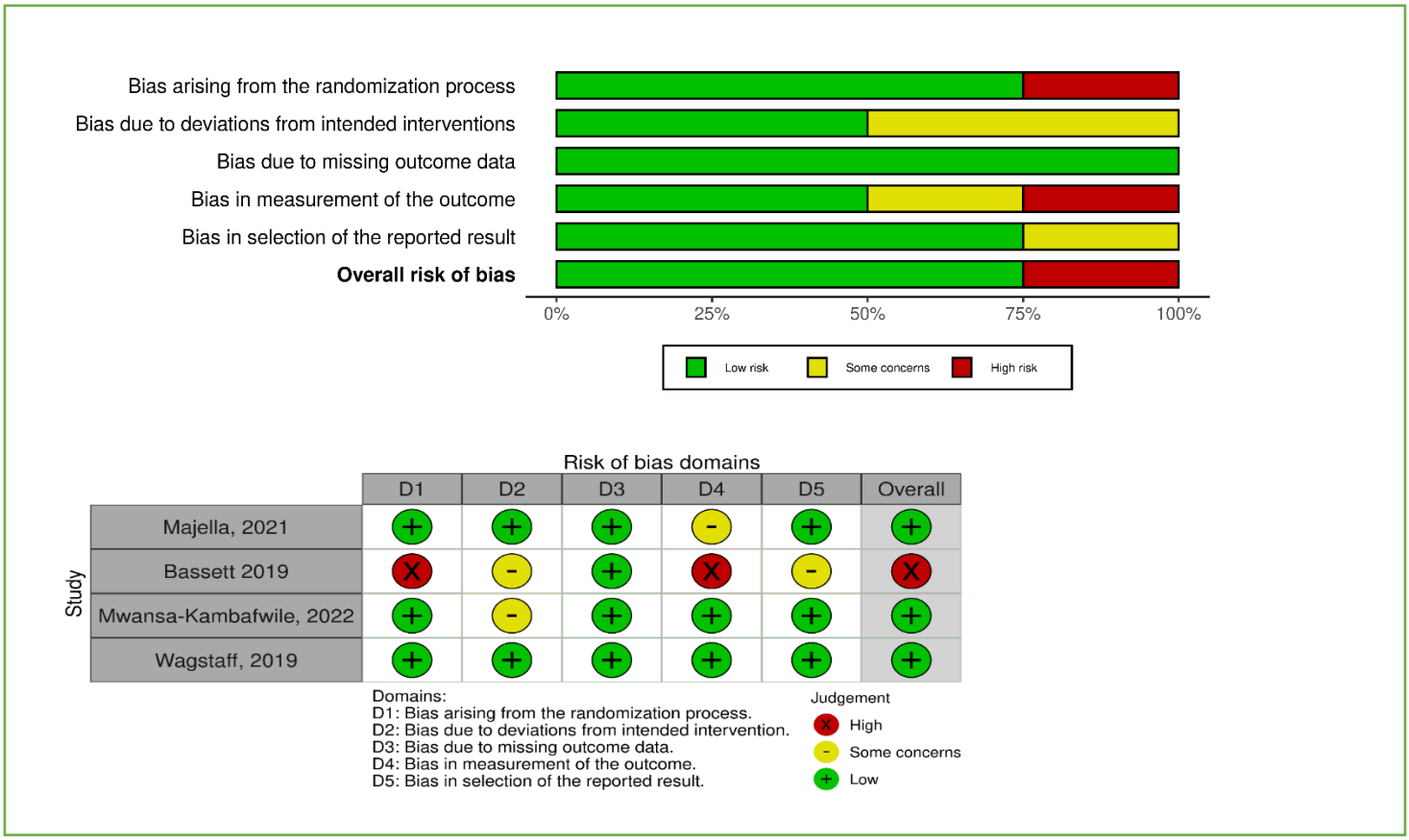


Figure 13: Risk of bias assessment among randomised controlled studies

Among the non-randomised studies, none of the studies had a low risk of bias with most (8) having moderate risk, 3 serious risk and 1 had a critical risk (Chadha et al., 2017). Most of the risk of bias arose from not controlling for potential confounders, lack of clarity on intervention classification and missing data (Figure 14).

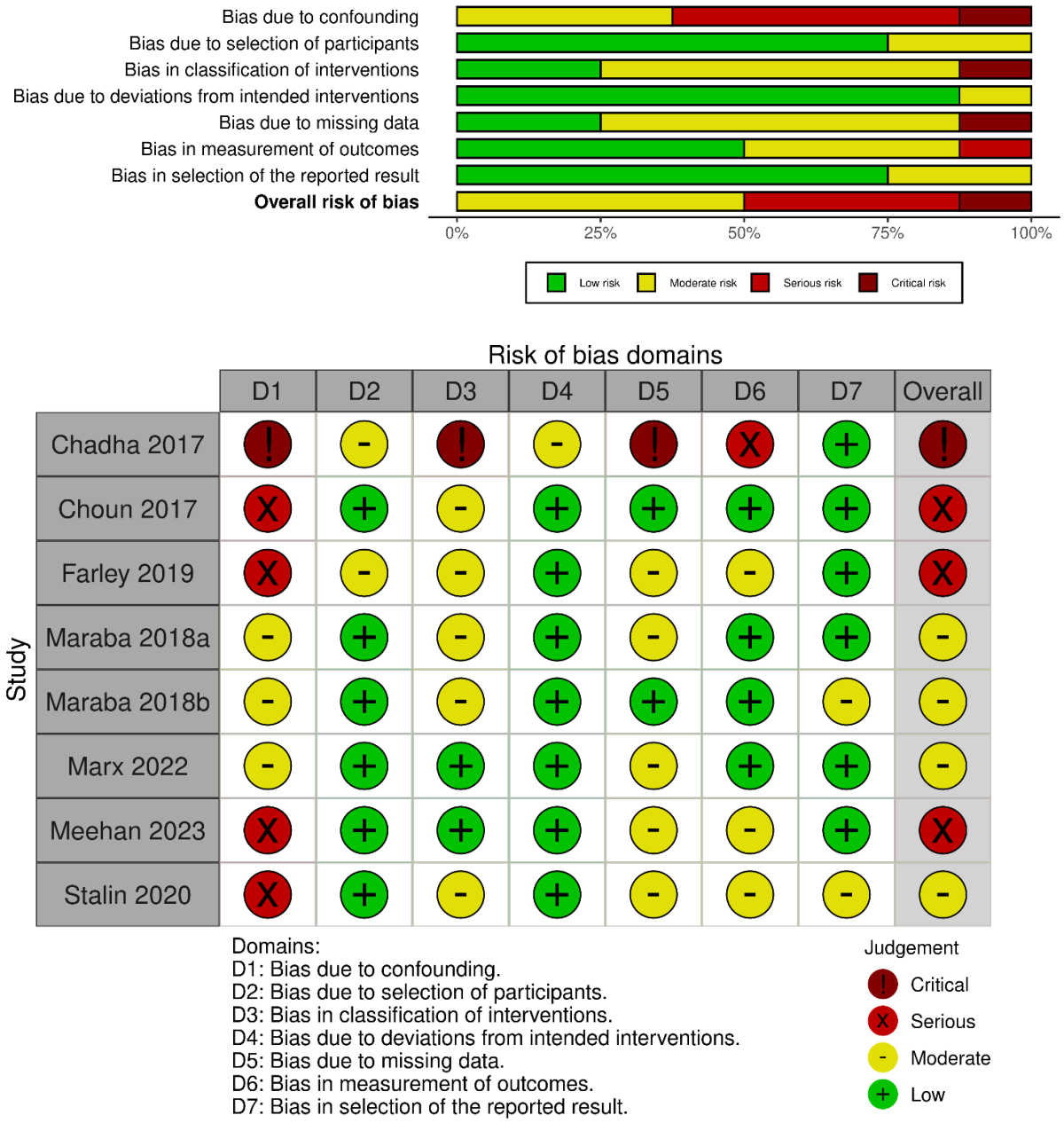


Figure 14: Risk of bias assessment among non-controlled studies

4.4 EFFECT AND FACTORS FOR USE OF AN SMS AND PHONE CALL INTERVENTION TO FOSTER COMPLETION OF THE TB DIAGNOSTIC PROCESS AMONG PEOPLE WITH PRESUMED TB IN CENTRAL UGANDA (SUB-STUDY 4)

Of 64,001 patients screened, 36.8% (2355/64001) were eligible, enrolled and randomized. Thirty two percent (1427/4565) of the participants had no mobile phone and 21.3% (668/3138) could not read and locate SMS hence were excluded. Only 3.9% (96/2470) declined to participate in the study and 0.8% (19/2374) were not willing to sign the informed consent form. A total of 99.1% (2334/2355) of the participants were followed up for 30 days.

For this study, we extracted and analysed participant records of only those who were randomized to the standard of care, SMS only and phone call only arms. Ninety nine percent (1773/1791) of the study participants were enrolled and randomized to; standard of care arm 27.1% (638), SMS reminders only 23.4% (551), and phone call only 24.8% (584). (Figure 15).

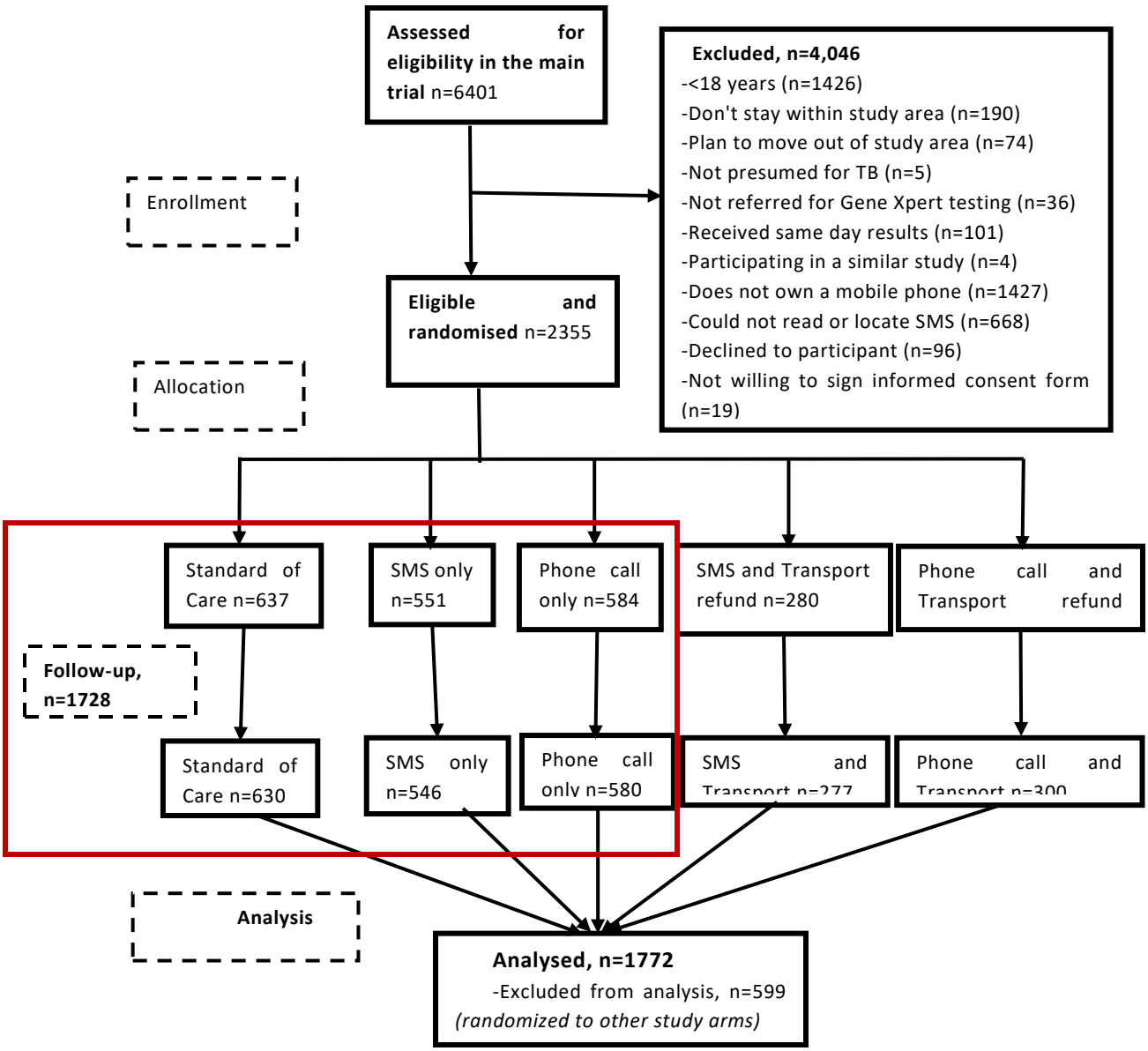


Figure 15: Flowchart of recruitment and randomisation of study participants

Characteristics of recruited participants

Most participants, 31% (549/1772) were aged between 31-44 years and the median age was 31, IQR: 24-42. Majority were females, 72.8% (1290/1771), had attained secondary education as the highest level, 48.1% (853) and were residing in an area less than or equal to 5kms from the study facilities 71.3% (1264/1772)- see Table 7.0. There were no statistically significant differences between participants randomized in the different study arms with regard to age, sex, level of education, religion, district of residence and monthly income. However, statistically significant differences were observed with regard to marital status (p=0.012) see Table 5.0.

Table 5.0: Baseline characteristics of study participants across the study arms in Central Uganda

Characteristic	Total N (%)	Standard of care	SMS reminders only	Phone call only	P-value
	(n=1772)	637 (35.9%)	551 (31.1%)	584 (33%)	
Age [median[(IQR)] years	31 (24-42)	31 (24-43)	31 (24-41)	31 (25-42)	0.178
Age group					
18 – 24	450 (25.4)	178 (27.9)	144 (26.1)	128 (21.9)	
25 – 30	402 (22.7)	135 (21.2)	119 (21.6)	148 (25.3)	
31 – 44	549 (31)	180 (28.2)	181 (32.9)	188 (32.2)	
45+	371 (20.9)	145 (22.6)	107 (19.4)	120 (20.6)	0.083
Sex					
Female	1290 (72.8)	471 (73.9)	396 (71.9)	423 (72.4)	
Male	482 (27.2)	166 (26.1)	155 (28.1)	161 (27.6)	0.705
Level of education					
None	26 (1.5)	12 (1.9)	5 (0.9)	9 (1.5)	
Primary	664 (37.5)	254 (39.9)	195 (35.4)	215 (36.8)	
Secondary	853 (48.1)	284 (44.6)	279 (50.6)	290 (49.7)	
Tertiary	229 (12.9)	87 (13.7)	72 (13.1)	70 (12)	0.323
Religion					
Catholic	599 (33.8)	206 (32.3)	180 (32.7)	213 (36.5)	
Anglican	381 (21.5)	132 (20.7)	128 (23.2)	121 (20.7)	
Muslim	313 (17.7)	116 (18.2)	101 (18.3)	96 (16.4)	
Pentecostal	360 (20.3)	134 (21.0)	106 (19.2)	120 (20.6)	
Other	119 (6.7)	49 (7.7)	36 (6.5)	34 (5.8)	0.667
Marital status					
Single	334 (18.9)	122 (19.2)	118 (21.4)	94 (16.1)	
Married/cohabiting	1127 (63.6)	383 (60.1)	348 (63.2)	394 (67.5)	
Widowed/divorced/separated	311 (17.6)	132 (20.7)	85 (15.4)	96 (16.4)	**0.012**
Distance (km) to health facility [median (IQR)]	3.0 (2.0-6.0)	3.2 (2.0-6.0)	4.0 (2.0-6.4)	4.0 (2.0-7.0)	0.744
Grouped Distance (km) to health facility					
<=5 km	1264 (71.3)	464 (72.8)	393 (71.3)	407 (69.7)	
>5 km	508 (28.7)	173 (27.2)	158 (28.7)	177 (30.3)	0.478

Continued Table 5.0: Baseline characteristics of study participants across the study arms in Central Uganda

Characteristic	Total N (%)	Standard of care	SMS reminders only	Phone call only	P-value
	(n=1772)	637 (35.9%)	551 (31.1%)	584 (33%)	
District					
Mukono	342 (19.3)	119 (18.7)	105 (19.1)	118 (20.2)	
Luwero	320 (18.1)	109 (17.1)	102 (18.5)	109 (18.7)	
Buikwe	71 (4.0)	33 (5.2)	22 (4.0)	16 (2.7)	
Wakiso	760 (42.9)	276 (43.3)	239 (43.4)	245 (42.0)	
Kampala	279 (15.7)	101 (15.8)	83 (15.1)	96 (16.4)	0.654
Health facility					
Mukono General Hospital	342 (19.3)	119 (34.8)	105 (30.7)	118 (34.5)	
Wakiso H/C IV	429 (24.2)	157 (36.6)	135 (31.5)	137 (31.9)	
Kawolo General Hospital	71 (4.0)	33 (46.5)	22 (30.9)	16 (22.5)	
Luwero General Hospital	320 (18.1)	109 (34.1)	102 (31.9)	109 (34.1)	
Entebbe Regional Referral Hospital	331 (18.7)	119 (35.9)	104 (31.4)	108 (32.6)	
Kiruddu National Referral Hospital	279 (15.7)	100 (35.8)	83 (29.8)	96 (34.4)	0.816
Average income per month (USD)					
Median (USD) (IQR)	53.3 (21.3-79.9)	53.3 (15.9-79.9)	53.3 (26.7-79.9)	53.3 (26.7-79.9)	0.349
<=15.9	407 (23)	161 (25.3)	117 (21.2)	129 (22.1)	
16-39.9	407 (23)	135 (21.2)	125 (22.7)	147 (25.2)	
40-79.9	549 (30.9)	188 (29.5)	181 (32.9)	180 (30.8)	
>=79.9	409 (23.1)	153 (24)	128 (23.2)	128 (21.9)	
HIV status (self-reported)					0.403
Positive	331 (18.7)	122 (19.2)	95 (17,2)	114 (19.5)	
Negative	1398 (78.9)	500 (78.5)	439 (79.7)	459 (78.6)	
Never tested	43 (2.4)	15 (2.4)	17 (3.1)	11 (1.9)	0.613

EFFECT OF THE SMS AND PHONE CALL INTERVENTION ON ENHANCING COMPLETION OF THE TB DIAGNOSTIC PROCESS AMONG PEOPLE WITH PRESUMED TB IN CENTRAL UGANDA

A total of 99.1% (1756/1772) of the participants were followed up for 30 days of whom, 98.4% (1728/1756) submitted a sputum sample for testing. Overall, a total of sixty eight percent of the

participants completed the TB diagnostic process within 30 days, 67.7% (1199/1772). Over all, completion of the TB diagnostic process was highest among participants randomized to the Phone call only arm, 74.3% (434/584) compared to those in other study arms (Table 6.0). In terms of socio-demographic characteristics, completion of the TB diagnostic process was highest among participants aged 45 years and above, males, those who have never tested for HIV and those who stay within 5kms from the health facility (Table 6.0). Completion of the TB diagnostic process also varied by health facility, highest at the national referral hospital (Kiruddu) and lowest in a health centre IV (Wakiso). A half of the participants completed the diagnostic process within the 3 days (IQR: 2-10) from the date of being presumed for TB. There was no difference in time to completing TB diagnosis between participants in the SMS and standard of care arms (Table 6.0).

Table 6.0: Effect of intervention on completion of the TB diagnostic process

Outcomes	% (n/N)
Primary outcome	
Completed the TB diagnostic process	
Overall	**67.7 (1199/1772)**
Study arm of completing the diagnostic process	
Standard of care	64.8 (413/637)
SMS only	63.9 (352/551)
Phone call only	74.3 (434/584)
Age group	
18 – 24	59.3 (267/450)
25 – 30	63.4 (255/402)
31 – 44	68.5 (376/549)
45+	81.1 (301/371)
Sex	
Female	63.5 (819/1290)
Male	78.8 (380/482)
HIV status (self-reported)	
Positive	68.3 (226/331)
Negative	67.2 (940/1398)
Never tested	76.7 (33/43)
Marital status	
Single	72.5 (242/334)
Married/cohabiting	64.2 (723/1127)
Widowed/divorced/separated	75.2 (234/311)
Grouped Distance (km) to health facility	
<=5 km	69.2 (875/1264)
>5 km	63.8 (324/508)
Health facility	
Mukono General Hospital	71.1 (243/342)
Wakiso H/C IV	62.2 (267/429)
Kawolo General Hospital	69.0 (49/71)
Luwero General Hospital	63.4 (203/320)
Entebbe Regional Referral Hospital	68.3 (226/331)
Kiruddu National Referral Hospital	75.6 (211/279)
Time to diagnosis	**Median (IQR)**
Overall	3 (2-10)
Study arm	
Standard of care	4 (2 - 10)
SMS only	4 (2 - 10)
Phone call only	3 (2 - 7)

Determinants of completion of the TB diagnostic process among participants

At multivariable analysis after controlling for marital status; participants in the phone call only arm (adj RR 1.16, 95% CI: 1.08,1.25) were more likely to complete the TB diagnostic process compared to those in the standard of care arm. There was no effect with SMS only arm, (adj RR 0.99, 95% CI: 0.91,1.08) see Table 8. Similarly, participants randomized to the Phone call arm only (adj RR 1.2, 95% CI: 1.21,1.59) were more likely to have early completion of the TB diagnostic process compared to those in the standard of care arm (Table 7.0). In the per protocol analysis, there was still no significant association between participant's completing the diagnostic process in the SMS arm (adj RR 1.01, 95% CI: 0.93,1.09) compared to the standard of care (Table 7.0).

Table 7.0: Crude and adjusted effect of SMS and Phone call reminders on completion of the TB diagnostic process

Outcomes	**% Completion of TB diagnosis**	**Unadjusted**		**Adjusted*(Intention to treat)**		**Adjusted* (Per protocol analysis**		
	% (n/N)	Relative Ratios	p-value	Relative Ratios	p-value	Relative Ratios		p-value
Primary outcome ***Completed TB diagnosis***						*Primary outcome* ***Completed TB diagnosis***		
Study arm								
Standard of care	64.8 (413/637)	Ref		Ref		Ref		
SMS only	63.9 (352/551)	0.99 (0.91,1.07)	0.733	0.99 (0.91,1.08)	0.800	1.01 1.09)	(0.93,	0.825
Phone call only	74.3 (434/584)	1.15 (1.06,1.23)	<0.001	**1.16 (1.08,1.25)**	**<0.001***	**1.10 1.18)**	**(1.03,**	**0.007***
Time to diagnosis	**Median (IQR)**	**Unadjusted**		**Adjusted***				
		Hazard ratios	p-value	Hazard ratios	p-value			
Study arm								
Standard of care	4 (2 - 10)	Ref		Ref				
SMS only	4 (2 - 10)	1.02 (0.88-1.17)	0.827	1.02 (0.85,1.13)	0.835			
Phone call only	3 (2 - 7)	1.16 (1.02-1.34)	0.028	1.16 (1.21,1.59)	0.029			

**Adjusted for age, marital status*

FACTORS THAT INFLUENCE USE OF THE SMS OR PHONE CALL REMINDERS INTERVENTION

Most participants in the qualitative interviews were females, 66.7% (14/21), and most aged between 31 and 40 years of age (12/21). Out of the 21 participants interviewed, 13 received SMS reminders while eight received phone calls. Sixteen of the participants had completed the diagnostic process while five had not. Of those who had completed the diagnostic process, nine were in the SMS arm while seven were in the phone call arm. Among those who were LTFU, four were in the SMS arm while one was in the phone call arm.

Findings on the influencing factors for the SMS and Phone call interventions were organised around the tenants of the social-ecological model (Figure 16). Findings were similar for both participants in the SMS and phone call arms hence they were combined. Three themes emerged as factors that influenced use of SMS and phone call interventions to enhance completion of the TB diagnostic process: i) facilitators, ii) barriers, and iii) user experiences.

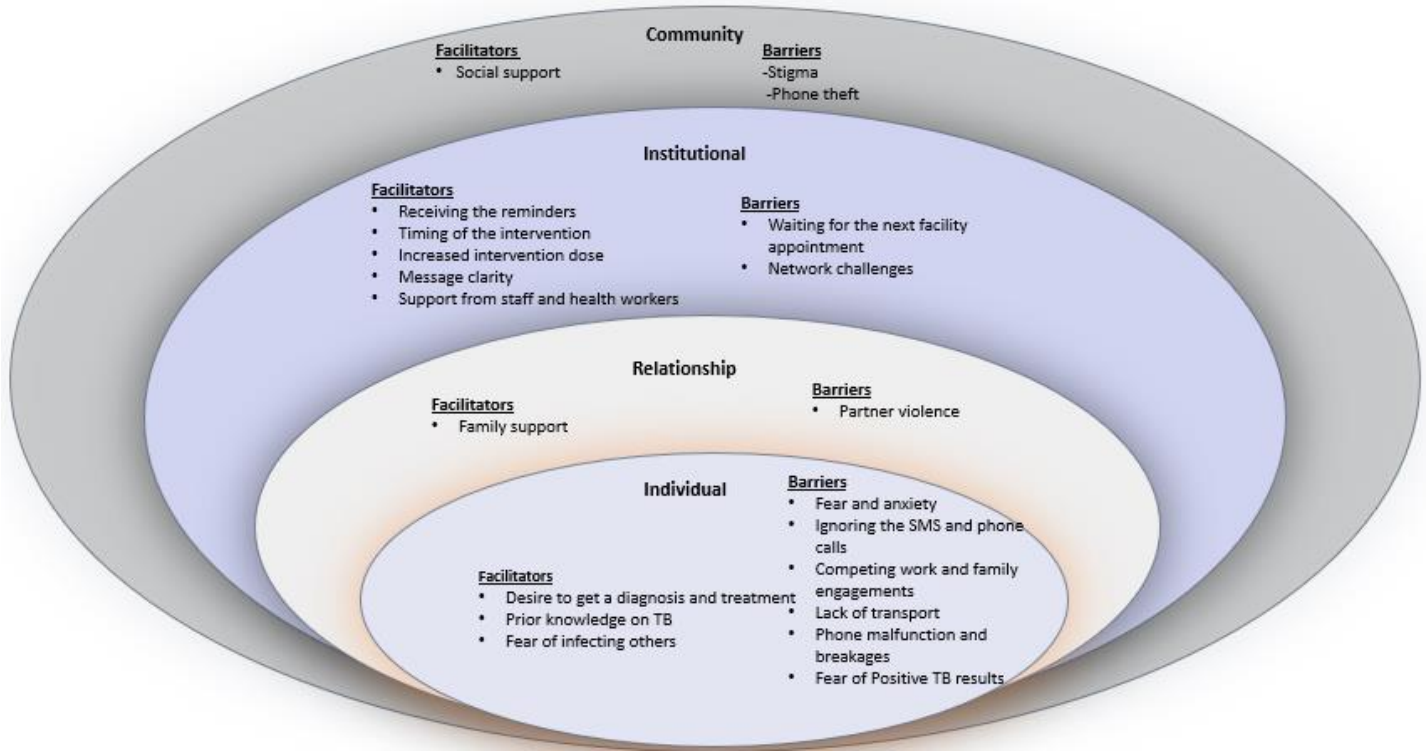


Figure 16: Factors that influence use of the SMS or phone call reminders intervention

A. FACILITATORS

Desire to get a diagnosis and treatment

Three quarters of the participants mentioned that they participated in the study and later on tested and collected results because they wanted to know what they were suffering from and get treatment. They described this desire to get a diagnosis after days of being ill without getting better.

> *"All I wanted was to know what was disturbing me, whatever they [health worker] told me was the disease I could tell him that let us treat it... My aim was to get well, so when he told me it could be TB, I didn't think about anything else. All I wanted was to go in the hospital get tested and I confirm whether it is TB then I start treatment."* ***(Female, completed diagnosis_SMS _Mukono)***

This desire was mentioned to be further amplified with the fear to infect others especially family members if they were indeed suffering from TB hence needed to test and get treatment. One participant narrated how this fear of infecting others encouraged him to test.

> *"…it meant that if I have TB I can infect my people at home so this motivated me to come and test because I wanted to prevent my people from getting TB. And once they get it, it will be my responsibility to treat them. So i said let me test and see if I have TB or not and if I have, I will make sure I protect them from acquiring it."* ***(Male, completed diagnosis_Phone call_Wakiso)***

Prior knowledge on TB

Out of the 21 participants, seven mentioned testing for TB and joining the study because they knew about TB either through health talks or had nursed TB patients or had heard about patients with TB. They mentioned understanding it as a deadly disease if not treated hence wanted to test and know their status.

> *"Like I told you before, because I cared for my son who had TB and I had the family, it meant that if I have TB I can infect my people at home so this motivated me to come and test because I wanted to prevent my people from getting TB"* ***(Female, completed diagnosis_Phone call_Mukono)***

Social support from family, friends and acquittances

Sixteen of the twenty-one participants, acknowledged the key role played by their family members, friends and acquaintances in encouraging them to proceed to test and collect their TB results. This support was mentioned throughout the who process from being encouraged to test to returning and collecting results. The support received was said to make them strong through the process as explained below:

"I met a lady she had also come for antenatal. That lady told me, what we need is life, let's go and test, that lady encouraged me to test, but me I was scared… Maybe I would also be among those who don't come back if I had not listened to the advice of the other woman that we should mind about our lives. That alone made me strong." ***(Female, Completed_SMS_Mukono)***

Support from the implementing (study) staff

All participants mentioned that the study staff were an important aspect of recruiting and retaining them in the study, ensuring that they returned to pick their results. They stated that the interactions they had with the staff were generally positive, respectful, encouraging and improved the clarity of their participation in the study as below:

"When I reached here, the way the health workers handle patients, it forced me to participate. They were polite, they explain something and you understand very well, and they handle you with dignity whether you have TB or not." ***(Female, completed diagnosis_Phone call_Mukono)***

Receiving the reminders

Receiving the intervention whether it was the SMS or Phone call reminders was mentioned by almost all participants as having influenced them to return and complete the TB diagnostic process as narrated below;

"When the results came back, she sent me a message which motivated me a lot. Because I was busy at work but I was forced to spare time like an hour and came back for my results." ***(Female, completed diagnosis_SMS _Mukono)***

Timing of the reminders

Two thirds of participants who received SMS mentioned receiving them in the evening hours after they had returned from work hence were more relaxed to read the messages and prepare to return to the health facilities in the morning. They mentioned if the messages had come during the day, they would have missed them.

> *"The time I received all the messages was good, especially the last message I received it at the right time because I was resting and i saw the message coming. I had the time to read the messages, i had nothing that was harrying me. It came in the evening. But if it came during working hours, it would be hard to read and at times you could forget reading it."* ***(Male Completed diagnosis_SMS_Wakiso)***

Similarly, some (5) of the participants in the phone call arm mentioned received the phone calls in the evening which favoured them since they were off at work and able to pick the calls but also it gave them time to plan to go back to the health facility the next day to complete the diagnostic process.

Increased dose of the reminders

Some participants, four out of thirteen participants in the SMS arm mentioned returning to the health facilities after receiving more than one message. They interpreted this as a sign of need for urgency to return to the health facilities when follow-on SMS reminders kept coming in addition to the 1st message.

> *"I received two messages. I didn't come at the first message but when I received the second message I came."* ***(Male Completed diagnosis_SMS_Kampala)***

B. BARRIERS

Fear of positive TB results, the associated treatment and stigma

Two out of the five participants, who did not return to complete the diagnostic test mentioned that they feared they could be having TB and yet they fear the medication which they had heard takes a long time and the drugs are big in size. Others also mentioned they feared they could be having HIV because they know that whoever has TB will likely get HIV and the stigma they might get from family and community members who might think that they also have HIV. So, they preferred not to return to the health facility to complete diagnostic process but rather leave with the unknown. The fear of positive TB results was commonly mentioned by male participants.

> *"I feared that I could be having TB yet I know that whoever has TB, has higher chances of having HIV. So, I was scared that I could also be having HIV."* ***(Male, LTFU_Phone call_Entebbe)***

Lack of transport to return to the health facility

Failure to get transport to return to the health facility to either submit a sputum sample or collect results hindered completion of the TB diagnostic process. This was commonly mentioned by females as narrated by a participant who received an SMS to return to the health facility after they had travelled in another district far away and could not afford transport to return: *"When the doctor sent me SMS I did not come, I was still in Nakasongola…I did not tell her I don't have transport money…I didn't come till today."* ***(Female, LTFU_SMS _Luwero)***

Competing work and family engagements

Competing obligations such as work and taking care of a sick person were frequently reported by female participants who failed to return and complete the diagnostic process. This was either because they could not get time off or they could only get time off when the health facility TB unit is non-

functional for outpatient clients. One participant explained her dilemma that made her not to return and finish diagnosis;

> *"My job, reason being i could go to work very early in the morning and I could come back late in the night very tired…so i could not come (to complete diagnosis) at night after work."* ***(Female, LTFU_Phone call_ Entebbe)***

Waiting for the next hospital appointment

Waiting for the next hospital appointment especially by those on antenatal care was a commonly reported reason for delay to pick results among females. Most mentioned that it a resource saving mechanism for both time and money. They preferred to return when coming to the health facility for another visit and use the same opportunity to collect their results. Other, especially the pregnant mothers mentioned being lazy and physically unable to make many hospital visits hence preferred to combine the antenatal appointment with collecting their TB results on one day.

> *"They called me but where I was staying, I could not come that very day, I had to wait for the appointment date for antenatal so that I save on transport."* ***(Female, LTFU_Phone call _Mukono)***

Ignoring the SMS and phone call reminders

Two out the five participants who did not return to complete diagnosis said it was because they ignored the SMS or phone reminders. For the SMS, they thought they were adverts from the telecom companies and for phone calls, they mentioned they ignored them since they did not know who the caller was as they were not saved in their phone book. As a result, they did not receive the reminders to return to the health facility. This was further mentioned by the study staff who obtained the same information

from participants who did not return to the health facilities claiming they thought they were messages from telecom companies hence they either ignored them or immediately deleted the messages.

Limited support from significant others

On the other hand, a few participants, a third, mentioned lack of support from family members and friends as having been the reason why they did not return to the health facilities to complete the diagnosis process despite receiving the reminders. This was commonly mentioned by female participants as narrated below;

> *"I told my husband that I am going to the hospital and he asked me that do you have money? Will they give you some transport? I told him I don't know because they had told me to go back on Friday…He told me if they are not giving you transport, leave it, don't go."* ***(Female, LTFU_SMS_Entebbe)***

Fear of TB and HIV stigma

Some participants mentioned the fear of stigma from family, friends and community as having contributed to their being lost before completing the diagnostic process. The fear was mainly on being mistaken to have HIV because of the myth that whoever has TB also has HIV and being discriminated. These fears were further amplified when said by friends and family members as below;

> *"The people I was living with kept demoralizing me that if my results come out positive, people will discriminate and isolate me. So, i feared when i had such things and did not come back."* ***(Female, LTFU_Phone call _Entebbe)***

Network challenges

One third of the participants mentioned experiencing network challenges where either the SMS did not come through or the they could not communicate clearly with the study team. This was further confirmed by the study staff who would try to make phone calls to the participants to return to the health facilities and they could not go through and would indicate network failure. They mentioned that sometimes the phones would go through but they could not interact with the participant due to the poor network. Network challenges were common among participants from rural areas that are far away from town centres.

> *"Some of them their numbers weren't reachable. Once they cross to their home villages, networks used to disturb us."* ***(Female study staff_Luwero)***

Phone theft, malfunction and breakages

Phones being stollen, malfunctioning or getting broken was reported by few participants which either deterred or delayed them from receiving the SMS or phone call reminders. For some, the phones were stolen before receiving any reminder and for others, after receiving some reminders. This was also attested to by the study staff who mentioned failure to make phone calls to participants who they had just recruited and tested the phone numbers if they are functional and on the mobile network. One participant narrated below how their phone had been stolen after being recruited.

> *"I had just left the hospital and my phone got lost, I got another one. I didn't know about the messages, I didn't see the messages."* ***(Male, LTFU_SMS_Luwero)***

Lack of clarity in the intervention or misunderstanding of the message received led to some missing out on coming back on time for their results. They had expectations of more information on which day to return to the health facilities and the time as below;

"They first sent me a massage but I think I didn't understand well. They used to send me messages that you must return to the hospital but I was waiting for them to tell me the date and that is where I failed to understand and I didn't reply to the messages." ***(Male Completed diagnosis_SMS_Wakiso)***

C. USER EXPERIENCES OF PARTICIPATION IN THE STUDY

SMS and phone call reminders perceived as useful

Eighteen out of twenty-one participants acknowledged the usefulness of SMS and phone call reminders for them to return to the health facility and complete the diagnostic process. They mentioned that chances of forgetting are high given the busy day to day schedules but the reminders sent to them were helpful in reminding them to return and collect results.

"I liked it because they were reminding me to come and pick my results because if someone doesn't send a message or call you, you may forget especially when you are not badly off or in a lot of pain or bedridden." ***(Male Completed diagnosis_phone call_Kampala)***

Less effort required to participate in the study

All participants mentioned requiring less effort to participate in the study. They mentioned that they had been sending SMS and receiving phone calls hence they did not need to do something extra. They only mentioned the need to keep their telephones near then so as not to miss the phone call or SMS and regularly checking their phones for any SMS or missed call.

"It only required me to keep my phone near me all the time so that I could get the messages she promised to send". ***(Female Completed diagnosis_SMS_Wakiso)***

Gratitude for being tested for TB

Most participants, three quarters, appreciated the opportunity to be tested for TB during the study, a process some thought was paid for in government health facilities while other mentioned they had never thought about testing despite having the cardinal symptoms. They viewed this as a rare opportunity to know their status and mentioned feeling good after testing. They acknowledged the fact that testing was for their benefit

> *"For me, I felt good because people fail to get opportunity to test for TB. So, for me I felt good when I got this opportunity to test for TB because it was of my benefit.* ***(Male Completed diagnosis_SMS_Mukono)***

Good care and communication from the study staff

All participants mentioned receiving good care from the study staff which was described as the way the staff talked to them, the counselling and services offered and later on giving them reminders to collect results. Participants interpreted this as being caring and thoughtful despite their profession and busy schedules which then motivated them to respond positively. Both males and females reported receiving the good care.

> *"The phone call I received motivated me because it showed me that the health worker that worked on me that day was caring. Because someone to take time and call you, he is so caring...This forced me to come back because I said if someone spared his time and called, it motivated me to come back."* ***(Male, Completed diagnosis_Phone call_Kampala)***

Informed significant others of their participation in the study

Out of the 21 participants, seventeen mentioned informing their significant others of their participation in the study and the anticipated intervention. These were mainly the people they live with, commonly

spouses and parents. Some mentioned that they informed them for support purposes while others feared they would know it if they did not tell them which would cause problems as below;

> *"I told my sister that they tested me for TB and they said they will send me a message. She was happy about it though I am not sure if she was genuinely happy...I had to tell her because there was no way I could leave work without letting her know where I was going because we work together."* ***(Female, Completed diagnosis_SMS_Kampala)***

Social support from family and friends

Most participants mentioned they received support when they informed their family members and friends that they had either been called or received an SMS to return to the health facility and complete diagnosis. The support given to the participants was in terms of either transport or time off to return to the health facility. Those who had informed their significant others of their participation in the study mentioned finding it easy to receive support from them when they received the reminders.

> *"My father has a motorcycle, I told him I have been called to pick my results, I explained to him and he gave me the motorcycle to come back (to the health facility)."* ***(Male, Completed diagnosis_Phone call_Luwero)***

Fear and anxiety

Two thirds of the participants in the phone call arm mentioned that they waited with anxiety for the phone call, with most insinuating that the call would mean they are positive for TB. However, this fear and anxiety did not keep participants away from returning to the health facility to compelte the diagnostic process.

"…I had feared the phone call I was going to receive… I got scared and said the moment I get a call from these people I will just know I have TB." ***(Female, Completed diagnosis_phone call_Entebbe)***

Even participants that were randomised to the SMS arm had earlier fears of receiving a phone call about their TB test results as narrated by a female participant who received an SMS in Kampala:

"…What amused me most was the message. I had feared the phone call I was going to receive. When I heard that they were going to send me a message and they sent me a sample of it, i was like even if I receive the message now, it will not scare me so much like a phone call" ***(Female, Completed diagnosis_SMS_Kampala)***

Partner violence

Only two women participants mentioned experiencing violence from their partners after they had received the phone call to return to the health facility and complete the TB diagnostic process. Both participants were in the phone call arms. Most of the violence was verbal and emotional.

"She called me and told me to come for the first time; I told her I am coming from the village so I will come. But the following day, I went to work and the man stopped giving me the phone." ***(Female, LTFU_Phone call_Entebbe)***

CHAPTER FIVE: GENERAL DISCUSSION

5.1 INTRODUCTION

The overall goal of this thesis was to assess the effect and implementation factors of mHealth interventions to reduce pre-diagnosis LTFU among people with presumed TB in Central Uganda. The study was implemented under four sub-studies. From the cohort analysis in sub-study 1, 28.3% (3,699/13.064) of the patients attending the selected health facilities in Central Uganda experienced pre-diagnosis LTFU and 13.7% (163/1187) of them did not initiate treatment within 14 days from the day they were diagnosed. Pre-diagnosis LTFU was more likely to occur among patients aged 0-14 years, females and those with no record of place of residence and phone contact.

In sub-study 2, key facilitators for completion of the TB diagnostic process included; obtaining same day results, prior TB knowledge, social support, caring health workers and calling of patients to collect results. Barriers were; TB and HIV stigma, lack of transport to return to the health facility, long turnaround time of results and unclear appointment for collection of results. From the systematic review in sub-study 3, phone calls and SMS were the commonly used mHealth interventions in the TB presumtpion phase mainly used as reminders to collect or deliver TB results. The evaluation of the SMS or phone call intervention revealed that completion of the TB diagnostic process was highest among participants randomised to the phone call arm compared to those in the standard of care 74.3% (434/584). There was no significant effect for those in the SMS arm. Individual factors, social influences, technological factors, intervention design factors, health system factors and participant experiences influenced implementation and use of the SMS or phone call intervention (sub-study 4).

This chapter provides a general discussion of all the results from these sub-studies in sync. The philosophical and theoretical underpinnings of this study are also discussed along with the methodological considerations. Study strengths and limitations are also highlighted in this chapter. This research was embedded in an ongoing study, MILEAGE4TB, which sought to use SMS

reminders, Phone call reminders and mobile money incentives to improve linkage to TB care in Central Uganda. This PhD generated data to explain the concept of pre-diagnosis LTFU, influencing factors and potential use of mHealth interventions. This information was used by the main study to inform contextual adaptation of the proposed intervention and evaluate its effect using a randomized controlled trial (RCT) (Nuwematsiko et al., 2025). In this section, I discuss findings that are relevant for my PhD research which sought to enhance completion of the TB diagnostic process using SMS and phone call reminders. Findings from the main study regarding contextual adaptation of the interventions and the effect of all intervention components are yet to be published in peer reviewed journals by the study team.

5.2 DISCUSSION OF MAIN FINDINGS

Sub-study one

This study assessed pre-diagnosis and pre-treatment LTFU and associated factors among patients with presumed TB and those diagnosed in selected health facilities in central Uganda. Twenty-eight percent of the participants experienced pre-diagnosis LTFU and thirteen percent of those who tested positive for TB did not initiate treatment within 14 days from the date of diagnosis. Over half of those who conducted the TB investigations required, did not have their results on the same day of being presumed, 52.8% (4983/9439). Pre-diagnosis LTFU was highest in 2019 and 2020 which decreased sharply in 2021 and 2022. Patients with no record of place of residence and no record of phone contact were more likely to experience pre-diagnosis and pre-treatment LTFU.

The high pre-diagnosis LTFU was attributed to no record of patient tracking information of place of residence and phone contact. Previous studies showed that patients withhold giving out their details or sometimes register wrong details because of mistrust and fear of stigma and being tracked by health

workers in their places of residence or work which could further stigmatise them in the community (Nong et al., 2022, Ajayi et al., 2023). Our study also revealed that half of the participants do not have results on the same day of being presumed for TB which requires repeat visits to the health facilities hence contributing to the LTFU as seen from previous studies (Zawedde-Muyanja et al., 2022, Sendagire et al., 2010). Similar pre-diagnosis LTFU proportions have been reported in studies in Zimbabwe (10%-25%), Tanzania (16%), India (30%) and in a study of 30 countries with a high-TB burden (35%) (Kim et al., 2019, Murongazvombo et al., 2019, Mando et al., 2023, Mgina et al., 2022, Pala et al., 2018, Padingani et al., 2018). However, a previous study in Uganda reported a higher proportion of LTFU of 40.7% (Ekuka et al., 2020). This could be because of the differences in the study setting, as the study by Ekuka et al. was conducted in a rural area where patients face more challenges in healthcare access. Indeed, studies have indicated that patients with presumed TB from rural health facilities tend to be LTFU (Murongazvombo et al., 2019, Padingani et al., 2018, Tedla et al., 2020). More so, Ekuka et al., study was conducted at a Health centre IV, which often face diagnostic challenges such as stock out of laboratory supplies, staff shortages in laboratories, high patient volumes and referral setbacks with patients self-referring to higher-level hospitals thus contributing to a higher LTFU (Muzeyi et al., 2025).

Pre-diagnosis LTFU threatens TB control by increasing the risk of community spread of the disease hence the need for health system strengthening solutions to ensure that every patient presumed to have TB is diagnosed. Considerations should be made to strengthen laboratory services in each health facility to provide same day results for patients so as to reduce chances of LTFU. Moreso, health workers should improve documentation of patient contacts and area of residences to ease patient follow-up for TB service provision. The government should consider fast tracking the scale up of the electronic medical system alongside training the users and enhancing data quality assessments which

have shown promise elsewhere in improving quality of routine data entry (Jedwab et al., 2022, Jamieson et al., 2017, Lemma et al., 2020).

Patients aged 0-14 years were more likely to experience pre-diagnosis LTFU before conducting the required TB tests compared to those aged 45 years and above. This may be because of the existing diagnostic challenges of TB among children, such as difficulty obtaining sputum and a lack of functional radiological investigations (X-rays) at health facilities (Gunasekera et al., 2022, An et al., 2023, Shitol et al., 2023, Dodd et al., 2014). More so, patients aged 0-14 years do not independently make decisions to seek care and hence depend on the availability and decisions of the care takers to seek care. Although our study revealed no association for pre-treatment LTFU among this age group, a study in Uganda revealed that 18.7% of smear-positive children were not initiated on treatment (Kizito et al., 2022). Early detection of TB especially in children and adolescents is crucial for improving treatment outcomes and preventing post TB lung impairment (Yayan et al., 2024, Graham et al., 2022, Nkereuwem et al., 2021).

Females were the most presumed patients for TB in the study period but were also more likely to be LTFU before collection of TB results. Women are more likely to be LTFU due to their decision and economic dependence on male counterparts before seeking care which often relies at the discretion of availability of funds and knowledge of TB by the male counterparts (Kerkhoff et al., 2023). A study in Pakistan for example revealed that women seeking TB care experience challenges such as limited autonomy in household financial decision-making and travel expressing dependence on their spouses (Habib et al., 2021). These findings are similar to studies elsewhere in Tanzania and Zambia which found males more likely to complete TB diagnosis compared to females (Mgina et al., 2022, Kerkhoff et al., 2023). More so, females have care-taking responsibilities that could derail their return to health facilities to complete care as this would require time off which is often not guaranteed (Mendoza-Hisey et al., 2023). However, some studies show men to have more challenges in TB health care

seeking due to their hesitance in seeking healthcare, working conditions that may not permit time off for health care and perceived stigma (Mendoza-Hisey et al., 2023, Rajarao and Rajesham, 2019). This reverse finding could be because of different cultural and social norms in the study settings which often affect how people perceive and seek care for TB (Alhassan et al., 2026).

Although our study showed no statistical significance between pre-diagnosis LTFU and HIV positive status, studies elsewhere have shown an association with those who are HIV positive most likely to be LTFU before completing TB diagnosis (Zawedde-Muyanja et al., 2020b, Padingani et al., 2018, Lungu et al., 2021). Relatedly, participants from the HIV clinic were less likely to be LTFU. This maybe because of the integration of HIV and TB services in our study facilities which provides synergies for follow-up of these patients especially during drug refills. More so, it maybe because of the existing rapport already created with the HIV positive patients by the same health workers which motivated the patients to complete diagnosis. However, patients with an unknown HIV status were more likely to experience pre-diagnosis and pre-treatment LTFU. This reveals gaps in implementation of the TB/HIV testing policy in these health facilities that subsequently leads to the LTFU of these patients before they are tested for TB or initiated on treatment when diagnosed. Integration of TB services with other services in the health facilities may therefore be a promising avenue for reducing LTFU before completing TB diagnosis.

Pre-diagnosis LTFU levels were highest in 2019 and 2020 and drastically decreased in 2021 and 2022 during the peak of the COVID-19 pandemic. The reduction in LTFU from 2020 to 2021 maybe attributed to the intensified efforts by the National TB and Leprosy Program (NTLP), which included the integration of TB and COVID-19 services; community campaigns such as TB Catch-up and Community Awareness, Screening, Testing, prevention and treatment to end TB Campaign (CAST TB), which involved community awareness of TB; and intensified screening and diagnosis of patients for TB (NTLP, 2023, MOH, 2021a). More so, the decline of the pre-diagnosis LTFU in 2021 and 2022

could have been because of the pandemic reset of health systems in Uganda leveraging on integration of services. These findings are similar to those of national and WHO reports showing that Uganda is one of the countries that quickly recovered from the effects of COVID-19 in terms of case notification of newly diagnosed TB patients (WHO, 2023c). The integration of health services, especially during outbreaks, is key to ensuring continuity of service delivery while harnessing the power of available resources (Semitala et al., 2023). More so in 2020, the WHO proposed new and updated recommendations related to TB screening and diagnosis favouring the molecular rapid diagnostic tests for TB such as Xpert MTB/RIF over microscopy. This wide adoption of Xpert MTB/RIF could have contributed to a reduced the turnaround time for results given its ability to produce results within two hours hence reduced pre-diagnosis LTFU (WHO, 2026).

Time to completing the TB diagnostic process was higher among participants in H/C IVs than those presumed in hospitals. This maybe because of the availability of the testing services on-site in the hospitals which enables a short turnaround time of results for patients. Most lower health facilities like the H/C IV depend on microscopy for testing and have to refer samples to a nearby health facility with the remaining testing services which process increases the turnaround time and the likelihood of patients incurring more time off work and transport costs to visit the health facility for their results hence LTFU when these resources are not available (MacPherson et al., 2013). These findings are similar to a study by Chilembo et al., in Zambia which showed that patients who were diagnosed with smear microscopy were more likely to be LTFU compared to those of Gene Xpert (Chilembo et al., 2020) and the one by Padingani et al., which showed participants in lower health facilities are likely to be LTFU (Padingani et al., 2018). The Gene Xpert assay has a short turnaround time for results but is expensive hence not available in all health facilities. These findings emphasize the need to ensure availability of on-site testing services to reduce on the turnaround time, additional health care costs to patients and LTFU.

Sub-study two

A follow-up qualitative study was conducted to explain facilitators and barriers to completion of the TB diagnostic process among people with presumed TB to in selected health facilities in Central Uganda. Key facilitators for completion of the TB diagnostic process included obtaining same day results, prior TB knowledge, social support, caring health workers, support from cough monitors and facility linkage officers and phone call to diagnosed patients to collect results. Barriers to completion of the TB diagnostic process were; TB and HIV stigma, failure to produce sputum, lack of transport high sample load, unavailable tests and stock out of supplies, unclear appointment for collection of results, missing and incorrect patient contact details and negative health worker attitude.

Obtaining same day results facilitated completion of the TB diagnostic process. This is because the patients got the diagnosis there and then and did not require more time off work and transport to return to the health facility, which were often cited as hard to get. This was further attested to by patients who did not complete the diagnostic process mentioning failure to obtain same day results as a barrier. Although the goal of all TB programs is to have patients with presumed TB obtain their results on the same day of testing, this is not realized yet (WHO, 2011). Evidence from a systematic review and meta-analysis in high-TB burden countries shows a health system delay for TB diagnosis of 14 days (Teo et al., 2021). Further, our formative study showed that over half of those who conducted the TB investigations required, did not receive their test results on the same day of being tested (Nuwematsiko et al., 2024). Failure to provide same day results was linked to high sample load, stock out of supplies in our study and inadequate laboratory personnel, and low laboratory capacity in studies elsewhere (Zawedde-Muyanja et al., 2022, Mulaku et al., 2023, Marahatta et al., 2020). Delay to provide a TB diagnosis exposes the community to possible infections and increases morbidity and mortality in the positive patients (Tiemersma et al., 2011, Getnet et al., 2019, Mugauri et al., 2018, Zawedde-Muyanja et al., 2020a).

Delayed results in this study consequently led to lack of transport to return to the health facilities, need to take time off work to return to the health facility and exposed participants to potential TB/HIV stigma due to the frequent trips to the health facility. This is similar to what other studies have found in Uganda and elsewhere (Fenta et al., 2023, Daka et al., 2022, Chilembo et al., 2020, Zawedde-Muyanja et al., 2022, Mulaku et al., 2023). The need for repeat visits to the health facilities increases health care costs for the patients which may derail progress towards achieving universal health coverage and the goal of eliminating catastrophic costs for TB services by 2035 (WHO, 2015a). Uganda is already struggling with high pre-diagnosis catastrophic costs of 30.6% (Walcott et al., 2020) hence this could further push patients to poverty. There is therefore need for issuance of same day results to patients on the day of the health facility visit.

Social support from family and community members were mentioned as a key facilitator to completing TB diagnosis. This support was commonly mentioned as from the significant people in patient's lives who have a form of influence such as spouses, parents and siblings. This could be because the social support system provides counselling, reminders, financial handouts and follows up these patients to complete the TB diagnostic process. These findings were found in other studies elsewhere where family members escort people with presumed TB to testing facilities, others provide transport means and other offer words of counsel and encouragement to visit the health facilities (Chilembo et al., 2020, Zawedde-Muyanja et al., 2022, Geadas et al., 2024). The social support is crucial given that TB is a highly stigmatized disease which could deter one from testing if not supported and motivated by a significant person in their life (Fenta et al., 2023, George et al., 2020).

Although the attitude and behaviour of health workers has been criticized over the years as deterring patients to seek care in health facilities, our study found otherwise (Agba et al., 2021, Mannava et al., 2015, Amare et al., 2022, Beena et al., 2020). Health workers who offer services to patients with presumed TB were described as caring. This motivated most participants to return to the health facility

and complete diagnosis. This finding is similar to recent studies that have showed high patient satisfaction with health worker behaviours and attitudes (Nkiruka et al., 2023, Safo, 2020). This may be due to increased awareness and engagements with health workers towards a patient-centred care approach that emphasizes improved communication with the patients which makes them feel cared for (Born and Laupacis, 2012, Delaney, 2018). Furthermore, it maybe because TB is a highly stigmatized disease with a long-term treatment period when tested positive hence the health care workers show empathy to foster compliance among patients. Previous studies have showed a positive correlation between improved knowledge and positive attitude hence the need for continuous engagement of health workers for attitude change to be able to provide better services to patients (Mohammed et al., 2016, Wondimu et al., 2021, McPhetres et al., 2019).

Prior knowledge on TB obtained through health education or interfacing with TB patients was mentioned to increase one's ability to complete the TB diagnostic process. This was because they already knew more details about TB such as the benefits of early testing and starting treatment and the fact that TB can be cured and some feared they may have been exposed hence motivated to test and know their status. These findings are similar to studies elsewhere that show previous history and experience with a TB patient increases the likelihood of testing for TB (Geadas et al., 2024). Previous studies elsewhere have found that limited awareness of TB is associated with delays in healthcare seeking (Teibo et al., 2024, Mulaku et al., 2023, Marahatta et al., 2020). This therefore calls for strengthening of community and facility health education programs on TB.

TB and HIV related stigma was a key barrier to completing diagnosis as has been found in other studies in Uganda, Kenya and across the globe (Garg et al., 2020, Teibo et al., 2024, Zawedde-Muyanja et al., 2022, Mulaku et al., 2023). The stigma was commonly due to the misconception of that whoever has TB has HIV hence the fear was more on being associated with HIV. Patients fear that they will be mistaken for having HIV and be stigmatised for life. HIV remains highly stigmatized despite on-going

efforts which are now consequently affecting the opportunistic infections complicating their control and management (George, 2019, George et al., 2020). This TB and HIV related stigma was further amplified by the same day HIV testing policy for all people with presumed TB. Patients are now aware that they will not only be tested for TB but also for HIV with some health facilities sending the patients for testing in the HIV/ART clinics which may portray an image of them being HIV positive by the outsiders hence the stigma. Sensitization efforts should focus on improving community knowledge on TB and dispelling these misconceptions.

Unclear appointment for collection of results limited the ability of patients to complete the TB diagnostic process. This was because the patients remained unsure of when to return to collect results, were uncertain if they would be contacted when results are ready but also those who were promised to be called mentioned not being contacted when results were ready. Studies elsewhere showed the same with patients citing poor communication as a barrier to completion of the diagnostic process (Mulaku et al., 2023). Given the structural and laboratory personnel inefficiencies in low-resource settings to provide same day TB results, emphasis should be placed on improving communication with patients once results are ready. From this study, those who were called back to collect results via phone calls, especially those who tested positive, mentioned this as a key facilitator. More so, there is overwhelming evidence on the effectiveness of phone call and SMS tools in improving health care seeking (Majella et al., 2021, Choun et al., 2017, Hasvold and Wootton, 2011). However, health workers indicated missing and incorrect patient contact details as a barrier even when there is an opportunity to contact the patient to return to the health facility. Lack of patient contact details has been seen in previous studies as a key contributor to LTFU of patients with presumed TB (Zawedde-Muyanja et al., 2020b, Thomas et al., 2018, Mulaku et al., 2024b). Improving patient-provider communication therefore requires comprehensive strategies comprising of proper documentation and availing the communication tools and resources.

Sub-study three

In this sub-study, a systematic review was conducted to identify potential mHealth interventions to address some of the facilitators and barriers to completion of the TB diagnostic process identified in sub-study two. These include unclear appointments of results collection which consequently leads to repeat visits at health facilities and stigma. Evidence showed that SMS and phone calls are the commonly used mHealth interventions in this phase to remind and track patients to return to health facilities and pick results and consequently initiate treatment if diagnosed with TB. Most studies used combined mHealth interventions sometimes alongside other interventions like home visits, health literacy and facility linkage/support officers. More patients returned to health facilities to collect results and initiate treatment with phone call interventions compared to the SMS and mobile applications.

Few mHealth studies were identified in this TB pre-diagnosis and pre-treatment phase which limits availability of evidence on their potential use and effect. Availability of few studies could be because of limited evidence on the LTFU in this phase with most focusing on the treatment phase where there is overwhelming evidence and limited resources to support the research. The limited number of mHealth studies targeting the TB presumptive phase indicates a significant evidence gap in the early stages of the TB care continuum. When there is insufficient evidence on whether mHealth interventions can effectively reduce pre-diagnosis LTFU, policymakers and healthcare providers may be reluctant to adopt these potentially effective solutions. Further research is needed to evaluate how mobile technologies can support undertaking the requested investigations, collection of results, referrals for treatment initiation, and reduce diagnostic delays, ultimately contributing to earlier TB detection and reduced transmission. Most mHealth interventions have been conducted in the TB treatment phase for reminders to patients either to take medicine or come for clinical appointments (Hermans et al., 2017, Guo et al., 2020, Musiimenta et al., 2023, Chen et al., 2023, Sekandi et al.,

2024, Sekandi et al., 2020a, Selvaraju et al., 2022). There is less attention to the presumption phase (the period before one is diagnosed with TB) yet increasingly that is where most patients are LTFU (Mwansa-Kambafwile et al., 2019, Iribarren et al., 2014, Liu et al., 2015, Kim et al., 2019, Nuwematsiko et al., 2024). The TB presumption phase presents an opportunity for early diagnosis and treatment initiation which are key components in TB control but also leads to better patient outcomes (WHO, 2010, Migliori et al., 2012).

SMS and phone call were the commonly used mHealth interventions to enhance completion of TB diagnosis and treatment initiation. This could be because they are low-cost interventions favoured by the increased ownership of mobile phones by most people (Hasvold and Wootton, 2011). As of 2025, 82% of the global population aged 10 years and above own a mobile phone with people in LMICs at 74% ownership (ITU, 2025). The use of SMS and phone calls has become a widely explored tool in the healthcare field, particularly in managing chronic conditions like TB and HIV for treatment adherence, tobacco control and reminders for appointments (Liu et al., 2015, Marcolino et al., 2018, Hall et al., 2014, Lester et al., 2019, Nglazi et al., 2013, Haberer et al., 2016, Hermans et al., 2017, Singh et al., 2017, Yasmin et al., 2016). These interventions are considered cost-effective methods to improve patient engagement, adherence to treatment, and overall health outcomes. With the increased ownership and use of mobile phones, their use to promote health care seeking should be optimized (Ibeneme et al., 2020, Adong et al., 2022). As of 2024, 60.42% of the world's population own a smart phone thus a great opportunity for use of technology (bankmycell, 2025).

Phone call interventions had more proportions of patients completing diagnosis and initiating treatment compared to the SMS and mobile applications. This could be because the phone calls allow interactive communication and gives room for more detailed discussion. Studies elsewhere that used phone call interventions also reported successful outcomes (Hasvold and Wootton, 2011)(Aku et al., 2024, Ouedraogo et al., 2024, Alturbag, 2024). Moreso, previously patients have showed more

preference (Hayat et al., 2020, Houser et al., 2013) and satisfaction (Ouedraogo et al., 2024, Braun et al., 2009) for phone call interventions mainly because of privacy, inability to read and the ability to interact back with a phone call (Ouedraogo et al., 2024). Although the phone calls are most preferred and increase the chances of better outcomes, they are costly and information on their cost-effectiveness limited.

Sub-study four

Based on the findings from sub-study three where SMS and phone calls were the commonly used mHealth intervention in the TB presumption phase, I leveraged on the already designed SMS and Phone call intervention in the primary study other than design a parrel intervention. Instead, findings from the review were used to refine the intervention design in the main trial and implementation strategies. The refined intervention was then adapted and implemented in the main study using an RCT. In this sub-study, i discuss findings from the evaluation of the RCT focusing on the SMS and phone call reminders arms only. From the evaluation, participants who received phone call reminders only were more likely to have early completion of the TB diagnostic process compared to those in standard of care. There was no significant association for those in the SMS arm compared to standard of care.

Phone call reminders fostered completion of the TB diagnostic process. This could have been because of the two-way interaction with the patients reminding them to return to the health facility unlike for SMS reminders. Patients perceive phone calls from the health facility as a sign of care and effective tool for providing feedback which motivates them to return to the health facilities (Buregyeya et al., 2023). This finding is similar to other studies where phone calls improved health care seeking for patients (Majella et al., 2021, Choun et al., 2017, Hasvold and Wootton, 2011). With the increased ownership and use of mobile phones, their use to promote health care seeking should be optimized

(Ibeneme et al., 2020). Moreso, 75% of clinic attendees in Uganda reported having access to a mobile phone and were willing to receive TB-related communication by either voice call or SMS which signifies an important opportunity to introduce the mHealth interventions (Ggita et al., 2018). Although effective, phone call interventions maybe a high-cost intervention compared to SMS. Additionally, phone calls require human time and resources which may constrain the already struggling health system that is marked with staff shortage. This therefore calls for innovations while adapting and scaling up phone call interventions. For example, partnerships with telecom companies can be explored for reduced costs as a form of corporate social responsibility and also leveraging on the use of Artificial intelligence and machine learning to automate some of the calling processes.

Although SMS reminders did not significantly increase completion of diagnosis in our study, some studies elsewhere have showed their effectiveness in i) improving surveillance and TB contact tracing; ii) providing health information on TB; iii) reminding patients to return to the clinics and complete diagnosis and iv) to deliver test results to patients who have gone through the diagnosis (Wagstaff et al., 2019, Liu et al., 2014, Babirye et al., 2019, Meyer et al., 2018, Maraba et al., 2018a, Ggita et al., 2020). Other studies in Argentina, Uganda and Pakistan did not find a significant outcome for SMS reminders sent to TB patients (Iribarren et al., 2012, Mohammed et al., 2016, Hermans et al., 2017). The SMS intervention did not yield significant results possibly because participants may have either not read them, or they were ignored or they were deleted. Formative phase findings of this study showed that patients were likely to ignore or delete SMS reminders because of fatigue from telecom companies and fear of unintended disclosure of their TB presumptive status which may explain why there was no association (Buregyeya et al., 2023) More so, the SMS may not have been significant because of the contamination in the standard of care where health facilities were also sending SMS alerts from the Xpert MTB/RIF machines. This could have led to the underestimation of the true effect

size leading to no association (Torgerson, 2001). Whereas SMS reminders are a low-cost intervention, they should be supplemented with other interventions for enhanced benefits (Willems et al., 2023).

Synthesis of all study findings

Collectively, the four sub-studies demonstrate that pre-diagnosis LTFU is a multifaceted problem intertwined in personal, health system and social realties and hence must be addressed using a multi-pronged multi-modal approach. The mixed-methods approach employed in this thesis provided complementary insights to identify how many are lost and who is lost and reasons why people with presumed TB drop out from care even in the face of interventions.

Completion of the TB diagnostic process remained lower (74%) than the WHO target of 90%, even after patients received phone call reminders (Fenta et al., 2023). This finding emphasizes the importance of using a holistic approach to address the underlying personal, health system and social factors that continue to increase vulnerability of LTFU (Zafar Ullah et al., 2022). Personal factors that lead to LTFU for example remained the same as in sub-study 1 and even after implementing the SMS and phone call reminders intervention in sub-study 4. These included; TB and HIV stigma, and lack of transport to return to the health facility. This emphasizes the fact that mHealth interventions should not be viewed as standalone solutions but rather as enablers that work synergistically with health system strengthening (Labrique et al., 2013).

Although long turnaround time for results was a major contributor of LTFU in sub-study 1, this was not the case after implementing the SMS and phone calls reminders intervention. This was because patients were assured of being reminded when to collect results no matter how long it took. This

implies that proper communication in the face of health system challenges may reduce a certain level of LTFU when patients remain informed.

From the systematic review, SMS and phone calls stood out as potential key interventions to support completion of the TB diagnostic process. In the previous studies, these interventions supported delivery of reminders and testing results which we leveraged on to address the communication challenge of uncertainty of when to collect results from the laboratory which was earlier mentioned by participants in sub-study 2 as a contributor for LTFU.

5.3 STUDY STRENGTHS AND LIMITATIONS

To the best of my knowledge, this is the first study in Uganda to utilise mHealth interventions in the TB presumption phase using an RCT. Most mHealth interventions have been utilised in the treatment phase to foster adherence and treatment completion. The TB presumption phase provides an opportunity for early diagnosis and medical interventions for better outcomes for patients. A key strength to this study is the use of mixed methods which complemented and supplemented each other for rich findings. Use of the RCT and a systematic review, which are the highest forms of evidence generation, are appropriate to support evidence based clinical practice and policy. Routine data from TB services was also analysed to identify factors associated with pre-diagnosis and pre-treatment LTFU. This enabled identification of gaps in TB health services in Uganda and thereafter making practical recommendations for health service improvement.

The systematic review on use of mHealth interventions in both the pre-diagnosis and pre-treatment phases of TB care was the first of its kind in LMICs. A recent study by (Mulaku et al., 2024b) conducted a scoping review to synthesize evidence on general interventions in the pre-treatment phase only including mHealth. This study therefore provides useful evidence for potential mHealth interventions to adopt and scale up in this phase.

The study had a few limitations. In sub-study 1, I utilized secondary data from health facility registers which often present with missing data and quality issues. I mitigated the likelihood of this by cross-matching data from the presumptive, laboratory and TB unit treatment registers during data collection to limit the missingness of data on key variables such as age, sex, date of sample collection and results received. This information is often recorded in at least two of the registers. Where data were completely missing on some variables, I used case analysis and deleted those entries. I acknowledge that this method often excludes potentially important data and reduces the statistical power. However, with the post-hoc power estimation, I still had power to conduct the analysis even after deleting the missing data. More so, availability of results in the presumptive TB register was used as a proxy for the completion of TB diagnosis, which may not translate to a patient receiving results for further management. A prospective study is recommended for future studies to establish the actual receipt of results by patients as an endpoint for the completion of TB diagnosis. Another limitation is that we could not verify whether the patients who were LTFU before completing TB diagnosis at one facility completed the diagnosis from another health facility or did not complete at all.

Participants for the qualitative interviews were sampled excluding those who did not have a record of telephone number since we could not obtain it to invite them for the interviews this may have created selection bais. All health facility registers were cross-checked for the telephone number before excluding the patient from the sampling frame. Home visits were not possible due to limited resources and poor or no locator information. This may have introduced selection bias where I missed a category of participants who did not have mobile phones and experience unique challenges. Also, social desirability bias may have occurred during primary interviews where the patients report contrary to what they do or did. This may have resulted in instances where I conducted the qualitative interviews as a lead investigator of the study. These effects were minimised by creating rapport with health workers and patients during the qualitative interviews and clearly explaining the goal of the study as

quality improvement than a fault-finding mission. More so, participants were assured of confidentiality in their responses and the data shared which likely reduce chances of modified behaviours. I also engaged another independent qualitative interview to reduce this social desirability bias from the respondents. More so, there might have been recall bias from qualitative participants where they might have inaccurately recalled the events surrounding their experience during the TB diagnostic process and post the SMS and phone call intervention. This was however mitigated by purposively selecting participants who had recently experienced our outcome of interest to reduce the recall bias.

The Hawthorne effect was likely due to the presence of the study in the health facilities and also patients knowing that they are being monitored hence altering behaviours of TB testing during the RCT which may have biased the findings. I further acknowledge limitations from the main RCT where I drew the secondary data to analyse for the effect of SMS and phone call reminders to enhance completion of the TB diagnostic process. First, the RCT was designed to exclude participants who did not own mobile phones and those who could not read. This was because the intervention was mobile phone-based and required reading of an SMS hence it would be difficult to deliver the intervention to those without phones and to people who could not read. Phone sharing was considered but deemed inappropriate due to fear of inadvertent disclosure of participant's TB testing status which would potentially introduce stigma. Excluding these participants may have introduced selection bias leading to an underestimation of the effect size making the results not generalisable to all people with presumed TB.

Further, the main RCT was an active controlled trial because the SOC arm was partially receiving an active intervention that is, SMS of results directly sent by the Xpert MTB/RIF and phone call to positive patients, which were also achieving the same outcome of informing the patient to collect their results just as the main RCT intervention. Because of this active intervention in the SOC arm, the

effect size may have been underestimated. It was not possible to have a true SOC arm because the SMS and phone call to positive patients were already in the SOC arm as stipulated by the Ministry of Health for some study facilities although this was not being done in all of them at the time of the start of the intervention. Even for the facilities where the SMS were being sent, it was inconsistently being done because of limited resources such as internet and time. This contamination was later anticipated in the remaining facilities which were not sending the SMS due to the Hawthorne effect, with facilities starting to send the SMS from the Xpert MTB/RIF machine as soon as the RCT was started. To account for this, data on possible contamination in all the study arms were collected along the data collection process. Hence, I conducted the per-protocol analysis to check for the differences in the effect size. From the analysis, there was no difference in the level of significance with the per-protocol analysis hence the contamination in the SOC arm may not have affected the findings.

A process evaluation andeconomic evaluation for cost-effectiveness of the SMS and Phone call intervention were not done due to limited resources hence I missed out on finding out the cost implication of these interventions to strengthen the recommendations regarding their uptake and scale up. I therefore recommend cost-effectiveness studies for SMS and phone call reminders for future research to provide this important information. More so, a process evaluation is recommended for future studies to understand the processes and mechanism under which the SMS works, why they did not become effective, for whom they work, when and how.

5.4 REFLEXIVITY AND POSITIONALITY

This refers to how the researcher's perspectives, biases, and experiences might have influenced the research process and findings (Olmos-Vega et al., 2023). As a PhD candidate, I coordinated the bigger RCT and my research only complemented it. Aware of potential biases from the two studies, I always ensured use of independent researchers and analysts for confirmability. For example, I analysed data with Biostatisticians who were not part of the main trial and engaged independent researchers to

support me in conducting qualitative interviews and the systematic review. For credibility and trustworthiness of qualitative data, all data collectors were trained, I included probes in interview guides and also triangulated data from different sources. More so, participants were varied to ensure responses from diverse categories of participants. For example, we interviewed both patients who had completed the TB diagnostic process and those who had not yet completed and also interviewed participants who received either SMS or phone calls during the qualitative study post the trial.

This was my first research in TB hence there were no undue influences due to previous work or experiences working in TB clinics. More so, this study was conducted in different settings other than my home town, Mbarara hence there were also limited biases and undue influences in sampling and other research processes. While the area of study was new to me, I was quick at creating rapport with health workers and district administrators for contextual understanding and smooth running of the study.

Results and findings have been presented in line with standard guidelines for comparability such as the Consolidated Criteria for Reporting Qualitative Research (COREQ) (Tong et al., 2007) and The Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols (PRISMA-P) 2015 guidelines were followed for conducting the systematic review and reporting .

5.5 METHODOLOGICAL CONSIDERATIONS

This was a sequential explanatory mixed methods study embedded in a bigger RCT whose aim was to foster linkage to care for patients with presumed TB. Embedding studies in ongoing research minimises resources, increases the evidence base in that area of research and increases the chance of usability of the findings when the studies complement each other (Akintola et al., 2024). Previous studies have documented increased research and evaluation capacity for embedded research models in areas where funding is limited with workforce pressures (Akintola et al., 2024, Kavanagh et al., 2024).

Mixed methods were considered for this study for triangulation of findings from different methods and data sources. This triangulation provided rich information on understanding completion of the TB diagnosis from perspectives of the patients and health care workers in the different settings. This information may inform planning for strengthening provision of TB services in the country.

A 30-day operational definition for completion of TB diagnosis was adopted for this study based on previous studies for comparison (MacPherson et al., 2013, Pala et al., 2018). This period was also selected because it takes into account the time taken for the different diagnostic tests with Xpert MTB/RIF taking between 2hrs to 72 hrs and other tests like microscopy between 1 and 2 days in addition to extra delays that maybe encountered by the patient and health system structures (Sekadde et al., 2013, Kwak et al., 2013). Whereas this cut-off has been previously used by similar studies and takes into account the possible delays, it may lead to an underestimation of the proportion of pre-diagnosis LTFU since the time is long enough for most patients to complete the diagnostic process. Also, with the recent guidelines of test and treat and improved diagnostics that yield results in a short time, this 30-day cut-off may have been high leading to an underestimation of LTFU but also presents opportunities for delayed treatment initiation for positive patients.

Whereas it was desirable to use cluster randomisation over individual randomisation because of its benefits in reducing contamination and increased chances of generalisability, individual randomisation was most preferred in sub-study 4 because it reduces selection bias and the available financial and time resources were limited. However, an individual randomised controlled trial still offers reliable and beneficial results with high internal validity most especially reducing selection bias. Internal validity is key while determining the effect of an intervention which information can be built upon by future studies using more robust methods to test its generalisability and scalability.

This study was conducted in six districts in Central Uganda which has a mixture of urban, semi-urban and rural populations hence some of the findings are generalizable and or transferable to other parts of Uganda given the similarities in the population and health system structures.

5.6 THE THEORETICAL FRAMEWORK AND PARADIGM USED IN THE STUDY

This study was guided by the socio-ecological model to predict completion of the TB diagnostic process. The SEM model was selected to guide this study because of its ability to identify multiple, interacting factors at different levels which contribute to a patient being lost to follow-up. The layers of the model reveal how factors do not exist alone but rather recognizes the complex interaction of individual, interpersonal, community, system and policy factors in fostering completion of the TB diagnostic process.

In sub-studies 1,2 and 4, we explored the individual, interpersonal, community, system and policy factors that fostered completion of the TB diagnostic process both with and without the SMS and phone call intervention. Even with the intervention, the factors affecting completion remained the same which indicates a complex interaction and existing of underlying causes that cannot just be solved with one intervention of improving communication.

Most factors identified were individual, interpersonal, community, system with few policy-related factors. The policy-related factor identified was the same day testing of TB and HIV which scares away patients and further confirms their fears of potential infection with HIV once they are presumed with TB. This was mentioned to further amplify TB stigma. More so, as much as personal and interpersonal factors contributed to LTFU, they were seen to be further amplified by system factors especially inefficiencies in the health system. For example, when the health system fails to deliver same day results or there is a long turn-around time, it compels the patients to make return visits to the health facilities which in turn require transport money, time off other duties or work and also leads

to stigma because of frequenting the health facilities to pick results. This implies the necessity for comprehensive interventions to foster completion of the TB diagnostic process and not just addressing a certain category of factors because all these are interconnected.

This study was hinged on pragmatism paradigm whose philosophical underpinning is that knowledge is not static and is as a result of experiences and perceptions in the social context (Kaushik and Walsh, 2019, Hildebrand, 2011). This paradigm dispels the use of one method of inquiry to understand a complex phenomenon (Shaw et al., 2010, Hall, 2013, Brierley, 2017). Therefore, findings presented across the four sub-studies demonstrated the use and justification of a pragmatic epistemological approach because knowledge was generated from multiple complementary forms of evidence that is; quantitative, qualitative inquiry, systematic review, and a randomised trial rather than using only one approach. This sequential application of methods to understand and solve the problem of pre-diagnosis LTFU is what Long et al. describes as the pragmatic application of complexity theory in healthcare, implying it is iterative, adaptive, and focused on useful change (Long et al., 2018).

In sub-study 1, quantitative data were used to determine the magnitude of pre-diagnosis LTFU and identify associated factors such as age, sex, missing residence information, and lack of phone contacts. This provided actionable knowledge about which patient groups were most vulnerable and where interventions should be targeted. In sub-study 2, the qualitative inquiry further explored patients' and health workers' experiences, revealing facilitators and barriers to completing the TB diagnostic process. Factors such as persistent symptoms, social support, and caring health workers facilitated completion, while stigma, transport challenges, delays in results, and poor provider attitudes hindered it. Pragmatism is reflected in the recognition that statistical associations alone in sub-study 1 could not fully explain patient behaviour, social and environmental factors that lead to pre-diagnosis LTFU. Experiential knowledge was therefore needed to understand the context and inform practical solutions in sub-study 4 during the trial of interventions.

Sub-study 3 further justified pragmatism through a systematic review that synthesized existing evidence on mHealth interventions. The review identified SMS, phone calls, WhatsApp messages, and mobile applications as strategies used during the TB presumption phase. By examining what had been implemented elsewhere, the study generated knowledge aimed at informing effective intervention design rather than merely developing theory. Finally, sub-study 4 evaluated the effectiveness of SMS and phone call interventions, the commonly used interventions from the systematic review. This application of the evidence obtained conformed to the fact that epistemology is empirical and action-oriented (Shaw et al., 2010). This sub-study also examined contextual factors influencing intervention use, including individual, social, technological, and health-system factors. This emphasis on determining "what works, for whom, and under what circumstances" is a central feature of pragmatism. Despite its strengths, the pragmatism approach used in this study has some limitations. The emphasis on generating practical solutions to reduce pre-diagnosis LTFU may have prioritized "what works" over a deeper examination of the underlying structural, political, and socioeconomic determinants of LTFU. For example, while factors such as stigma, transport challenges, and health worker attitudes were identified, the broader policy systems and power dynamics that produce these barriers were not have been fully explored. More so, the pragmatic approach is highly context-dependent hence findings such as the effectiveness of phone calls may not be easily transferable to other settings with different health system capacities, patient populations, or technological infrastructure.

5.7 IMPLICATIONS OF THIS STUDY

The findings of this study were disseminated in workshops, conferences, seminars, and meetings. In particular, findings were presented to the 2022 and 2023 World Union Conference on Lung Health online and in France respectively. Results were also shared in the research forum of the National TB and Leprosy Program of the ministry of Health to increase likelihood of uptake of the findings by

different stakeholders who attend the forum. Reports of the findings will be shared with the study facilities to inform their practice.

Public health

This study generated essential information on effect and implementation factors of an SMS or phone call intervention to foster completion of the TB diagnostic process. These findings will provide information for designing public health interventions to support early diagnosis and treatment initiation of people with presumed TB to reduce community spread of the infection. Several facilitators and barriers were identified which implementers may take up to address especially barriers around turnaround time for results and waiting time for patients.

mHealth interventions are increasingly becoming popular hence this study's findings will provide insights into designing similar interventions to improve practice. The study's results could be used to advocate for the integration of mHealth technologies, specifically phone calls, into national TB control programs and further strengthen the existing SMS system.

Policy

Findings from this study may be taken up to guide design and operationalisation of policies to increase completion of the TB diagnostic process. Whereas guidelines recommend same day TB and HIV testing policy, this study highlights the need to increase awareness of this policy among patients and dismiss myth around the co-infection which increases stigma and further deters away people from testing for TB.

5.8 ACADEMIC CONTRIBUTIONS

This study adds on the body of knowledge on promoting completion of the TB diagnostic process among people with presumed TB. First, it shows that the problem of LTFU before completing the TB

diagnostic process still persists and the facilitators and barriers for this loss. Secondly, the study provides evidence on the use of SMS and phone call reminders to enable patients complete the TB diagnostic process and influencing factors for the use of these mHealth interventions. Lastly, this research shows what other effective mHealth interventions are available for use to support completion of the TB diagnostic process. The use of mixed methods along with an experimental study design and a systematic review, the highest level of evidence, strengthen the evidence provided by this study. Publications from the four sub-studies arising from this research will be read by a wide community across the world ultimately disseminating knowledge beyond the confines within which the work was done.

5.9 PRACTICAL USE

The study focused on fostering completion of TB diagnosis which has not been largely explored with mHealth interventions yet it presents an opportunity for early diagnosis and treatment initiation which are key components in TB control but also lead to better outcomes (Subbaraman et al., 2020, WHO, 2010). Findings from this study on effectiveness of an mHealth intervention maybe taken up to guide policy, scale-up and improve implementation of mHealth based interventions in the TB presumptive phase.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

Findings from sub-study one show high proportions of pre-diagnosis (28%) LTFU of people with presumed TB. These high proportions are facilitated by individual factors (TB and HIV stigma, inability to produce sputum, lack of transport to return to the health facility); and health system factors (long turnaround time of results, stock out of supplies, unclear appointment for collection of results, inadequate patient contact details and negative health worker attitude). On the other hand, obtaining same day results and prior TB knowledge, social support, caring health workers and calling of patients to collect results enhances completion of the TB diagnostic process.

Existing evidence shows that SMS and phone call reminders are potential and commonly used mHealth interventions to promote completion of the TB diagnostic process with phone calls showing a likely higher effect than SMS. However scanty evidence existed on the effect of these interventions using robust methods hence an RCT was designed to assess the effect. Indeed, with the RCT, phone calls provided a much higher completion rate of the TB diagnostic process compared to the standard of care. The SMS showed no statistically significant effect (adj RR 0.99, 95% CI: 0.91,1.08), implying that completion of the TB diagnostic process is similar for patients who receive SMS reminders and those who receive nothing. Overall, less than three quarters of the participants completed the diagnostic process even with the intervention in place. This reveals continued gaps in completion of the TB diagnostic process. Efforts should therefore be focused on building the health system especially capacity of laboratories to provide same day results to patients with presumed TB. Individual, social, technological factors, intervention design and experiences influenced the use and outcomes of the SMS and phone call interventions in fostering completion of the TB diagnostic process.

6.2 RECOMMENDATIONS

Recommendations presented in this chapter arise from the results obtained from the three sub-studies. These recommendations will inform design and implementation of strategies and interventions to enhance completion of the TB diagnostic process.

Recommendations for policy makers

1. Enhance availability and functionality of the point-of care tests such as the Xpert MTB/RIF so as to provide same day results for patients. Enhancing availability of these tests is critical in ensuring timely diagnosis and management of TB. This may include investment in the diagnostic equipment, adequate reagent supply to avoid stock outs, and regular maintenance. Same-day results reduce the turnaround time for results, which in turn minimizes delays in treatment initiation, reduces patient anxiety, and helps prevent TB transmission. Additionally, patients are spared the burden of multiple visits, which often entail more transport money, loss of work time and other socio-economic disruptions. Assessments for the cost, feasibility and workforce requirements for achieving same-day results should be conducted first for informed decision making.
2. Enhance social support from the community and health workers through peer to peer or peer-led interventions. Peer-led models offer a unique advantage by providing relatable, culturally sensitive, and empathetic support to patients. Individuals who have experienced TB treatment can serve as peer educators and community advocates.
3. Strengthen data quality improvement programs to ensure all patient details are entered correctly in registers to enable tracking where need be. Lessons maybe drawn from past data quality assurance programs and assessments to determine the technical and resources required for this proposed activity.

4. Implement community stigma reduction strategies on TB and HIV to dispel myths about Tb and HIV which stood out as a major barrier. Stigma remains a major barrier for TB and HIV care. Community-led interventions that use education, media, local champions, and inclusive dialogue can help shift attitudes and dismantle harmful myths. The community interventions should be championed by all stakeholders that is: the community, NGOs, government, community health workers, CSOs because they all have an active role to play.
5. Incorporate phone calls into routine care for people with presumed for TB to enhance completion of the TB diagnostic process. Considerations for partnerships with telecom companies for subsidised or free airtime packages as part of their social corporate responsibilities and innovations by leveraging the use of Artificial Intelligence and Machine learning should be explored to overcome possible financial and human resource challenges in implementing phone calls.

Recommendations for health workers

1. Improve documentation of patient contacts and area of residences to ease patient follow-up for TB service provision.
2. Strengthen sensitisation of patients on the signs and symptoms of TB so that they volunteer to be screened. Sensitisation should also focus on appropriate care seeking for children presumed to have TB emphasizing to care givers the importance and consequences of undiagnosed and untreated childhood TB.

Engage partners of patients in the TB testing process to avoid possible domestic violence once one discovers that their spouse tested for TB.

Recommendations for patients

1. Embrace social systems and networks with trusted people such as spouses and immediate family members and disclose the testing status where possible so as to receive support. Disclosure of the testing status could limit potential domestic and intimate partner violence. Community health workers may support in the creation of the social support systems and networks in the community and link them to health facilities for more technical support. These social networks may include family members or close friends to the patients and formulation of patient networks.
2. Parents and care givers should endeavour to seek appropriate health care for children under the age of 15years who are presumed to have TB as these are more likely to be LTFU before completing the diagnostic process. Untreated TB has severe and long-term effects on children hence parents should seek appropriate care.

6.3 AREAS FOR FUTURE RESEARCH

Future studies should explore whether the TB diagnostic process is completed elsewhere through the use of patient pathway analysis and more robust triangulation methods across health facilities.

There is need for a realist evaluation into how SMS work for whom they work, when and how to establish why it is not as effective as a phone call. More so, considerations should be made for trials with a combined intervention of SMS and phone call to establish their combined effect. Further, an economic evaluation for SMS and phone call interventions should be considered to establish their cost-effectiveness before they can be adapted and rolled out. Also, an exploration of how SMS and phone call reminders are influenced by the social context should be done.

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APPENDICES

Appendix 1: Summary of the methods per sub-study and objective

Sub-study	Study objective	Study design	Data collection methods	Study population	Outcomes	Analysis
Sub-study 1	1. To determine the proportion of pre-diagnosis LTFU among people with presumed TB and factors associated in Central Uganda.	Cohort analysis of secondary data	Quantitative -Data extraction- Records from presumptive TB and TB laboratory. -Total enumerative sampling Qualitative - 30 IDIs - 12 KIIs -Purposive sampling Purposive sampling (time presented to the facility, having an address recorded or a functional phone number)	People with presumed TB who presented to the study facilities between January 2019 and December 2022. -People with presumed TB who presented to the study facilities between November and December 2022 and either completed or did not complete diagnosis (IDIs) -Health workers involved in the study facilities involved in	-Pre-diagnosis LTFU -Factors associated with pre-diagnosis LTFU -Facilitators and barriers to completing TB diagnosis	-Univariate analysis for the proportions of LTFU - Factors associated- Bivariate and multivariate using either logistics or modified Poisson regression -Thematic analysis

				TB care (KIIs)		
Sub-study 2	2. To explore facilitators and barriers for completion of the TB diagnostic process in Central Uganda	Qualitative	Qualitative - 25 IDIs - 9 Focus group discussions - 12 Key informant interviews	- Presumptive patients who present to the study facilities one month before data collection (FGDs) - Health workers who offer TB care (KIIs) -Health workers involved in TB care, policy makers, researchers (Insight workshop)	- Perceptions on the use of an SMS or phone call intervention to reduce pre-diagnosis and pre-treatment LTFU - Contextually adapted SMS or phone call intervention	Thematic analysis
Sub-study 3	3.To synthesize evidence on effectiveness of mHealth interventions to reduce LTFU in the TB presumptio	Systematic review	-Data extraction tool -Databases: PUBMED/ Medline, Scopus, Web of science, Embase, ScienceDirect and the Cochrane Central	Studies from LMICs that used mHealth interventions to reduce LTFU for presumptive TB from the year 2000 to 2022	- mHealth interventions in the TB presumption phase to reduce LTFU -Effectiveness of the mHealth interventions in the TB presumption phase to reduce LTFU	Descriptive analysis

	n phase in LMICs		Register of Controlled Trials			
Sub-study 4	4.To assess the effect of a contextually adapted SMS or phone call intervention to reduce LTFU among people with presumed TB in health care facilities in Central Uganda.	3-arm multi-centre Individual Randomized controlled trial	1410 participants; 1:1:1 (470 per arm) - Face to face interviews	- People with presumed TB ages 18 years and above who present to the study facilities during data collection	- Completed diagnosis (Yes/ No) - Initiated treatment if positive (Yes/ No) - Median time to completing diagnosis and initiating treatment	-Primary- Intent to treat -Sub-group analysis - Log-binomial regression or Modified Poisson with robust variance will be used to obtain the outcome measure inthe intervention, as compared to the control
	5. To explore factors that influence use of a contextually adapted SMS or phone call intervention to foster completion of the TB diagnostic process in	Qualitative evaluation (implementation factors-context and acceptability)	Qualitative -20 IDIs -9 KIIs	-People with presumed TB in the trial (IDIs) -Research Assistants in the trial	-Factors that facilitated and hindered uptake of the intervention -Factors that facilitated and hindered implementation -Perceptions on performance and effort of the intervention.	-Thematic analysis

	Central Uganda.				- Experiences and perceptions of the participants (social norms and facilitating factors) -Experiences and perceptions of the implementers	

Appendix 2:

Paper 1-Pre-diagnosis and pre-treatment loss to follow-up and associated factors among patients with presumed tuberculosis and those diagnosed in Uganda (Nuwematsiko et al., 2024)

RESEARCH **Open**

Pre-diagnosis and pre-treatment loss to follow-up and associated factors among patients with presumed tuberculosis and those diagnosed in Uganda

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Abstract

Background Loss to follow-up (LTFU) of patients with presumed tuberculosis (TB) before completing the diagnostic process (pre-diagnosis LTFU) and before initiating treatment for those diagnosed (pre-treatment LTFU) is a challenge in the realization of the End TB Strategy. We assessed the proportion of pre-diagnosis and pre-treatment LTFU and associated factors among patients with presumed TB and those diagnosed in the selected health facilities.

Methods This was a retrospective cohort study involving a review of routinely collected data from presumptive, laboratory and TB treatment registers from January 2019 to December 2022. The study was conducted in three general hospitals and one lower-level health centre IV in Central Uganda. We defined pre-diagnosis LTFU as failure to test for TB and obtain results within 30 days from the date of being presumed and pre-treatment LTFU as failure to initiate TB treatment within 14 days from the date of diagnosis. Modified Poisson regression was used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) of factors associated with pre-diagnosis and pre-treatment LTFU.

Results Of the 13,064 patients with presumed TB, 39.9% were aged 25 to 44 years, and 57.1% were females. Almost a third, 28.3% (3,699/13.064) experienced pre-diagnosis LTFU and 13.7% (163/1187) did not initiate treatment within 14 days from being diagnosed. Pre-diagnosis LTFU was more likely to occur among patients aged 0-14 years (adj PR 1.1, 95% CI: 1.06,1.24), females (adj.PR=1.06, 95% CI: 1.01, 1.12) and those with no record of place of residence (adj. PR=2.7, 95% CI: 2.54, 2.93). In addition, patients with no record of phone contact were more likely to be LTFU, (adj. PR=1.1, 95% CI: 1.05, 1.17). Pre-treatment LTFU was also more likely among patients with no record of place of residence (adj PR 7.1, 95% CI: 5.13,9.85) and those with no record of phone contact (adj PR 2.2, 95% CI: 1.63,2.86). Patients presumed from the HIV clinics were 40% less likely to experience pre-treatment LTFU compared to those in the outpatient departments (adj PR 0.6, 95% CI: 0.41,0.88).

Conclusion High proportions of pre-diagnosis and pre-treatment LTFU were observed in this study. This calls for urgent interventions at these time points in the TB care cascade to be able to realise the End TB Strategy.

Keywords Tuberculosis, loss to follow, Up, pre, Diagnosis loss to follow, Up, pre, Treatment loss to follow, Up, Uganda

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Introduction

Tuberculosis (TB) remains a global public health challenge and is the second leading cause of death from a single infectious agent after COVID-19 [1]. Although the global incidence has been reduced by approximately 2% for most of the decades, delays in TB diagnosis and treatment initiation remain globally, requiring more effort to find the missing patients and achieve the 2035 End TB strategy [2, 3]. In 2022, there were an estimated 10.6 million new TB patients out of which 3.1 million, around 30%, were either not diagnosed or were not notified to national TB programs [1]. One of the biggest gaps in the TB care cascade in both high- and low-TB burden countries is the significant number of patients who are not diagnosed [4].

Pre-diagnosis loss to follow-up (LTFU) has been estimated to range between 8% and 55% in Asia and Africa [5–12]. Similarly, a comparison study between 30 high and 153 low-TB burden countries revealed that 35% of TB incident cases in high-TB burden countries were not diagnosed compared to 20% in low-TB burden countries [4]. Moreso, in a systematic review in low- and middleincome countries (LMICs), pre-treatment LTFU was estimated to be between 6% and 38% in Africa, excluding Uganda [13].

Pre-diagnosis and pre-treatment LTFU increase community transmission of TB, TB severity and poor patient outcomes [7, 13–16]. Earlier studies revealed some of the associated factors for pre-diagnosis and pre-treatment LTFU as being HIV positive, residing far from the health facility, no record of tracking information such as phone contact and place of residence, poor communication between health workers and patients, long waiting time and need for repeat visits at health facilities [7, 8, 17–19].

In Uganda, a few studies have assessed this LTFU in the TB care cascade with Ekuka et al., reporting a pre-diagnosis LTFU of up to 40.7% and Zawedde et al., reporting a pre-treatment LTFU of 19.6% [12, 16]. Both studies focused on one type of loss in the TB care cascade that is; pre-diagnosis LTFU only for Ekuka et al., [12] and pretreatment LTFU only for Zawedde et al., [16] which limits understanding of the extent of these losses in Uganda. Therefore, the aim of this study was to assess the proportion of both pre-diagnosis and pre-treatment LTFU and associated factors among patients with presumed TB and those diagnosed in Uganda over a four-year period.

Methods

Study setting

The study was conducted in four selected health facilities in Mukono, Buikwe and Mityana districts, Central Uganda. The health facilities included three general hospitals (2 government-owned and 1 private-not-for profit) and one lower-level health centre IV (governmentowned). The selection of study facilities was based on high volume and to ensure representation of the different levels of the health care system and type of facility ownership, whether government or private-not-for profit owned. In the study facilities, patients are screened for symptoms of TB and presumed from any entry point of the health facility, including the outpatient department (OPD), HIV clinic, Pediatric clinic and Antenatal clinic. The symptomatic screening is in accordance with the cardinal symptoms of TB: persistent cough of two weeks or more, night sweets, fever of more than two weeks, weight loss, previous contact with a TB patient and if a child, poor weight gain [20]. After the patient has been presumed, they are referred for TB tests (Fig. 1).

TB diagnosis is performed using GeneXpert (Xpert MTB/RIF), which is the recommended first diagnostic test [21]. Depending on the availability of tests and how the patient presents, other diagnostic tests are available, including sputum microscopy, chest X-ray and urine TB lipoarabinomannan (LAM), mainly for HIV-positive patients [21, 22]. A diagnosed TB patient is defined as one who is bacteriologically confirmed by either Xpert MTB/RIF, smear microscopy or TB LAM or those confirmed by chest X-ray. Patient socio-demographic information, contacts, address of residence, clinical details and dates of registration are recorded in the national standardized paper-based registers at each care entry point, as described in Fig. 1. All study health facilities provide TB diagnostic and treatment services. More details on the flow of the patients right from when they arrive at the health facility are provided in the flow chart in Fig. 1.

Study design and population

This was a retrospective cohort study involving a review of routinely collected data of patients with presumed TB presenting. The study included patients of all ages who presented to the study facilities with the cardinal symptoms of TB from January 2019 to December 2022. The four-year period was selected to allow comparison of the pre-diagnosis and pre-treatment LTFU; before and during the COVID-19 pandemic. We referred to 2019 as before the COVID-19 pandemic and 2020–2022 as during the pandemic based on WHO periods of declarations of COVID-19 as a public health emergency of international concern [23, 24]. We excluded patient records with any of the missing variables of age, name, sex and date of registration when presumed for TB because these were identifiers for duplicates. ***Sampling***

We used total enumerative sampling, where all records meeting the inclusion criteria were extracted from the residence and date of being identified with presumed TB. The presumptive TB register was the starting point after

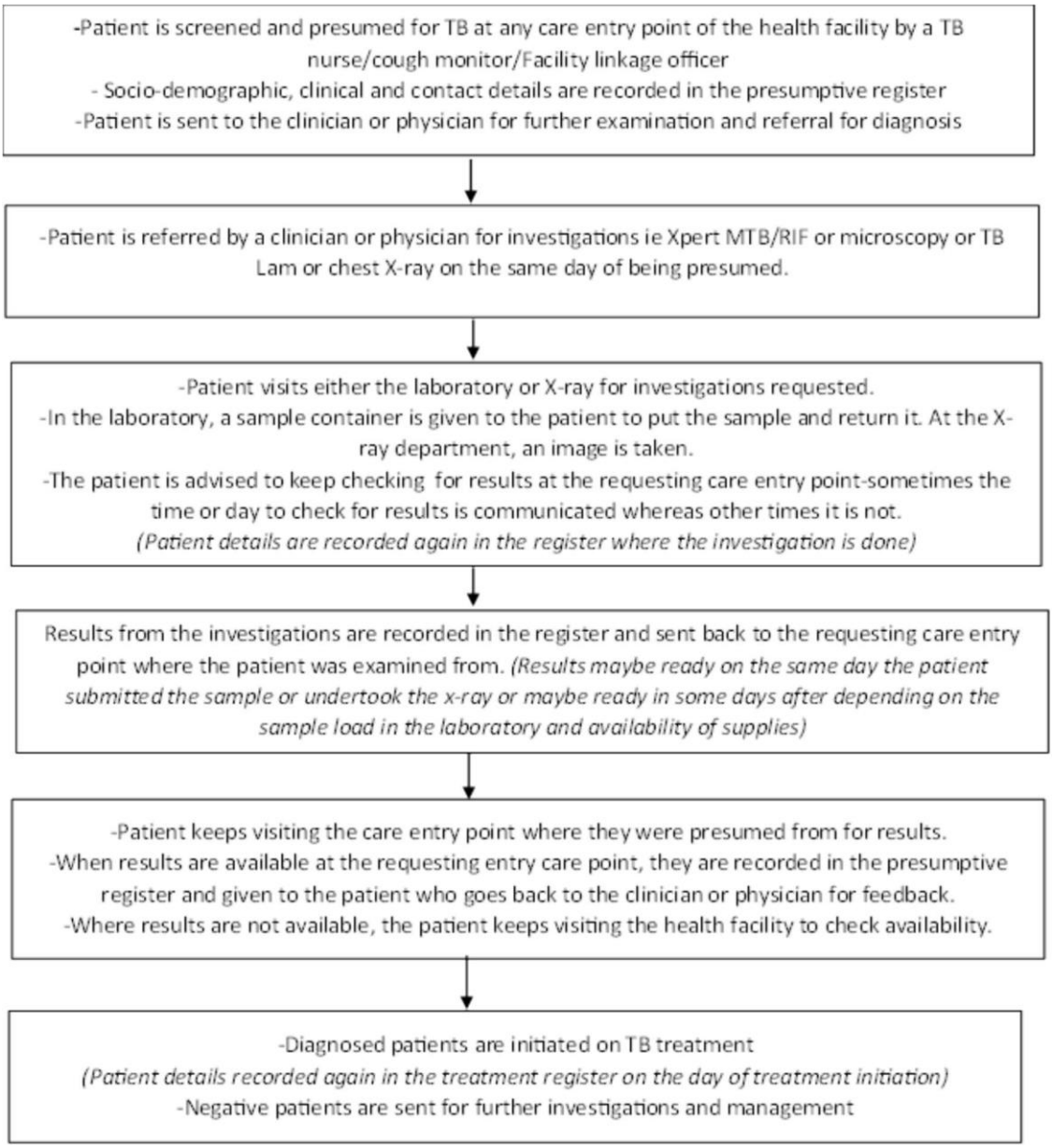


Fig. 1 Patient flow at the health facility for the diagnosis and treatment of TB

registers. A post hoc power estimation was performed using the Stata software version 14 to estimate whether we had the power to conduct the analysis.

Data collection procedures

Data were collected and cross-matched from paper-based TB registers (presumptive, laboratory, radiology and treatment). Four variables were used for cross-matching the data in the different registers: patient name, age, place of

which the patient with presumed TB was manually followed up by trained research assistants in the laboratory or radiology or treatment registers using the crossmatching variables. Data on patients with presumed TB who presented to the study health facilities were extracted from the presumptive TB registers at all screening points/units. These patients were then followed up in the laboratory and radiology registers for completion of the TB diagnostic process within 30 days from the date of being identified with presumed TB. Completion of the TB diagnostic

process referred to undertaking the requested TB investigation and obtaining results from the test within 30 days. Patients with presumed TB who tested positive for TB were followed up in the facility treatment register for treatment initiation within 14 days from the date they were diagnosed. Patients appearing in the laboratory or radiology or treatment registers who were not recorded in the presumptive TB registers were not included in the study. This is because they were referrals from other health facilities and had a different pathway. All the facilities included in this study receive referred patients for both testing and treatment initiation from other health facilities. Patients who were missing any of the four cross-matching variables in the presumptive TB register were excluded. This was because they could not be subsequently cross-matched in the other registers. Patient records which were not matching in the subsequent registers were treated as unique and crossmatched separately.

Data were collected using an extraction tool adapted from a similar study conducted in Zimbabwe [8]. The data extraction tool was pre-tested, and the refined tool was uploaded to the *KoboCollect* mobile data collection app. The following variables were extracted: age, sex, place of residence recorded (Yes/No) and phone contact recorded (Yes/No), TB disease type, HIV status and dates of presumption, diagnosis and initiation of treatment for the patients who tested positive. Data on these variables were primarily extracted from the presumptive registers at the study facilities except for variables of diagnosis and treatment initiation. In case data on any of the variables were missing in the presumptive register, effort was made to retrieve it from other registers either laboratory, radiology or treatment at the point of cross-matching the data and entered. This is because all the health facility registers used for this study record patient's demographics and clinical data.

Research assistants with experience in research and extracting data from large databases were recruited and trained in a three-day workshop for data collection. Meetings were held at the end of each data collection day to check for adherence to the data collection procedures and operational definitions, consistency, and completeness of the data collected. **Key definitions**

Patient with presumed TB: a person who presents with symptoms or signs suggestive of TB. That is; persistent cough of two weeks or more, night sweets, fever of more than two weeks, weight loss, previous contact with a TB patient and if a child, poor weight gain.

Diagnosed TB patient: a patient who is bacteriologically positive for TB by either Xpert MTB/RIF, smear microscopy or TB Lam or those detected by chest X-ray.

Completion of the TB diagnostic process: Undertaking the requested TB investigations and obtaining results (as evidenced in the TB presumptive registers) from the test within 30 days from the date of being identified with presumed TB.

Pre-diagnosis loss to follow-up: failure to test for TB and obtain results within 30 days from the date of being presumed.

Pre-treatment loss to follow-up: failure to initiate TB treatment within 14 days from the date of diagnosis.

Variables and measurements

Pre-diagnosis LTFU was measured as the proportion of patients who were lost before testing for TB and receiving results within 30 days from being identified with presumed TB out of the total number of all patients with presumed TB registered in the study period. The 30-day follow-up period was selected based on previous studies for comparison [10, 13]. Having results documented in the presumptive TB register was used as a proxy for receipt of results by the patient. The presumptive TB register was preferred for extracting data on receipt of results over the laboratory register because patients return to points of care where they were presumed for TB to obtain their results. At these points of care, patient's results are recorded and handed over to them.

Pre-treatment LTFU was defined as failure to initiate TB treatment within 14 days from the date of diagnosis based on previous studies [16, 18, 25]. This was measured as the proportion of diagnosed TB patients who were lost before initiating treatment within 14 days from when they were diagnosed out of the total number of diagnosed TB patients registered in the study period. **Data security and storage and management**

The data were submitted daily to the server and checked for accuracy and any errors which were communicated to the research assistants for correction during subsequent data extraction. The data collection phones and server were password protected. The server was only accessed by the Biostatistician and study investigators.

The final dataset was downloaded from the *Kobocollect* mobile app into an Excel spreadsheet and exported to Stata

software version 14 for cleaning and analysis. Duplicate records were removed using identifiers of age, name, and registration date when the patient is presumed for TB. Patients with presumed TB who were missing dates of registration when presumed, sample collection and results date were also excluded because these were key variables for analysis. We dropped anyone with a duplicate registration date within three days which signified double registration. We used complete case analysis where entries with missing data were deleted.

Statistical methods

Descriptive statistics such as frequency distributions, median and interquartile ranges (IQRs) were computed. The trends of pre-diagnosis LTFU over time were compared using a line graph. A modified Poisson regression analysis model via generalized linear models with family (Poisson) and a log link was constructed to obtain the estimates for factors associated with pre-diagnosis LTFU [26]. Modified Poisson regression was preferred over logistic regression because of higher proportions of pre-diagnosis and pre-treatment LTFU (i.e greater than 10%) hence, odds ratios would provide biased estimates of prevalence ratios [27, 28]. Independent variables that were statistically significant at the bivariate analysis with p-value<0.2 and those known from the literature to be associated with pre-diagnosis LTFU were entered into a model to establish factors independently associated while controlling for known confounders. The level of statistical significance was set at a p-value ≤ 0.05. An exploratory logical model-building method following the conceptualization of the study outcome and literature review was used to generate the final model. Variables in a model that were found to be consistently insignificant and did not add any value in terms of goodness of fit were eliminated. Selection of the final model was performed using likelihood ratio tests.

Results

A total of 13,496 records of patients with presumed TB were abstracted from the facility records. Of these, 432 records were excluded from the analysis (Fig. 2).

Socio-demographic and clinical characteristics of study participants

Thirty-nine percent (5,213/13,064) of the patients were aged 25 to 44 years, with a median age of 35 years (IQR, 24–50). Over half of the patients 57.1% (7,462/13,064) were female. The percentage of patients with presumed TB was highest in the year 2022 at 34.2% (4,464/13,064) and lowest in 2020 at 14.9% (1956/13,064) see Table 1. Forty-two percent of the patients were living with HIV, 42.9% (5,605/13,064) see Table 1.

Pre-diagnosis LTFU and factors associated among patients with presumed TB

Overall, 28.3% (3699/13064) experienced pre-diagnosis LTFU (Fig. 2). Over half of those who conducted the TB investigations required, did not have their test results documented in the laboratory or chest x-ray register on the same day of being presumed, 52.8% (4983/9439). TB was diagnosed among 12.7% (1187/9365) patients (Fig. 2). Pre-diagnosis LTFU among the study participants was highest in 2019 at 48.7% (1,832/3760) and 42.9% (840/1956) in 2020. This was followed by a sharp decline in 2021 to 14.3% (413/2884) and 13.8% (614/4464) in 2022 (Fig. 3).

Factors associated with pre-diagnosis LTFU among patients with presumed TB

At multivariate analysis, females (adj PR 1.1, 95% CI: 1.01,1.12), those aged 0–14 years (adj PR 1.1, 95% CI: 1.06,1.24) and patients presumed from the private not for profit (PNFP) (adj PR 1.2, 95% CI: 1.11,1.28) were more likely to experience pre-diagnosis LTFU. In addition, patients with no record of place of residence (adj PR 2.7, 95% CI: 2.54,2.93) and no record of phone contact (adj PR 1.1, 95% CI: 1.05,1.17) were also more likely to experience pre-diagnosis LTFU compared to those whose details were recorded in the registers. On the other hand, patients presumed from hospitals (adj PR 0.7, 95% CI: 0.69,0.81) and those presumed to have TB between 2020 and 2022 were less likely to be lost before completing TB diagnosis (Table 2).

Pre-treatment LTFU and factors associated among diagnosed TB patients

Thirteen percent (163/1187) of the patients who were diagnosed with TB experienced pre-treatment LTFU (Fig. 2). Pre-treatment LTFU was highest in 2019 at

15.0% (36/240) which slightly decreased in 2020 to

13.7% (20/146) and 13.2% (50/378) in 2022.

Patients who had no record of place of residence (adj PR 7.1, 95% CI: 5.16,9.88) and no record of phone contact (adj PR 2.2, 95% CI: 1.63,2.86) were more likely to experience pre-treatment LTFU compared to those whose details were recorded in the registers. Those with an unknown HIV

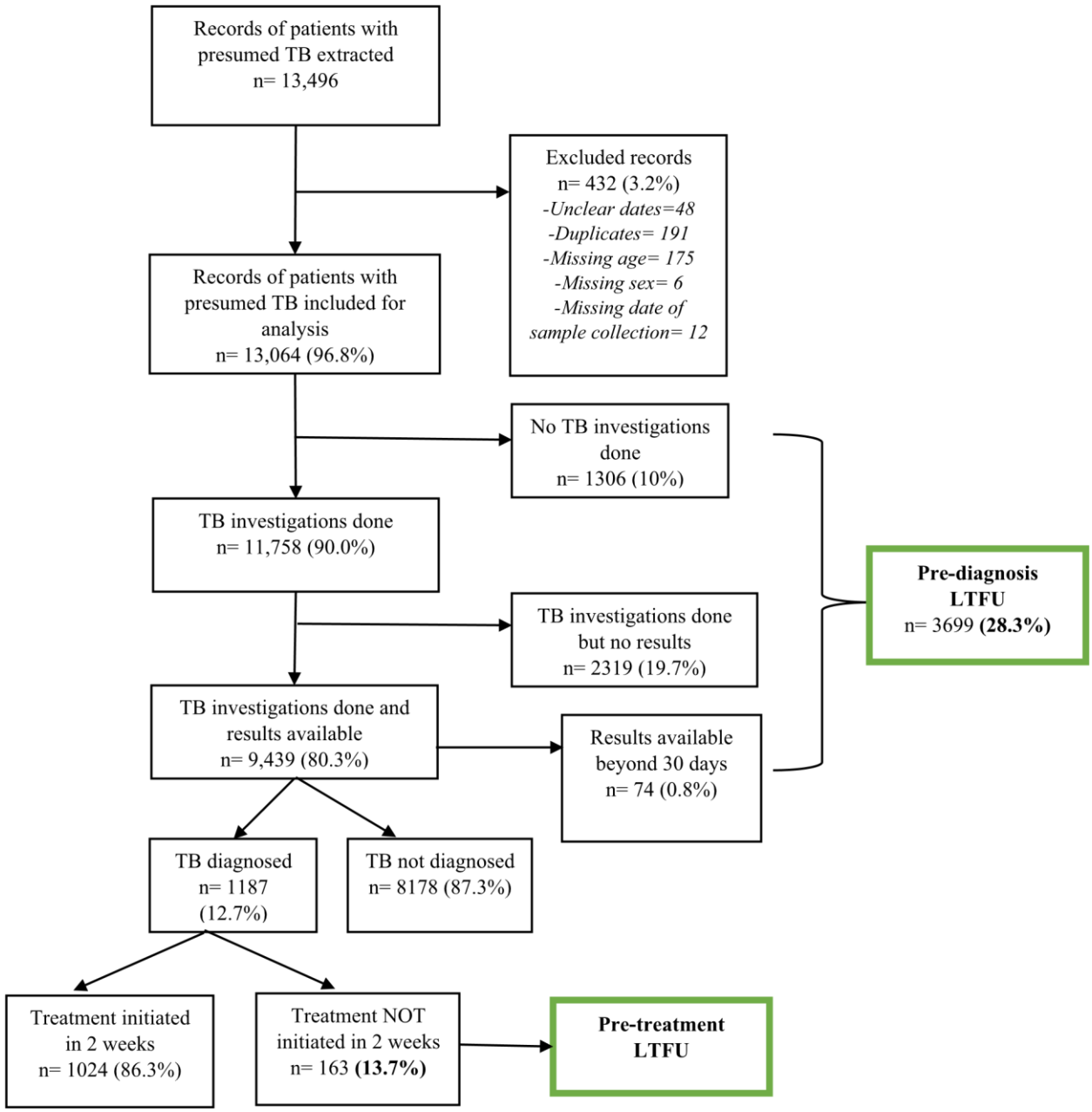


Fig. 2 Flow diagram of the data extracted and analysed

status were 1.9 times more likely to experience pre-treatment LTFU compared to those who were HIV negative, (adj PR 1.9, 95% CI: 1.09,3.27)**.** Patients presumed from the HIV clinics were 40% less likely to experience pre-treatment LTFU compared to those presumed from the outpatient departments (adj PR 0.6, 95% CI: 0.41,0.88). Patients presumed to have TB in 2022 were less likely to be lost before initiating treatment compared to those presumed to have TB in 2019 (adj PR 0.6, 95% CI: 0.42,0.96) see Table 3.

Discussion

This study assessed pre-diagnosis and pre-treatment LTFU and associated factors among patients with presumed TB and those diagnosed from 2019 to 2022 in selected health facilities in central Uganda. Twenty-eight percent of the participants experienced pre-diagnosis LTFU and thirteen percent of those who tested positive for TB did not initiate treatment within 14 days from the date of diagnosis. Over half of those who conducted the TB investigations required, did not have their results on the same day of being presumed, 52.8% (4983/9439). Pre-diagnosis LTFU was highest in 2019 and 2020 which decreased sharply in 2021

and 2022. Patients with no record of place of residence and no record of phone contact in the health facility

Table 1 Socio-demographic and clinical characteristics of the participants

Variable	***N* = 13,064 (%)**
Age (median =35, IQR; 24, 50)	
0 to 14	1603 (12.3)
15 to 24	1907 (14.6)
25 to 44	5213 (39.9)
45+	4341 (33.2)
Sex	
Male	5,602 (42.9)
Female	7,462 (57.1)
Record of place of residence available	
Yes	11,002 (84.2)
No	2,062 (15.8)
Record of phone contact available	
Yes	8,679 (66.4)
No	4,385 (33.6)
Facility unit of screening for patients with presumed TB	
Outpatient department	4302 (32.9)
TB Unit	2,995 (22.9)
Maternity	398 (3.1)
HIV clinic	3,506 (26.8)
[a]Pediatric clinic	1,284 (9.8)
[b]Community outreach programs	579 (4.4)
Year of presumption	
2019	3,760 (28.8)
2020	1,956 (14.9)
2021	2,884 (22.1)

2022	4,464 (34.2)
Facility ownership	
Public (Government funded)	10,220 (78.2)
Private not for Profit (PNFP)	2,844 (21.8)
Facility level	
Health centre IV	1,668 (12.8)
Hospital	11,396 (87.2)
Accessibility to TB testing services at the health facility	
Multiple services (Gene Xpert, microscopy, TB LAM, Chest Xray)	11,396 (87.2)
Only microscopy	1,668 (12.8)
District of presumption	
Buikwe	4615 (35.3)
Mityana	3937 (30.1)
Mukono	4512 (34.6)
HIV status	
Negative	5,936 (45.4)
Positive	5,605 (42.9)
Unknown	1,523 (11.7)

[a] These numbers were from the hospitals, the health centre IV does not have a pediatric clinic [b] Patients with presumed TB from the community outreach programs were documented only in the health centre IV a presumptive TB register at the outpatient department

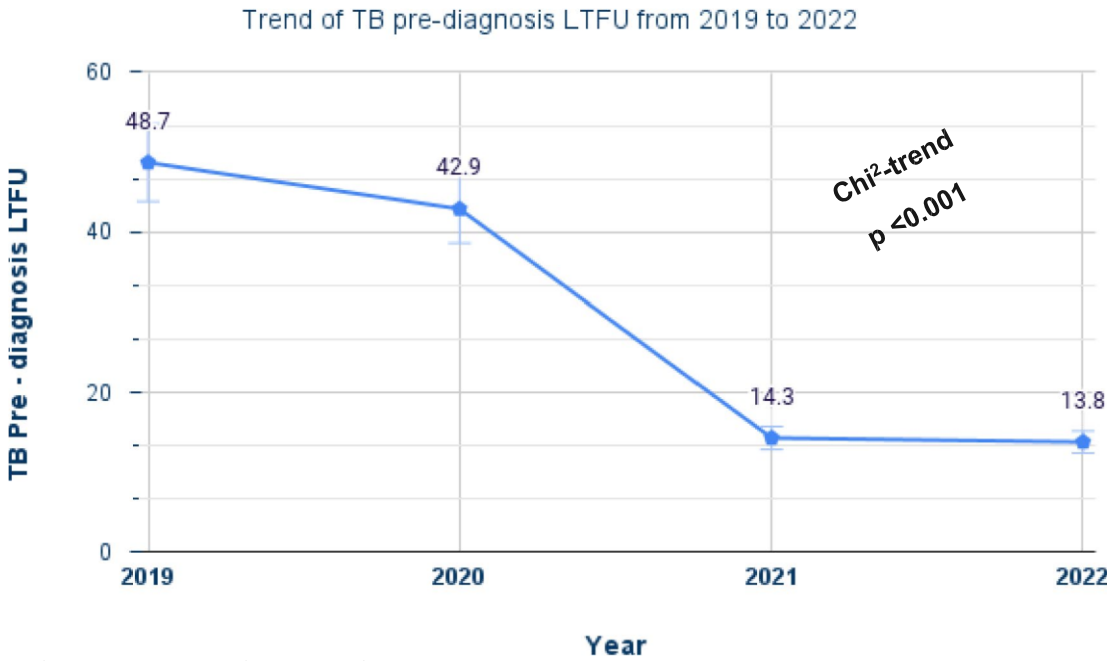


Fig. 3 Trend of pre-diagnosis LTFU of participants from 2019 to 2022

registers were more likely to experience pre-diagnosis and pre-treatment LTFU.

The high pre-diagnosis LTFU was attributed to no record of patient tracking information of place of residence and phone contact. Our study revealed that half of the participants do not have results on the same day of being presumed for TB which necessitates patients to be contacted to return and collect their results. Hence patients whose tracking information is missing and do not return on their own initiative are likely to be LTFU. Having no same day results also requires repeat visits to the health facilities hence contributing to the LTFU as seen from previous studies [29, 30]. Similar pre-diagnosis LTFU proportions have been reported in studies in Zimbabwe (10%−25%), Tanzania (16%), India (30%) and in a study of 30 countries with a high-TB burden (35%) [4, 5, 8, 10, 31, 32]. However, a previous study in Uganda reported a higher proportion of LTFU of 40.7% [12]. This could be because of the differences in the study setting, as the study by Ekuka et al. was conducted in a rural area where patients face more challenges in healthcare access. Indeed, studies have indicated that patients with presumed TB from rural health facilities tend to be LTFU [8, 32, 33]. Pre-diagnosis LTFU threatens TB control by increasing the risk of community spread of the disease hence the need for health system strengthening solutions to ensure that every patient presumed to have TB is diagnosed. Considerations should be made to strengthen laboratory services in each health facility to provide same day results for patients so as to reduce chances of LTFU. Moreso, health workers should improve documentation of patient contacts and areas of residence to ease patient follow-up for TB service provision. The government should also consider fast tracking the scale up of the electronic medical system alongside training the users and enhancing data quality assessments which have shown promise elsewhere in improving quality of routine data entry [33–35].

Similarly, the high pre-treatment LTFU reported in this study was associated with non-availability of patient tracking information of place of residence and phone contact coupled with the failure of health facilities to provide patients with same day results. Other studies have found the same reason of no patient tracking records, poor patient-provider communication, older age, history of TB disease, distance of residence from the health facility, complexity of navigating the system, and health care worker attitude as contributing factors to the pretreatment LTFU [17–19, 25, 36–38]. This proportion of pre-treatment LTFU is comparable to that in other studies, which reported a range of 4–42% [13, 16, 18, 25, 36]. The lack of timely treatment initiation for TB patients increases the severity of the disease and the likelihood of poor treatment outcomes [14, 16, 39, 40].

Patients aged 0–14 years were more likely to experience pre-diagnosis LTFU compared to those aged 45 years and above. This may be because of the existing diagnostic challenges of TB among children, such

Table 2 Factors associated with pre-diagnosis LTFU from 2019 to 2022 in study health facilities in Uganda

Characteristic	Pre-diagnosis LTFU % (n/N)	Crude PR (95% CI)	Adjusted PR (95% CI)	*P*-value
Age				
45+	28.7 (1246/4341)	1 (Ref)	1 (Ref)	
0 to 14	33.9 (543/1603)	1.2 (1.09–1.28)	**1.1 (1.06–1.24)**	**<0.001***
15 to 24	27.8 (531/1907)	1.0 (0.89–1.06)	1.0 (0.89–1.05)	0.477
25 to 44	26.5 (1379/5213)	0.9 (0.86–0.98)	1.0 (0.90–1.01)	0.120
Sex				
Male	27.4 (1537/5602)	1 (Ref)	1 (Ref)	
Female	28.9 (2162/7462)	1.1 (0.99–1.11)	**1.1 (1.01–1.12)**	**0.019***
Record of place of residence available				
Yes	26.5 (2913/11002)	1 (Ref)	1 (Ref)	
No	38.1 (786/2062)	1.4 (1.35–1.53)	**2.7 (2.54–2.93)**	**<0.001***
Record of phone contact available				
Yes	27.1 (2354/8679)	1 (Ref)	1 (Ref)	
No	30.7 (1345/4385)	1.1 (1.07–1.19)	**1.1 (1.05–1.17)**	**<0.001***
Facility unit of screening for patients with presumed TB				
Outpatient department	33.7 (1449/4302)	1 (Ref)	1 (Ref)	
TB Unit	35.3 (1056/2995)	1.0 (0.98–1.12)	**1.1 (1.03–1.17)**	**0.005***
Maternity	35.7 (142/398)	1.1 (0.92–1.21)	1.1 (0.96–1.26)	0.183
HIV clinic	21.6 (756/3506)	0.6 (0.59–0.69)	**0.8 (0.74–0.87)**	**<0.001***
Pediatric clinic	21.1 (271/1284)	0.6 (0.56–0.70)	**0.9 (0.79–0.99)**	**0.036***
Community outreach programs	4.3 (25/579)	0.1 (0.09–0.19)	**0.2 (0.14–0.31)**	**<0.001***
HIV status				
Negative	28.0 (1664/5936)	1 (Ref)	1 (Ref)	
Positive	24.9 (1399/5605)	0.9 (0.84–0.95)	1.0 (0.94–1.08)	0.784
Unknown	41.8 (636/1523)	1.5 (1.39–1.60)	**1.4 (1.30–1.51)**	**<0.001***
Year of presumption				
2019	48.7 (1832/3760)	1 (Ref)	1 (Ref)	

2020	42.9 (840/1956)	0.9 (0.83–0.94)	**0.9 (0.84–0.95)**	**<0.001***
2021	14.3 (413/2884)	0.3 (0.27–0.32)	**0.2 (0.22–0.26)**	**<0.001***
2022	13.8 (614/4464)	0.3 (0.26–0.31)	**0.2 (0.21–0.24)**	**<0.001***
Facility level				
Health centre IV	25.8 (430/1668)	1 (Ref)	1 (Ref)	
Hospital	28.7 (3269/11396)	1.1 (1.02–1.21)	**0.7 (0.69–0.81)**	**<0.001***
Facility ownership				
Public (Government funded)	29.8 (3042/10220)	1 (Ref)	1 (Ref)	
Private not for Profit (PNFP)	23.1 (657/2844)	0.8 (0.72–0.84)	**1.2 (1.11–1.28)**	**<0.001***
Accessibility to TB testing services at the health facility				
Only microscopy	25.8 (430/1668)	1 (Ref)		
Multiple services (Gene Xpert, micros- copy, TB LAM, Chest Xray)	28.7 (3269/11396)	1.1 (1.02–1.21)		
District of presumption				
Buikwe	31.9 (1470/4615)	1 (Ref)		
Mityana	29.0 (1142/3937)	0.9 (0.85–0.97)		
Mukono	24.1 (1087/4512)	0.8 (0.71–0.81)		

* Statistically significant at <0.05

as difficulty obtaining sputum and a lack of functional on the availability and decisions of the care takers to seek radiological investigations (X-rays) at health facilities care. Although our study revealed no association for pre[41–44]. Moreso, patients aged 0–14 years do not inde- treatment LTFU among this age group, a study in Uganda pendently make decisions to seek care and hence depend revealed that 18.7% of smear-positive children were not

Table 3 Factors associated with pre-treatment LTFU from 2019 to 2022 in study health facilities in Uganda

Characteristic	**Pre-treatment LTFU % (n/N)**	**Crude PR (95% CI)**	**Adjusted PR (95% CI)**	***P*-value**
Age				
45+	15.4 (57/371)	1 (Ref)	1 (Ref)	
0 to 14	15.4 (18/117)	1.0 (0.61–1.63)	1.2 (0.77–1.93)	0.394
15 to 24	13.2 (22/167)	0.9 (0.54–1.35)	0.8 (0.54–1.29)	0.416
25 to 44	12.4 (66/532)	0.8 (0.58–1.12)	1.0 (0.73–1.35)	0.968
Sex	11.9 (87/730)	1 (Ref)	1 (Ref)	

Male				
Female	16.6 (76/457)	1.4 (1.05–1.86)	1.2 (0.93–1.61)	0.149
Record of place of residence available				
Yes	10.4 (117/1129)	1 (Ref)	1 (Ref)	
No	79.3 (46/58)	7.7 (6.17–9.50)	**7.1 (5.16–9.88)**	**<0.001***
Record of Phone contact available				
Yes	10.6 (101/953)	1 (Ref)	1 (Ref)	
No	26.5 (62/234)	2.5 (1.89–3.32)	**2.2 (1.63–2.86)**	**<0.001***
Facility unit of screening for patients with presumed TB				
Outpatient department	16.9 (64/378)	1 (Ref)	1 (Ref)	
TB Unit	12.9 (46/355)	0.8 (0.54–1.09)	0.8 (0.56–1.13)	0.209
Maternity	25.00 (4/16)	1.5 (0.61–3.55)	1.4 (0.62–3.03)	0.439
HIV clinic	11.1 (37/334)	0.7 (0.45–0.95)	**0.6 (0.41–0.88)**	**0.010***
Pediatric clinic	10.6 (10/94)	0.6 (0.34–1.18)	0.7 (0.36–1.43)	0.341
Community outreach programs	20.0 (2/10)	1.2 (0.34–4.16)	2.4 (0.64–9.26)	0.190
HIV status				
Negative	13.4 (74/553)	1 (Ref)	1 (Ref)	
Positive	12.5 (76/610)	0.9 (0.69–1.26)	1.1 (0.77–1.50)	0.667
Unknown	54.2 (13/24)	4.0 (2.65–6.19)	**1.9 (1.09–3.27)**	**0.024***
Year of presumption				
2019	15.0 (36/240)	1 (Ref)	1 (Ref)	
2020	13.7 (20/146)	0.9 (0.55–1.52)	1.0 (0.58–1.58)	0.871
2021	13.5 (57/423)	0.9 (0.61–1.32)	0.8 (0.55–1.20)	0.303
2022	13.2 (50/378)	0.9 (0.59–1.31)	**0.6 (0.42–0.96)**	**0.032***
Facility level				
Health centre IV	10.2 (14/137)	1 (Ref)	1 (Ref)	
Hospital	14.2 (149/1050)	1.4 (0.83–2.33)	1.1 (0.63–1.90)	0.758
Facility ownership				
Public (Government funded)	13.9 (137/988)	1 (Ref)	1 (Ref)	

Private not for Profit (PNFP)	13.1 (26/199)	0.9 (0.64–1.39)	1.1 (0.71–1.59)	0.760
Accessibility to TB testing services at the health facility				
Only microscopy	10.2 (14/137)	1 (Ref)		
Multiple services (Gene Xpert, microscopy, TB LAM, Chest Xray)	14.2 (149/1050)	1.4 (0.83–2.33)		
District of presumption				
Buikwe	15.5 (50/323)	1 (Ref)		
Mityana	13.8 (73/528)	0.9 (0.64–1.25)		
Mukono	11.9 (40/336)	0.8 (0.52–1.13)		

* Statistically significant at <0.05

initiated on treatment [45]. Early detection of TB especially in children and adolescents is crucial for improving treatment outcomes and preventing post TB lung impairment [46–48].

Although our study showed no statistical significance between pre-diagnosis LTFU and HIV positive status, studies elsewhere have shown an association with those who are HIV positive most likely to be LTFU before completing TB diagnosis [32, 49, 50]. This maybe because of the integration of HIV and TB services in our study facilities which provides synergies for follow-up of these patients especially during drug refills. More so, it maybe because of the existing rapport already created with the persons living with HIV by the same health workers which motivated the patients to complete diagnosis. However, patients with an unknown HIV status were more likely to experience pre-diagnosis and pre-treatment LTFU. This reveals gaps in implementation of the TB/HIV testing policy in these health facilities that subsequently leads to the loss of these patients before they are tested for TB or initiated on treatment when diagnosed. Integration of TB services with other services in the health facilities may therefore be a promising avenue for reducing LTFU before completing TB diagnosis.

Pre-diagnosis and pre-treatment LTFU levels were highest in 2019 and 2020 and drastically decreased in 2021 and 2022 during the peak of the COVID-19 pandemic. The reduction in LTFU from 2020 to 2021 was attributed to the intensified efforts by the National TB and Leprosy Program (NTLP), which included the integration of TB and COVID-19 services; community campaigns such as TB Catch-up and Community Awareness, Screening, Testing, prevention and treatment to end TB Campaign (CAST TB), which involved community awareness of TB; and intensified screening and diagnosis of patients for TB [51, 52]. These findings are similar to those of national and WHO reports showing that Uganda is one of the countries that quickly recovered from the effects of COVID-19 in terms of case notification of newly diagnosed TB patients [1]. The integration of health services, especially during outbreaks, is key to ensuring continuity of service delivery while harnessing the power of available human resource.

Patients presumed from hospitals had a less likelihood of pre-diagnosis LTFU for presumptive TB patients compared to those in lower-level health facilities. This maybe because of the availability of the testing services on-site and increased staffing which enables a short turnaround time of results for patients. Patients in the lower-level health facility depend on microscopy for testing which has a low sensitivity hence their samples have to be referred to nearby hospitals for Xpert MTB/RIF which process increases the turnaround time and the likelihood of patients being LTFU [53]. These findings are similar to a study by Chilembo et al., in Zambia which showed that patients who were diagnosed with smear microscopy were more likely to be LTFU compared to those of Gene Xpert [54] and other studies which showed participants in lower-level health facilities are likely to be LTFU [8, 32, 55]. The Xpert MTB/RIF assay has a short turnaround time for results but is expensive hence not available in all health facilities. These findings emphasize the need to increase investment in Xpert MTB/RIF assays for lowerlevel health facilities in order to reduce the turnaround time for TB results, reduce sample loads referred to higher facilities but to also save patients additional health care costs associated with repeat visits to the health facilities.

The numbers of patients with presumed TB mirror the TB screening gaps at the study facilities where it is lowest among the children, adolescents and young people compared to patients aged 25 years and above. Moreso, screening is not systematically done at all entry care points as per the Uganda ministry of health guidelines that recommend TB screening of all patients presenting to health care facilities [56]. Screening of patients enables early detection of TB and treatment initiation which subsequently improves on the patient outcomes [46]. The maternity unit, where pregnant women receive antenatal care, had as low as 3.1% of patients with presumed TB which indicates a low screening level. This may be due to the low suspicion levels of the health workers at these maternity entry points but also the TB symptoms such as weight loss, fever and night sweats mimic the physiological changes that occur during pregnancy hence may easily be ignored [57, 58]. TB in pregnancy leads to poor outcomes for both the neonate and the mother including maternal anaemia, miscarriage and deaths hence the need to enforce the screening of pregnant women for early detection [58, 59]. The ministry of health should enforce systematic TB screening at all care entry points in health facilities by ensuring sensitisation of patients on the signs and symptoms of TB so that they volunteer to be screened and refresher trainings for health workers on TB screening.

A key strength to our study is the use of routine data from TB services to identify factors associated with prediagnosis and pre-treatment LTFU. This enabled identification of gaps in TB health services in Uganda and thereafter making practical recommendations for health service improvement. Another strength is the analysis of data giving a perspective of one year before the COVID19 pandemic (2019) and three years into the pandemic (2020–2022). This provides information on the effect of disease outbreaks on the continuity of service provision and health seeking behaviors of the patients. This information may inform preparedness and response planning for future outbreaks and pandemics. We also had a large sample size of 13,064 which improved the precision of the estimates.

However, we utilized secondary data which often presents with missing data and quality issues. We mitigated the likelihood of this by cross-matching data from the presumptive, laboratory and TB unit treatment registers during data collection to limit the missingness of data on key variables such as age, sex, date of sample collection and results received. This information is often recorded in at least two of the health facility registers. Where data were completely missing on some variables, we used complete case analysis and deleted those entries. We acknowledge that this method often excludes potentially important data and reduces the statistical power. However, with the post-hoc power estimation, we still had power to conduct the analysis even after deleting the missing data. Moreso, availability of results in the presumptive TB register was used as a proxy for the completion of the TB diagnostic process, which may not translate to a patient receiving results for

further management. A prospective study is recommended for future studies to establish the actual receipt of results by patients as an endpoint for the completion of the TB diagnostic process. Another limitation is that we could not verify whether the patients who were LTFU before completing the TB diagnostic process completed the diagnosis from another health facility elsewhere or did not complete at all. We recommend that future studies explore whether the TB diagnostic process is completed elsewhere through the use of patient pathway analysis and more robust triangulation methods across health facilities.

Conclusion

In this retrospective cohort analysis study in central Uganda, we found a high pre-diagnosis LTFU of 28% among the patients with presumed TB and pre-treatment LTFU of 13% among those diagnosed. This calls for urgent interventions to reduce these losses in the care cascade to be able to realise the End TB Strategy. Over half of participants who conducted the TB investigations required did not have results on the same day of being presumed. There is need to strengthen the capacity of laboratories to provide same day results for patients so as to reduce chances of LTFU. No record of place of residence or phone contact in the patient registers was significantly associated with LTFU, which calls for improved documentation at health facilities to ease patient followup for TB service provision and contact tracing.

Abbreviations

Adj	Adjusted
ART	Antiretroviral therapy
CAST TB	Community Awareness, Screening, Testing, prevention and treatment to end TB Campaign
CI	Confidence Interval
COVID-19	Coronavirus disease
HIV	Human immunodeficiency virus
IQR	Interquartile ranges
LMICs	Low- and middle-income countries
LTFU	Loss to follow-up
MOH	Ministry of Health
NTLP	National TB and Leprosy Program
PNFP	Private-not-for-profit
PR	Prevalence ratio
TB	Tuberculosis
UN	U nited Nations
WHO	World Health Organization

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Authors' contributions

RN co-conceptualised the study with EB and coordinated the implementation including manuscript writing. STW, MN, AND LN participated in study implementation, data analysis and manuscript writing. NK, HL, ST, JNS and LA provided technical support during implementation of the study and guided the contextual interpretation of the results during analysis and manuscript writing. EB conceptualised the study and provided overall technical guidance during implementation and manuscript writing. All authors read and approved the final manuscript.

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Data availability

The data and materials supporting results of this manuscript are available through the Research and Ethics Committee of Makerere University School of Public Health. They can be contacted at hdrecadmin@musph.ac.ug.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki [60].

Approval to conduct the study was obtained from the Research and Ethics Committee of Makerere University School of Public Health (#SPH-2023-427), and the study was registered with the Uganda National Council of Science and Technology (HS3000ES). The privacy and confidentiality of all the data obtained was ensured by limiting access of the data to only the study investigator and data manager. Since this was a review of records with no face-to-face interviews with patients, the need for informed consent was waived by the ethics committee.

Consent for publication Not applicable.

Competing interests

The authors declare no competing interests.

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Appendix 3: Paper 2-Facilitators and barriers for completion of the diagnostic process among people with presumed tuberculosis in Central Uganda (Nuwematsiko, 2025)



RESEARCH ARTICLE

Facilitators and barriers for completion of the diagnostic process among people with presumed tuberculosis in Central Uganda

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Abstract

Uganda has improved its tuberculosis (TB) diagnostic processes over the years since the scale up of the Xpert MTB/RIF testing in 2012. However, there are continued

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delays in diagnosis and missing people with TB who are either not diagnosed or noti-fied. We explored facilitators and barriers for completion of the TB diagnostic process among people with presumed TB in selected health facilities in Central Uganda.

This was a qualitative exploration involving 25 in-depth interviews with people with presumed TB and six sex stratified focus group discussions with people with TB who had recently initiated treatment. We also conducted 20 key informant interviews with health workers providing TB services. All interviews and discussions were audio recorded and transcribed verbatim. Thematic analysis was carried out using Atlas.

ti software version 6.0 guided by the constructs of the socio-ecological model. Key facilitators for completion of the TB diagnostic process included; individual factors (persistent symptoms and the desire to get better, obtaining same day results and prior TB knowledge); community (social support); and health system factors (caring health workers and calling of patients to collect results). Barriers were; individual fac-tors (TB and HIV stigma, inability to produce sputum, lack of transport to return to the health facility); and health system factors (long turnaround time of results, stock out of supplies, unclear appointment for collection of results, inadequate patient contact details and negative health worker attitude). Completion of the TB diagnostic process is influenced by individual, health system and community related factors. To enhance completion, there is need for availing same day results, making clear appointments for collection of results and improving health worker attitudes at the health facility level. At the individual and community level, TB/HIV stigma reduction interventions,

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Data availability statement: All the data and materials supporting this manuscript are within the paper and the supplementary file, also accessed at the Zenodo repository (https://doi.org/10.5281/zenodo.16944363). More information can be requested through the Research and Ethics Committee of Makerere University School of Public Health. They can

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community health education on TB and provision of social support to patients with presumed TB should be emphasized.

Introduction

Tuberculosis (TB) remains a significant global health challenge and in 2023 it was ranked the leading cause of death from a single infectious agent [1]. The Sustain-able Development Goals (SDGs) call on all countries to find the missing TB patients in order to end the TB epidemic by 2035 [2,3]. This has however been challenged by the continued loss of people with presumed TB before they complete the diag-nostic process (pre-diagnosis loss) and before initiating treatment if diagnosed with TB (pre-treatment loss) [4,5]. People with presumed TB are adults or children with symptoms suggestive of TB; cough, fever, night sweat, weight loss and previous contact with a TB patient. Pre-diagnosis and pre-treatment loss of patients facilitates continued spread of TB in the community, poor treatment outcomes for persons with TB and death [4–8]. In Sub-Saharan Africa, 48.5% of people with presumed TB are lost before receiving a diagnosis according to a systematic review and metanalysis of studies [9]. This burden of people with presumed TB getting lost before being diagnosed is shared across all TB-burden countries although it is highest in high-TB burden countries compared to low-burden countries [4,6].

Uganda is among the 30 TB/HIV high burden countries [1] with an incidence of 198 cases per 100,000 people [10]. In 2023, the country's TB case notification rate decreased to 178 cases per 100,000 people up from 200 cases per 100,000 in 2022, indicating a gap in diagnosis and notification [1,10]. Relatedly, studies in Uganda

by Ekuka et al., [11] and Nuwematsiko et al., [12] showed that 40.7% and 28% of patients who are presumed with TB do not complete the diagnostic process respec-tively. In order to improve case detection and notification, the country adopted the World Health Organization (WHO) TB systematic screening and testing strategy at all health facilities but its implementation is low at 75.1%, below the 100% target [10,13]. Although this intervention is in place to foster increased case detection, people with presumed TB continue to be lost in Uganda before completing the diagnostic process and initiating treatment. Completion of the TB diagnostic process refers to undertak-ing the requested TB investigations and obtaining results from the test within 30 days from the date of being identified with presumed TB [12].

There is paucity of data on factors for the loss of patients before completing the TB diagnostic process in Uganda. A previous study by Zawedde-Muyanja et al., [14] explored factors for the loss of patients largely before treatment initiation leaving gaps on an in-depth analysis of the phase before one is tested and diagnosed for TB. Understanding factors that influence completion of the TB diagnostic process will pro-vide in-depth contextual insights into these factors which will inform local strategies for improving the Uganda TB response thus contributing to the global goal of ending TB by 2035. This study therefore explored facilitators and barriers for completion of the diagnostic process among people with presumed TB in selected health facilities in Central Uganda.

Methods and materials

Study design and setting

We utilised an explanatory qualitative phenomenological study design to explore facilitators and barriers for completion of the TB diagnostic process. This was part of a study to evaluate the TB diagnostic process and linkage to care in Cen-

tral Uganda. Quantitative findings of the evaluation showed that 28% of the people with presumed TB were lost before completing the diagnostic process [12]. We hence sought to understand the influencing factors for the loss of patients and facilitators for completion of the diagnostic process. Focus group discussions (FGDs), Key informant interviews (KIIs), and in-depth interviews (IDIs) were conducted. The Consolidated Criteria for Reporting Qualitative Research (COREQ) guided the study-*S1 File* [15].

The study was conducted in purposively selected four health care facilities in Central Uganda that is; St. Francis Hospi-tal Nagalama (Private-not-for profit) and Kojja health centre four (IV) in Mukono district (lower-level health facility); Kawolo Hospital in Buikwe District and Mityana Hospital in Mityana District. Selection of study facilities was based on level of facility (hospital or health centre) and ownership type that is either public or private-not-for profit to ensure rich information. Health care services in Uganda are offered by both the government (public) and private providers. The health system is arranged in a tier-system including national referral hospitals, regional referral hospitals, district (General) hospitals and health centres, four (IV), three (III) and two (II) [16]. General hospitals serve districts and provide general medical and surgical services targeting a population of approximately 500,000 people. Health centre IVs serve a county or municipality with a population of approximately 100,000 people. They provide emergency surgery and blood transfusion services in addition to all general medical services [16]. TB services are offered from health centre III up to the national referral hospi-tals. More than half of the households, 72% in Mukono, 68% in Buikwe and 72% in Mityana districts are within 5 km radius to the nearest public health facilities [17]. Over half of the population, 56%, own mobile phones in the Buganda region of the country where the study sites, Mukono, Mityana and Buikwe districts are located as indicated in the recent National Population and Housing Census results of 2024.

In all the study facilities, both the health centre IV and general hospitals, the TB diagnostic process runs from being screened for TB symptomatically to receiving test results. Systematic TB screening is done at the different points of ser-vice delivery using the Intensified Case Finding Form [13]. A patient is presumed with TB if they have any of the cardinal symptoms: persistent cough of two weeks or more, night sweats, fever of more than two weeks, weight loss and if a child, poor weight gain and previous contact with a person with TB. Patients with presumed TB are then sent for laboratory or radiological investigations depending on the presenting condition. Xpert MTB/RIF is the recommended first diagnostic test in Uganda but also microscopy, urine lipoarabinomannan (LAM) and chest X-ray are used [13]. Patients' results are then sent to the point of service delivery that referred the patient. Patients are expected to return to the service delivery points and collect the results. Patients either receive results that same day of testing or are asked to return another day and check for their results hence they make several trips to the health facility until the results are ready. Diagnosed patients who test positive for TB and did not receive same day results are often called back to the health facilities through phone calls and initiated on treatment through the TB clinics [12,14]. Calling of patients is however inconsistently done due to resource limitations. Patients who test negative for TB are rarely called back; they are expected to return on their own whenever ready to collect the results. Patient demographics, address, telephone contacts and clinical details are recorded in the registers at every service delivery point for tracking and accountability purposes [13].

Study population, sample, and data collection

We conducted 25 IDIs among patients identified with presumed TB in the study facilities. Participants were selected from the presumptive TB registers at each health facility by the research team supported by health workers. We included patients who were aged 18 years and above and were presumed for TB in the past one month. Purposive sampling was

used to select participants for the IDIs based on their completion status of the TB diagnostic process (completed diagnos-tic process for TB within 30 days from when they were presumed for TB/not completed at all). Selection ensured repre-sentation of both males and females. Conducting IDIs among patients who had completed the diagnostic process and those who had not and with the different sexes was to ensure rich and diverse perspectives of the findings. People with presumed TB who reported being critically ill were excluded. The IDI interview guide was developed containing open-ended questions on facilitators and barriers to completion of the TB diagnostic process as well as suggestions on increas-ing completion *(S2 File)*. Some of the questions included understanding of the patients' knowledge on TB, experiences

as they navigated the TB diagnostic process, facilitators and barriers to submitting a sample for testing and collecting of results. The interview guide included probes to elicit more responses from participants but also to guide the interviewers on making checks for responses of previous participants to ensure credibility of the findings. The IDI guide was translated to Luganda, the most common language in the study area and pretested in one health facility in Wakiso district to ensure it yields the data needed. To limit bias in the study findings, the pretest was conducted in one health facility in Wakiso dis-trict, which had similarities with the study sites in Mukono, Mityana and Buikwe districts such as being in Central Uganda and having both urban and semi-urban catchment populations. The tool was then revised based on the feedback obtained from the pre-test to improve on the clarity of questions and include more probes. Interviews were conducted in *Luganda* and lasted about 40–60 minutes.

Six FGDs were also conducted with TB patients aged 18 years and above who had been on treatment for one month to understand their experiences as they went through the diagnostic process after being identified with presumed TB.

The selection of one month was to limit the recall bias from the participants. The FGDs were organized to be sex-specific groups. This is because TB is a highly stigmatized disease hence participants in the opposite sexes would not be comfort-able inadvertently disclosing their TB status and sharing experiences leading to potential biased responses. Participants were purposively selected by the research team from the TB unit treatment registers at each health facility based on the inclusion criteria with the support of health workers. A focus group discussion guide was developed containing open-ended questions and probes on facilitators and barriers to completion of the TB diagnostic process as well as suggestions on increasing completion *(S2 File)*. The discussion was conducted in *Luganda* by a trained researcher and lasted between 50 minutes and 1 hour.

Names of eligible participants for both the IDIs and FGDs sampled from the presumptive and TB unit treatment regis-ters were handed over to the TB facility linkage officers who contacted the patients through phone calls using the contacts recorded in the registers at the health facilities. The TB facility linkage officers were introduced to the study and taken through the objectives and procedures for inviting participants for the interviews. During the phone conversation, they introduced the study to the potential participant as guided by the research team and invited the participant to come to the health facility for the interview if willing to participate. Selected patients whose phone contacts were unreachable at the time of data collection were contacted through the next of kin whose contacts are also recorded in the registers.

In addition, 20 KIIs with TB focal persons, heads of outpatients' departments (OPD), HIV/ART clinics, in-patient depart-ments, laboratories and TB community linkage officers were conducted. The KIIs were selected purposively based on those who often interact and offer services to patients with presumed TB and those diagnosed in each study facility. That is, health workers who either provide TB screening or health education or counselling or testing or treatment to those diag-nosed. Health workers who were on leave during the time of data collection were excluded from the study. We developed the KIIs interview guide containing open-ended questions with probes on experiences providing services to patients with presumed TB right from the point of screening to initiating treatment if diagnosed *(S2 File)*. We also explored their per-spectives on likely facilitators and barriers to completing the TB diagnostic process and suggestions on increasing com-pletion. Interviews with the health workers were conducted mainly in English.

The three methods of data collection that is; FGDs, KIIs and IDIs were used to enable triangulation of findings from the different methods

and participants so as to obtain more rich data. All interviews were conducted between 18th April and

7th June 2023 by two trained qualitative researchers (RN and VK), male and female who hold a master's degree in Public Health and Sociology respectively. The two researchers were involved in the design of the study and drafting of the inter-view guides *(S2 File)*. A two-day training on data collection was conducted for the interviewers together with the rest of the study team to ensure quality of the data to be collected. The training covered basic information on TB and the diagnostic process, ethics of conducting research, skills and procedures in conducting qualitative interviews and an overview of the interview guides. All interviews were conducted at the study health facilities in a place deemed safe, private and comfort-able for both the research assistant and respondent and there were no non-participants during the interviews to ensure privacy. All interviews and discussions were audio recorded after obtaining written informed consent from the participant and notes taken by a trained note taker. Meetings were held at the end of each day between the qualitative researchers who were conducting interviews and other study investigators to check for adherence to the data collection standard oper-ating procedures and to discuss emerging codes and themes about completion of the TB diagnostic process.

Data management and analysis

Audio recordings were transcribed verbatim in English by the researchers who conducted the interviews (VK and RN). The transcripts were cleaned and checked against the original audios to ensure quality and that complete data is available for analysis. Thematic analysis was done following the steps suggested by Braun and Clarke [18]. Two researchers (VK and RN) experienced in qualitative research read through selected transcripts to familiarise themselves with the data. The research-ers then read through the transcript the second time to develop codes independently using an abductive approach. For confirmability, the independent lists of codes from the two researchers were reviewed by other core study team members (EB, RN and LA) to assess agreement. Any discrepancies were clarified and resolved by comparing each coder's results with raw data until consensus was reached. The codes were then applied for line-by-line coding using ATLAS.ti software (version 6). The codes were analysed to formulate themes *(S3 File)* which were further refined guided by the constructs of the socio-ecological model and researcher's experiences during data collection. The socio-ecological model is based on the notion that behaviours are as a result of the complex interaction between humans and the environment where the two influence each other. The model conceptualizes this influence at different levels of; individual, interpersonal relationships, community and policy by Bronfenbrenner, 1994 [19]. Findings from this study were shared back with participants during an insight workshop for their feedback which further guided the interpretation of the results. The research team triangulated data from all interviews at analysis to improve on the credibility of the findings. Relevant quotes were selected to represent the main themes. We conducted methods and data source triangulation where we used various data collection methods that is; IDIs, KIIs and FGDs. These methods further included varied participants to ensure collection of data from different sources. These included participants who had completed the TB diagnostic process, and those who had not completed
at all or initiated TB treatment if diagnosed for the IDIs; TB patients who had recently initiated treatment for the FGDs and TB health care workers. Data from these different methods and participant categories were coded independently by the researchers and later harmonized in the analysis meetings with all study investigators.

Ethical considerations

Makerere University School of Public Health Research and Ethics Committee granted approval for the study *(Protocol number:799)*. The study was further registered with the Uganda National Council of Science and technology *(HS993ES)*. We obtained written informed consent and all participants signed the forms before participation in the study. All partici-pants consented to be audio-recorded during the interviews and discussions. We maintained confidentiality of all data obtained by limiting access of the data to only the study investigator and data analysts. People with presumed TB who did not complete the diagnostic process, those who still had symptoms suggestive of TB and those diagnosed who had not started treatment were referred to the TB focal persons at the study sites for further management. Field researchers

practiced infection prevention and control measures at all times during the data collection to protect themselves and the participant against COVID-19, which measures also doubled for protection against acquiring the TB infection. Some of these measures included masking, handy hygiene with an alcohol-based sanitizer and keeping a social distance of 2 meters *(S4 File).*

Results

Characteristics of study participants

Out of 25 in-depth interview participants interviewed, 15 were female and almost a third aged between 45 years and above. Almost half (11/25) were farmers by occupation. We conducted six focus group discussions with 42 participants ranging between 6–8 per group, an average of seven participants. Most participants of the focus group (14), were aged 31–39 years of age and more than half (23), were females. Of the 20 key informants; three-quarters of them were female and most aged between 20–30 years (6) and 31–40 years (6).

Interviews from the patients (IDIs and FGDs) and health workers (KIIs) showed similar views on the facilitators and barriers to completing the TB diagnostic process, therefore the presentation of the results is integrated. Where necessary the similarities or differences across participant categories are highlighted. The findings are presented according to the categories of individual, health system and community factors. Six themes were obtained that is; i) individual level facil-itators ii) individual level barriers, iii) health system facilitators iv) health system barriers v) interpersonal and community facilitators and vi) interpersonal and community barriers. Findings are summarized in Fig 1.

Facilitators for completion of the TB diagnostic process

Three themes with corresponding sub-themes emerged under facilitators for completion of the TB diagnostic process: i) individual facilitators (persistent symptoms and the desire to get better, obtaining same day results and prior TB knowl-edge) ii) health system facilitators (caring health workers, support from cough monitors and facility linkage officers,

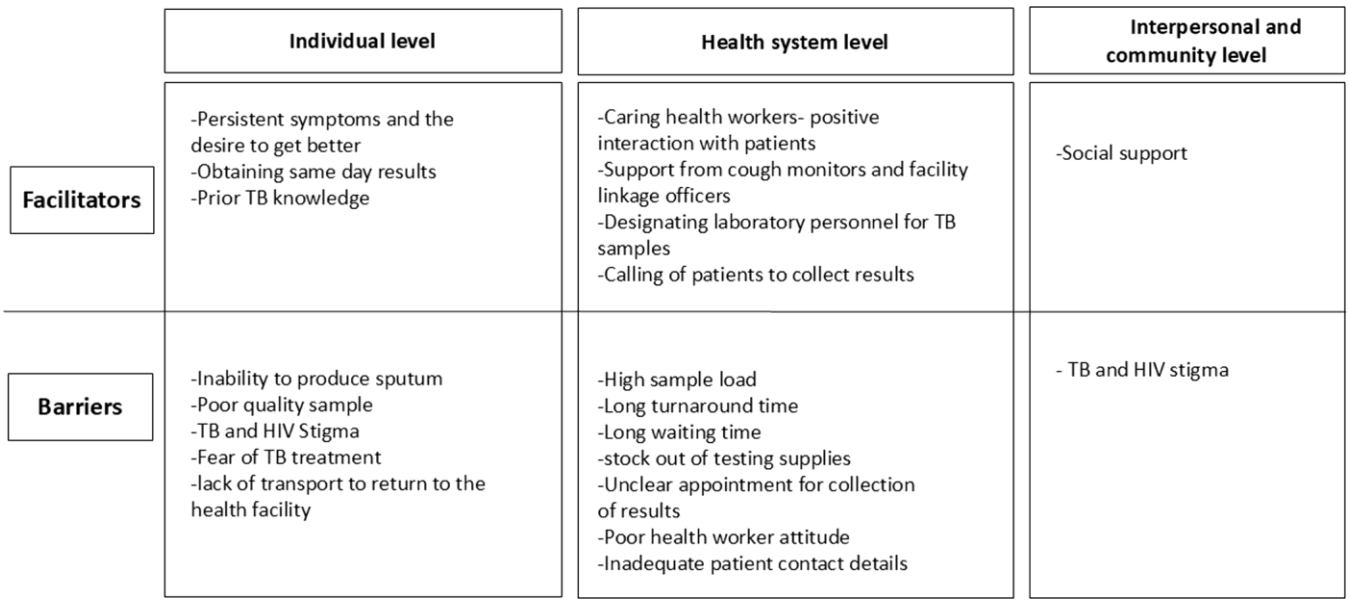


Fig 1. Results framework based on the socio-ecological model [19].

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designated TB laboratory personnel and calling of diagnosed patients to collect results) and interpersonal and community facilitators (social support).

Individual level facilitators

Almost all IDI participants who completed the TB diagnostic process and those in all FGDs, mentioned that experienc-ing persistent TB symptoms and the desire to get better was a facilitator for completing the diagnostic process. Par-ticipants stated that the pain alone from the persistent symptoms was a motivation to go through the whole process of getting a diagnosis and initiating treatment if diagnosed with TB in order to get better. In some instances, participants mentioned taking medication either from private clinics or pharmacies to get relieved of the symptoms which still per-sisted thus prompting them to get tested for TB. Persistent cough with chest pain was the commonly mentioned symp-tom mentioned by most participants, cutting across females and males. Relatedly, compared to females, more males expressed coming to the health facilities when already in too much pain hence motivated to complete the diagnostic process.

"It was the pain that I was going through that motivated me to do everything that the health workers asked me to do. I always had fevers, would cough a lot and had been on treatment for a long time with no change…." **39-year-old female IDI participant, completed the diagnostic process**

Obtaining same day results: few participants mentioned receiving results on the same day of being presumed for TB and attributed their completion of the diagnostic process to that. They said it was because they were able to wait and get their results without the need to return to the health facility which was associated with more transport costs, need for time off work and potential stigma from repeat visits to the health facility. Obtaining same day results was commonly mentioned by participants in the private not-for profit health facility. One participant in a female FGD affirmed that if she had not received results that very day, she would never have come back to complete the TB diagnostic process for fear of being stigma-tized by her family.

"I feared people at home to know that I have TB…if I was not told that I have TB on that same day and also given drugs, I do not think I would have come back to the hospital" **25-year-old female FGD participant, Hospital**

Having prior knowledge on TB was mentioned as another key facilitator to completing the TB diagnostic process. This was because the patients already knew about TB, the benefits of testing and wanted to know the results. This was commonly mentioned by IDI and KII participants. The knowledge was obtained through previous experience with people with TB either by nursing or living with them, having a history of TB and interaction with people with TB in the community. Com-pared to females, males were less knowledgeable on TB. Additionally, sensitization from health workers in previous health facility visits was mentioned as a source of TB knowledge for some participants. In one of the KII, a participant explains how prior knowledge motivates the patients:

"There are clients that we get who come straight to be tested for TB. They do not wait to be screened. They see the signs and symptoms and come. We get those too a lot. So, someone like that easily complies with the processes… Sometimes the client has a TB patient at home, so when they start to cough, they turn up to be tested too." **47-year-old female KII_TB unit, Hospital**

On the other hand, in all FGDs, it was mentioned that some patients don't submit the sputum samples and return to collect results because they have limited knowledge on TB. The knowledge gap was specifically on the benefits of testing, not knowing that TB can be cured and consequences of not getting treatment if one has TB.

Health system facilitators

Caring health workers: The positive interaction with healthcare workers motivated patients to get tested for TB. This was mentioned by most IDI participants who completed the TB diagnostic process and in most FGDs. The care was reported in the form of counselling, talking to them politely, guidance on the next steps in the diagnostic process and giving them extra information on TB. The care from health workers was also described to motivate patients who were diagnosed with TB to proceed further and start treatment. This was pointed out mainly by males and adults above 30 years across all the health facilities.

"According to what you have gone through while suffering from what you don't know, you can come here and ask for the tests yourself. The health workers are caring in a way that when you come, they immediately attend to you. The health worker's attitude and how they talk to us motivates us. These health workers always help to show us what to do and where to go." **51-year-old male FGD participant, Hospital**

From the health system perspective, the care and support from cough monitors (health workers designated to assist in cough monitoring for a sputum sample from people with presumed TB) and TB facility linkage officers enables sensitiza-tion, symptomatic screening of patients and patient follow-up for samples and treatment initiation as mentioned by most KIIs. In the KIIs, it was noted that patient screening and follow-up would have been challenging with the heavy workload and low staffing especially in the hospitals. Having these support staff was therefore viewed as a strong pillar for support-ing patients to complete the diagnostic process since they are mainly designated to do that with limited competing work. Furthermore, staff from the TB departments were described by all laboratory personnel as caring, supportive and respon-sible. They described their support in; sample collection, following up submitted samples for results, calling back patients (those with poor quality samples or whose samples were lost) and sometimes collecting the printed results and dispatch-ing them to the requesting departments. This was mentioned to reduce the work load of the laboratory staff thus reduc-ing the turnaround time of the results. In one health facility, staff from the TB departments were mentioned to support in sample collection from patients at the different service delivery points to reduce on the waiting time at the laboratory. One key informant mentioned how the support from the TB focal person helps them not to miss out on testing any patient;

"There is a close link with the TB personnel who really support us a lot...The good thing is that the TB focal person for the facility is really active. So, he always comes in and then checks on how many patients were worked on, what are the details, what could be the results." **36-year-old female KII_laboratory, Health centre IV**

Having designated laboratory personnel to run TB samples was mentioned in most KIIs as a strong facilitator for having a diagnosis for patients. These designated personnel prioritize the TB samples in addition to the other laboratory workload and ensure that all samples received are run on time and sends back results to the requesting departments. It was noted that these personnel also take the initiative to alert the requesting unit and TB focal person once a patient's result comes out positive. This is to ensure that the patient is called back to the health facility to initiate treatment. In two health facil-ities, it was mentioned that this laboratory person prioritizes patients with presumed TB for sample collection to reduce their waiting as a way to motivate them to complete the diagnostic process. Additionally, one key informant, a laboratory manager, mentioned that not all staff want to process and analyse TB sputum samples because they find them unpleas-ant. She explained that previously, most of the laboratory staff would leave the sputum samples unanalyzed for her to pro-cess when on duty. This prompted her to designate specific personnel to analyze these samples so that

patient's results are not delayed.

Calling of patients diagnosed with TB to collect results also facilitated almost all participants who were diagnosed to collect results and start treatment. In the majority of the KIIs, participants said they always call back patients who are diagnosed with TB to return to the health facilities and initiate treatment immediately. This happens in cases where the patient had left the health facility without collecting their results. Health workers contact patients by telephone using the contact details recorded in the health facility registers or those of the next of kin if the patient is unreachable on their personal telephone. Participants in some of the IDIs and all FGDs also said the same, that the phone call helped them to come back to the facility, collect results and initiate treatment.

"The health worker called me directly and told me that the results from my sputum show that I have TB and also asked me if I can go there on Monday and start taking drugs. I was going through a lot of pain. I had coughed for weeks…
I was looking forward to Monday to go to hospital and start my medications." **39-year-old female FGD participant, Hospital**

However, some KIIs stated that calling of patients was sometimes challenged by no airtime to make the phone calls and poor record taking of the patient contact details. It was noted that some health workers do not record the contact num-bers of the patients or record incomplete numbers. On the other hand, other KIIs pointed out that patients submit wrong or incorrect contact numbers when they feel they don't want to be contacted. This was mentioned to be common among young people and those who stay in distant places.

"The other problem I have seen is amongst the youth and the people on islands, some of them forge numbers (tele-phone contacts). They give us forged telephone numbers. There is a client that we received I think in 2021 from Buvuma (an island). The lady turned TB positive, we tried to call and the phone was not available. It was not available on the network. So that is a problem too." **23-year-old male KII_TB Unit, Hospital**

Interpersonal and community facilitators

Receiving social support was mentioned by most IDI participants and few FGDs as a key factor that encouraged them to get tested for TB, collect results and initiate treatment when diagnosed. The support came mostly from parents, spouses and close relatives in the form of accompanying them to the health facility, advising and counselling them to get tested, and giving them money for transport and food while visiting the health facility. The social support was more pronounced among females and the young people under 35 years of age as narrated below;

"My mother encouraged me to come for testing to see what is wrong with them. She also counselled me and told me whatever the results I will not be the first." **23-year-old female IDI participant, completed diagnosis**

Barriers for completion of the TB diagnostic process

We identified three themes under barriers for completion of the TB diagnostic process: i) individual-level barriers (inabil-ity to produce sputum, TB and HIV stigma, lack of transport to return to the health facility, fear of TB treatment) ii) health system barriers (long turnaround time for results, high sample load, stock out of testing supplies, unclear appointment for collection of results, poor health worker attitude, inadequate patient contact details) and interpersonal and community barriers (TB and HIV stigma).

Individual-level barriers

A few IDI participants who did not complete the TB diagnostic process mentioned that they were unable to provide a sputum sample into the laboratory specimen container for testing. They mentioned trying all they could to produce the

sputum but were unable and eventually went home. Very participants mentioned that they returned to the health workers for advice when they were unable to produce the sputum. These were advised to get an early morning sample while other participants said they simply left the health facility without consulting. For some participants, they were still unable to pro-duce the early morning sputum sample and others were successful. Those who were unable to produce the sputum com-pletely mentioned not returning to the health facility for fear of being reprimanded by the health workers if they came back without a sample. Because of the fear to go back to the health workers, patients ended up either submitting a poor-quality sample or disappearing from the health facility.

"I wanted to know the results truthfully but I did not have sputum. I do not know what I put in there. I coughed, coughed, and coughed…but I did not have it. When they asked for it (sputum), I did what I did and spat in the container but it was not sputum." **39-year-old female IDI participant, lost to follow-up (LTFU)**

A few KIIs explained that some patients are unable to produce sputum because health workers rarely tell patients the techniques of sputum production during sensitization and counselling sessions. It was noted that patients are also not informed of other available tests in instances where one is unable to produce sputum which causes patients to disap-pear from the health facilities. It was further mentioned that limited sensitization also leads to poor quality samples from patients with some submitting either saliva or an insufficient sample. A key informant narrates below how patients do not return to the health workers once they are unable to produce sputum.

"There are some patients when they are told to collect sputum, they find it difficult to get that sputum, so when they fail, they just give up. When they are asked to collect sputum, they go in that area where they are supposed to collect the sputum from and when they fail, they just lose hope and sometimes they are not explained to the other options. So, they just give up and go away." **34-year-old male KII_TB Unit, Hospital**

TB and HIV related stigma was reported to lead to loss from the TB diagnostic process. The drivers of the stigma were;
i) fear of association with HIV/AIDS, ii) fear of social exclusion and iii) fear of spreading TB to the rest of the family mem-bers. Participants in the IDIs and FGDs feared being labelled as people living with HIV because of the community under-standing that whoever has TB also have HIV. They also expressed the fear of being stigmatized and socially excluded
in the community by family members if they found out that they were being presumed for TB. Hence, they feared to be isolated, gossiped about, being seen using TB services and taking medication. The stigma was reported across all ages and sexes, and by participants in all IDIs and in all FGDs.

*"It is because of fear. Personally, I was initially afraid as well. I imagined what it would be like if I were seen taking TB drugs, and my mom telling me not to take them from here. I also thought about how people would gossip about me
if they saw me taking those drugs. So, I decided to leave it up to them and not take the drugs because I was worried about how people would perceive me."* **27-year-old female FGD participant, Hospital**

The barrier of TB and HIV stigma was also attested to by key informants who mentioned that the community associates TB to HIV/AIDS which discourages people with presumed TB from testing for fear of being labelled by the community as people living with HIV. A key informant in one of the hospitals explained how stigma makes patients not to test for TB:

"Stigma makes them disappear because most people think that when you have TB you are HIV positive…So these patients fear seeing them in the line of people testing for TB and HIV…that kind of fear causes the patients to get lost and fail to complete the diagnostic process. The person is asked to produce the sample and they instead choose to leave the facility" **43-year-old male KII TB Unit, Hospital**

The TB/HIV testing policy being implemented in the study facilities was mentioned to further increase the stigma which deters away some patients when presumed for TB. Majority of the participants in KIIs and IDIs and in few FGDs said patients know that they will not only be tested for TB but also for HIV and this scares them so much. The main fear was getting HIV positive results once tested followed by daily swallowing of drugs for the rest of their lives which scared them away. Participants stated that some community members thus prefer to live in ignorance of their HIV status than face this reality of swallowing drugs daily. The fear of being tested for HIV was commonly mentioned among males and participants under 40 years of age.

"Some people are told to go and test but they refuse because they fear and they know they are not only going to be tested for TB but they also have to be tested for HIV and this thing scares them so much" **36-year-old male FGD par-ticipant, Hospital**

Lack of transport to return to the health facility either to submit a sample or collect results from the test was also reported as a barrier for completion of the TB diagnostic process. This was mentioned by participants who did not get a spot spu-tum sample and needed to take back the sample the next day and by those who did not collect results or initiate treatment on the day of the health facility visit. Participants reported that they do not receive results on the same day they are pre-sumed for TB hence the need to return to collect results or initiate treatment which requires money for transport. This was commonly mentioned by females and those who reside in areas far away from the health facilities. Participants who stay far said it is worse for them compared to those who stay in nearby places. Close to half of the participants across IDIs, KIIs and in all FGDs mentioned the lack of transport as a major barrier.

"The distance and the transport fees made it difficult for me. If it were nearby, I would have returned even that very day…. But the distance is long and you have to first gather some money before you can be able to come back to the facility."." **50-year-old male IDI participant LTFU**

The fear of TB results and treatment was mentioned in all FGDs and by most IDI and KII participants as a key contributor to loss before completing the TB diagnostic process. It was noted that generally some people fear taking drugs hence they will disappear from the health facilities before knowing the results. The fear of taking TB drugs is further amplified by the TB and HIV stigma with participants fearing to be seen taking TB drugs and be mistaken for swallowing HIV drugs. Other participants mentioned knowing that TB treatment is for six months hence see it as a long time, which makes them not to proceed to test for TB preferring to live in ignorance of their status. Other participants who had seen the drugs perceived them as big tablets hence feared swallowing them. All these perceptions on the TB drugs and duration were reported to discourage patients from testing for TB.

"Some people fear to know the results and also fear taking the drugs. Some people have fear within themselves and also do not imagine themselves taking the TB drugs especially when they have seen the drugs. Tablets are too big and are taken for a long time. Some people feel sorry for themselves and say that they do not want to take drugs. This makes them not to come back." **52-year-old male FGD participant, Hospital**

More so, people living with HIV were cited to fear the potential pill burden in case the results come back positive for TB. This is because they are already swallowing ARVs daily and perceive the addition of other daily TB drugs as cumbersome hence they shy

away from the diagnosis. This causes them to not test for TB or even collect their results.

"Another thing that makes people to not want to complete the process (TB Diagnosis) is the fact they are already taking HIV drugs. They imagine how they will be able to take both drugs concurrently and so they will decide to stay on the HIV drug only…The fact that the TB drugs are also taken for a long period of six months and yet the HIV drugs are already for a lifetime makes them to stay away from completing TB diagnosis. They just have hope that they will some-how recover from the TB without drugs yet that is not possible". **40-year-old male FGD participant, Health centre IV**

Health system barriers

High sample load from lower-level health facilities was mentioned in the two public hospitals as a barrier for same day analysis of samples. These hospitals receive many samples from different referring facilities in addition to those collected from the patients seen in their facility departments. This was further complicated by the type of Xpert MTB/ RIF machines available in the facilities which can only analyse few samples at a time. This led to a long turnaround time for results and consequently long waiting time for the patients. In most cases, they asked the patients to return and collect results either the next day or after some days which led to some of them getting lost from the diagnostic process.

"We work on samples from lower facilities and in a day, we can work on thirty (30) or more than that throughout the district. This gene expert takes one hour to run, just running and when it comes to sample collection, we can give it like three (3) hours in total. You find that time for patients to wait is long. It is too hard for them to wait...As I have told you, when they go back to the village, coming back is a problem." **30-year-old male KII_laboratory, Hospital**

Relatedly, long waiting time for results was mentioned by over half of the participants in IDIs, KIIs and all FGDs. Patients reported a long waiting time either on the day of sample submission when told to wait for results that very day or long wait-ing in days when one is told to return because the results will not ready on the same day of sputum submission. The long waiting time was said to lead to frustration and one making a decision to either return or not return to collect the results.
For patients who are told to return on another day and collect results, it was mentioned that some health workers attempt to give them a date to return with the hope that results will be ready then. However, it was not always guaranteed that the patients will find results on the given date. Some participants mentioned the possibility of not finding results on that day they are told to return and collect them. This therefore meant more waiting time and the need for another return visit to the health facility. Participants narrated that every return to the health facility necessitated time off work and more transport money beyond that which was originally planned at the first visit. This was therefore seen to make completion of the TB diagnostic process tedious and costly.

"The long waiting time for results also makes them disappear. For example, those who have given in their sample on Tuesday are told to come for their results on Friday. But remember he may come on Friday and be told to come back on Monday. All that is money wasted on transport." **44-year-old female KII_TB Unit, Hospital**

On the other hand, some participants mentioned not being given clear appointment dates when to collect the results which left them in uncertainty causing them to make random visits to the health facilities before obtaining results. Unclear appointments for collection of results coupled with poor communication was reported by majority of the IDIs and in three FGDs as a barrier. This meant patients making several back and forth trips to the health facility checking for readiness of results which was mentioned by some participants to expose them to stigma and doubt by the people around them.

*"They did not call me and they also did not give me a date so that when the date reaches, I go back. But they did not tell me so I didn't know. When they did not give me a return date or call me, I went silent…what scared me was fre-quenting the hospital and what people would say and think about it, especially my mother. Had they called me, I would have come back.***" 37-year-old female IDI participant_LTFU**

"I thought that they would give me the results on that day, but they told me that they would call me and tell me when to return…They did not call me and they also did not give me a date. When they did not give me a return date or call me, I went silent." **52-year-old female IDI participant_LTFU**

Stock out of testing supplies at the health facilities also hindered patients from completing the diagnostic process. Labo-ratory staff in the hospitals mentioned a common stock out of Xpert MTB/RIF cartridges which forces them to halt sam-ple collection and processing. More so, a few participants said that some tests not being available at the health facility increases the likelihood of patients being lost from the process. In such cases, patients are sent for testing outside of the health facility, which was often associated with costs. In that process, the patients do not return to the health facilities either because of the cost or they are unable to get time and transport to return to the health facility. Chest x-ray was the commonly missing test in the public facilities and patients were often referred to the private facilities with the machine which came at a cost.

"It (Chest x-ray) is not so common because it has got a cost and it's not within our health facility and area, so one has to travel to Mukono town for x-ray. So then coming back with results is not common. It may be a handful of them who come back." **29-year-old male KII_TB unit, Health centre IV**

Poor health worker attitude towards TB was also reported as a barrier when screening and handling patients with pre-sumed TB in all FGDs and in some IDIs. Some KIIs especially in hospitals reported that health workers handle these patients with a negative attitude in terms of the way they screen them, send them for sputum samples and respond to them when they ask questions or have made an error in any of the health facility processes. Relatedly, some patients mentioned being stigmatized by health workers who shout at them to wear masks when coughing and to extend far when talking to them. This attitude made the patients feel unwanted hence feared to return to the health worker when asked to submit the sputum sample.

"TB is so painful. The health worker was asking me questions and I could not answer the questions. She asked me if I did not have a mouth to speak. I had the mouth, but was unable to speak. I did not know what to tell the health worker." **41-year-old female IDI participant, completed diagnosis**

Health workers also acknowledged the fact that the negative attitude of their fellow staff demotivates patients to complete the diagnostic process. Patients were mentioned to seek care when in pain and after trying many different options to get healed but in vain, including going to the traditional healers. This was mentioned as costly and frustrating for patients which requires handling them with care when they finally come to the health facilities.

"The health workers bad and negative attitude towards the patient scares them away. At times these patients come here when they no longer love themselves because of the pain. Actually, some sacrifice their stuff to witch doctors to get healed so they need to be handled well." **55-year-old male KII_TB Unit, Hospital**

Inadequate patient contact details: **s**ome of the key informants noted poor documentation of patient tracer information such as telephone contact and home address as a key barrier for receiving results and initiating treatment. Participants described this as either contacts not being collected at all or contacts available but incorrect. This tracer information was mentioned to aid health workers with patient follow-up especially when a patient's results are positive for TB and contact tracing as below;

"One of the reasons (for the loss of patients) is poor documentation. So, you presume someone and you don't write their phone numbers and not even their next of kin phone number. Those people you can hardly find them… You find

that all you know about that person is where they live and the area is very big. Even people have the same names, so some people are lost in that way." **38-year-old male KII_ OPD, Health centre IV**

Discussion

This was a qualitative exploration of facilitators and barriers to completion of the TB diagnostic process among patients with presumed TB, those diagnosed with TB and health workers providing TB services in selected health facilities in Central Uganda. Key facilitators for completion of the TB diagnostic process included; social support, obtaining same day results, prior TB knowledge, caring health workers (positive interaction with patients who were helpful, caring and com-passionate) and calling of patients to collect results. Barriers were; long turnaround time, lack of transport to return to the health facility, TB and HIV stigma, unclear appointment for collection of results, inadequate patient contact details and negative health worker attitude.

Social support from family and community members were mentioned as a key facilitator to completing the TB diag-nostic process. This support was commonly mentioned from the significant people in patient's lives who have a form of influence such as spouses, parents and siblings. This was found in studies elsewhere where family members escort peo-ple with presumed TB to testing facilities, others provide transport means and offer words of counsel and encouragement to them to visit the health facilities [14,20,21]. The social support is crucial given that TB is a highly stigmatized disease which could deter one from testing if not supported and motivated by a significant person in their life [22,23].

Obtaining same day results facilitated completion of the TB diagnostic process. This is because the patients got the diagnosis there and then and did not require more time off work and transport to return to the health facility, which were often cited as hard to get. This was further attested to by patients who did not complete the diagnostic process mention-ing failure to obtain same day results as a barrier. Although the goal of all TB programs is to have patients with presumed TB obtain their results on the same day of testing, this is not realized yet [24]. Evidence from a systematic review and meta-analysis in high-TB burden countries shows a health system delay for TB diagnosis of 14 days [25]. More so, our formative study showed that over half of people with presumed TB who conducted the TB investigations required, did

not receive their test results on the same day of being tested [12]. Failure to provide same day results was linked to high sample load, stock out of supplies in this study and studies elsewhere showed additional factors of inadequate laboratory personnel, and low laboratory capacity [14,26,27]. Delay to provide a TB diagnosis exposes the community to possible infections and increases morbidity and mortality in people with TB [8,28–30].

Relatedly, long turnaround time and waiting time for results in this study led to the need for return visits to the health facilities to collect results which contributed to the loss of patients before completing the diagnostic process. Return visits required transport money, taking time off work and exposed participants to potential TB/HIV stigma due to the frequent hospital visits. This is similar to what other studies have found in Uganda and elsewhere [6,14,21,22,31,32] where long turnaround time for results and need for repeat visits leads to loss of patients from TB care. The need for repeat visits to the health facilities increases health care costs for the patients which may derail progress towards achieving universal health coverage and the goal of eliminating catastrophic costs for TB services by 2035 [33]. Uganda is already struggling with high pre-diagnosis catastrophic costs of 30.6% [34] hence this could further push patients to poverty. There is there-fore need for increased commitment for both financial and human resources to enable issuance of TB results to patients on the same day of the health facility visit.

Unclear appointment on the day for collection of results limited the ability of patients to complete the TB diagnostic process. This was because the patients remained unsure of when to return to collect results, were uncertain if they would be contacted when results are ready but also those who were promised to be called mentioned not being contacted when results were ready. Studies elsewhere showed the same with patients citing poor communication as a barrier to comple-tion of the diagnostic process [35]. Given the structural and personnel inefficiencies in low-resource settings to provide

same day TB results, emphasis should be placed on improving communication with patients once results are ready. From this study, those who were called back to collect results via phone calls, especially those who were diagnosed with TB, mentioned this as a key facilitator. More so, there is overwhelming evidence on the effectiveness of phone call and SMS tools in improving health care seeking [36–38]. However, health workers indicated inadequate patient contact details as a barrier even when there was an opportunity to contact the patient to return to the health facility. Lack of patient contact details has been seen in previous studies as a key contributor to loss to follow-up of patients with presumed TB [12,39–41]. Improving patient-provider communication therefore requires comprehensive strategies comprising of proper documenta-tion and availing the communication tools and resources.

TB and HIV related stigma was a key barrier to completing the TB diagnostic process as has been found in other studies in Uganda, Kenya and across the globe [14,32,42,43]. This was mainly perceived stigma due to the misconception that whoever has TB has HIV hence the fear was more on being associated with HIV. This stigma was further complicated by the WHO and Uganda national guidelines on TB/HIV testing where patients are expected to test for TB and HIV at the same time which breeds stigma and fear especially if the HIV testing is offered in a facility that serves people living with HIV [44–46]. HIV remains highly stigmatized despite on-going efforts which is now consequently affecting the oppor-tunistic infections complicating their control and management [23,47]. More so, there was fear of being socially isolated once one is known to be presumed or diagnosed with TB. Literature shows that community members often do not want to interact with people with TB for fear of being infected, even when they do, they express and show discomfort [23,48]. This social isolation reduces the patient's self-esteem and self-efficacy to seek care leading to delayed diagnosis, treat-ment initiation, poor adherence to treatment and poor mental health including suicidal thoughts [49–52]. A study in LMICs revealed that poor mental health combined with TB infection leads to worse outcomes than TB infection alone hence the need for urgent action [53]. Sensitization efforts should focus on improving community knowledge on TB and dispelling TB misconceptions to reduce the stigma. This will consequently encourage social support to the patients as has been seen in previous studies where patients who received social support were less likely to experience stigma [49,54,55].

Prior knowledge on TB obtained through health education or interfacing with people with TB was mentioned to increase one's ability to complete the TB diagnostic process. This was because they already knew more details about TB such as the benefits of early testing and starting treatment and the fact that TB can be cured and some feared they may have been exposed hence motivated to test and know their status. These findings are similar to studies elsewhere that show previous history and experience with a person with TB increases the likelihood of testing for TB [20]. Previous studies elsewhere have found that limited awareness of TB is associated with delays in healthcare seeking [27,35,43]. This there-fore calls for strengthening of community and facility health education programs on TB.

Although the attitude and behaviour of health workers has been criticized over the years as deterring patients to seek care in health facilities, our study found otherwise [56–59]. Health workers who offer services to people with presumed TB were described as caring indicating a positive interaction finding them helpful, caring and compassionate. This moti-vated most participants to return to the health facility and complete diagnosis. This finding is similar to recent studies that have showed high patient satisfaction with health worker behaviors and attitudes [60,61]. This may be due to increased awareness and engagements with health workers towards a patient-centred care approach that emphasizes improved communication with the patients which makes them feel cared for [62,63]. Furthermore, it maybe because TB is a highly stigmatized disease with a long-term treatment period hence the health care workers show empathy to the patients. Pre-vious studies have showed a positive correlation between improved knowledge and positive attitude hence the need for continuous engagement of health workers for attitude change to be able to provide better services to patients [64–67]. On the other hand, a few participants were dissatisfied with the health care workers attitudes especially during screening of people with presumed TB hence the need for more behavior change programs among health workers.

A key strength to our study is the triangulation of findings from different interview methods that is; IDIs, FGDs and KIIs. More so, we triangulated data from different levels of health facilities to explore these factors from a health system

perspective. This triangulation provided rich information on understanding completion of TB diagnosis from perspectives of the patients and health care workers in the different settings. This information may inform planning for strengthening provision of TB services in the country. We conducted sex-specific FGDs for homogeneity but also to mitigate the likely gender-related TB and HIV stigma among participants which promoted a conducive environment for free and open participation.
However, there might have been recall bias from participants in the FGDs who had initiated treatment within one month. They might have inaccurately recalled the events surrounding their experience during the TB diagnostic process. This was however mitigated by purposively selecting most from those who initiated within two weeks to reduce the recall bias. Further, despite efforts to maintain objectivity, our social identities, prior experiences and perceptions may have shaped interactions with participants during interviews and the interpretation of data during analysis. This was minimized by using the same interview guides throughout and disseminating preliminary findings among different stakeholders for their insights but also triangulating data from the patients and health workers. In addition, adoption of the socio-ecological model comes with challenges in fitting the results accurately to express the dynamic interplay between factors within and at different levels, with some levels not being well represented like the policy level.

Conclusion

This study reveals persistent gaps in Uganda's TB response for people with presumed TB which need urgent attention to prevent more people from dropping out before completing the diagnostic process if the country is to achieve the 2035 End TB strategy. Obtaining same day results, social support, caring health workers and prior knowledge on TB facilitate completion of the TB diagnostic process while long turnaround time for results, TB and HIV stigma, poor health worker attitude and inadequate patient contact details contribute to the loss of patients. Addressing diagnostic and resources challenges to enable same day results, improving health worker to patient communication and enhancing social support from the community should be considered to enhance completion of the TB diagnostic process.
The national policy for same day testing of TB and HIV should be accompanied with heightened community awareness and counselling to minimize the associated stigma that comes with HIV testing which was not anticipated by the patients.

Supporting information

S1 File. The Consolidated Criteria for Reporting Qualitative Studies (COREQ) Checklist.
(DOCX)

S2 File. Interview guides.
(DOCX)

S3 File. Analysis framework for factors for completion of the TB diagnostic process among patients with presumed TB in Central Uganda.
(DOCX)

S4 File. The study risk mitigation plan.
(PDF)

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Appendix 4: Supplementary publication-"Effect of SMS Reminders, Telephone Calls, and Transport Incentives on Enhancing the Completion of Tuberculosis Diagnosis and Initiation of Treatment for Diagnosed Patients: Protocol for a Randomized Controlled Trial (Nuwematsiko, 2025)

Protocol

Effect of SMS Reminders, Telephone Calls, and Transport Incentives on Enhancing the Completion of Tuberculosis Diagnosis and Initiation of Treatment for Diagnosed Patients: Protocol for a Randomized Controlled Trial

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Abstract

Background: Globally, tuberculosis (TB) programs have enhanced efforts to improve case detection, treatment initiation, and monitoring of treatment outcomes. However, less attention has been given to reducing the number of persons with presumed TB who never get tested for TB or those with confirmed TB who never start treatment in endemic regions such as Uganda. Such losses hinder progress toward attaining the 2035 End TB goals. The World Health Organization recommends mobile health (mHealth) interventions such as SMS reminders, telephone calls, mobile apps, and digital monitoring devices to foster universal health coverage. To our knowledge, there is limited evidence on whether these mHealth interventions can increase linkage to care for persons with presumed TB, particularly in sub-Saharan Africa.

Objective: We aim to conduct a randomized controlled trial (MILEAGE4TB) whose aim is to assess the effect of SMS reminders, telephone calls, and transport incentives on improving completion of TB diagnosis among persons with presumed TB and initiation of treatment for diagnosed patients in Uganda.

Methods: This will be a 5-arm individual randomized controlled trial among persons with presumed TB aged 18 years or older who are referred for Xpert MTB/RIF testing. Participants will be randomly assigned (2:2:2:1:1) to (1) standard of care,

(2) SMS reminders only, (3) telephone calls only, (4) SMS reminders and a transport incentive, and (5) telephone calls and a transport incentive. An estimated sample size of 2389 participants will be considered. The primary outcome will be completion of TB diagnosis, defined as submitting a sputum sample for Xpert MTB/RIF testing and receiving test results within 30 days of being identified as having presumptive TB. The secondary outcomes will include (1) TB treatment initiation, which will be defined as starting TB treatment within 30 days of being diagnosed; (2) median turnaround times for TB diagnosis and treatment initiation; and (3) acceptability and feasibility of the interventions. Participants will be followed for 30 days to check whether they have tested for TB and collected their results. Chi-square tests will be performed for categorical

outcomes. Analysis will be by intention to treat. Modified Poisson regression models will be used to estimate the effects of the interventions on completion of TB diagnosis and treatment initiation.

Results: The study was funded in June 2020 and data collection for the trial started in August 2023. Results from this trial are not yet available. As of August 28, 2025, a total of 2355 participants had been recruited. Data from the preliminary analysis will be ready by December 2025 after all trial activities.

Conclusions: This randomized controlled trial will provide insights on the use of mHealth interventions to improve the completion of TB diagnosis among persons with presumed TB and initiation of treatment for diagnosed patients.

Trial Registration: ClinicalTrials.gov NCT05964842; https://www.clinicaltrials.gov/study/NCT05964842

International Registered Report Identifier (IRRID): DERR1-10.2196/70325

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Keywords: tuberculosis; TB; presumptive tuberculosis; SMS; telephone calls; transport incentives; linkage to TB care

Introduction

Background

Tuberculosis (TB) remains one of the leading causes of death from a single infectious agent despite the fact that it is preventable [1]. The End TB Strategy of the World Health Organization (WHO) calls for reduction of TB incidence by 90%, deaths by 95% and eliminating catastrophic costs for TB-affected households by 2035; however, progress is hindered by the loss to follow-up (LTFU) of patients along the continuum of care [2]. Patient LTFU can occur after they are identified with presumptive TB but are never tested, while those who are tested and are confirmed to have TB can also undergo LTFU and never initiate TB treatment. This is in addition to the number of patients who never access a TB diagnostic test [3]. In 2023, an estimated 10.84 million people fell ill with TB, of whom 8.16 million were diagnosed and notified to national TB programs, leaving out 2.7 million patients (25%) [1]. A study by Kim et al [4] on TB care cascades of 30 high TB burden countries found that 35% of people with TB did not receive a diagnosis, while 5% of people who were diagnosed did not initiate treatment.

The WHO recommends the use of mobile health (mHealth) for improved service delivery and continuation of health care, given its timeliness, popularity, and affordability [2,5]. SMS reminders, telephone calls, and mobile apps are some of the interventions being used to support TB care and reduce patient LTFU during the treatment phase [6-10]. These mHealth interventions have shown promise in improving adherence to TB treatment in previous studies [11-14]; therefore, they have the potential to also support persons with presumed TB to complete the diagnostic process. Incentives given to patients have also been found to improve health care outcomes elsewhere [15-19]. However, there is limited evidence on the application of mHealth interventions and incentives during the phase when one is being presumed for TB and on how they can improve completion of the diagnos-tic process.

have reported prediagnosis LTFU of up to 40% [20] and pretreatment LTFU of 19% [21]. Diagnosis and initiation of Uganda's TB burden has persisted over the years, and the country is still ranked among the 30 countries in Africa with a high burden of both TB and HIV, with an incidence of 198 cases per 100,000 population [1]. Recent studies from Uganda

TB treatment are critical for controlling TB transmission and achieving good patient outcomes, particularly when medication adherence is maintained [2]. Therefore, this situation calls for bold actions and innovations to reduce the number of patients lost to follow-up before completing TB diagno-sis (prediagnosis LTFU) and those lost to follow-up before initiating treatment when diagnosed (pretreatment LTFU). In Uganda, mHealth interventions have emerged as promising tools to enhance TB care by improving patient outcomes and health care processes. These mHealth interventions have been used to address challenges in TB care, including contact investigation, delivery of test results, adherence to appointments, linkage to care, and treatment adherence [6,22].

The consequences of prediagnosis and pretreatment LTFU are serious. Patients with untreated TB remain infectious and can transmit TB to others, while failure to initiate treatment contributes to increased morbidity and mortality [23-26]. Therefore, monitoring the outcomes of persons with presumed TB is an important aspect of TB control [5]. This study will thus assess the effect of SMS reminders, telephone calls, and transport incentives on enhancing completion of TB diagnosis and initiation of treatment in Uganda. Assess-ing the effect of these interventions will provide evidence on whether reminding patients using SMS reminders or telephone calls, with or without conditional cash incentives, can enhance completion of TB diagnosis and initiation of treatment for improved patient outcomes and hence aid in designing targeted interventions and policies.

Goal of the Study

This randomized controlled trial aims to assess the effect of SMS reminders, telephone calls, and transport incentives sent to persons with presumed TB and those with confirmed TB on enhancing completion of TB diagnosis and initiation of treatment for diagnosed patients. The TB care continuum comprises 4 steps: screening, diagnosis, treatment initiation, and treatment completion [3,4]. This study will address LTFU along the TB care continuum at 2 time points: before diagnosis and before treatment. Prediagnosis LTFU refers to the failure to test for TB and obtain results within 30 days from the date of being presumed. Pretreatment LTFU refers to failure to initiate treatment after TB has been confirmed.

The proposed intervention will use SMS reminders and telephone calls to improve communication between patients and health care providers, while the transport incentives will help address the economic barriers to diagnosis completion and treatment initiation.

Objectives and Hypothesis

The primary objective is to assess the effect of SMS reminders, telephone calls, and transport incentives on completion of TB diagnosis among persons with presumed TB and initiation of treatment for diagnosed patients. The secondary objectives are to determine the median turnaround time for TB diagnosis and treatment initiation and to examine the acceptability and feasibility of the interventions. We hypothesize that compared to standard of care (SOC), each individual intervention—SMS reminders alone or telephone calls alone—will improve completion of TB diagnosis and initiation of treatment by reducing prediagnosis LTFU by a minimum of 40% (from 24% to 14.4%), while a combined intervention—SMS reminders or telephone calls coupled with transport incentives—will reduce prediagnosis LTFU by 50% (from 24% to 12%). This protocol follows the SPIRIT (Standard Protocol Items: Recommendations for Interven-tional Trials) reporting guidelines [27].

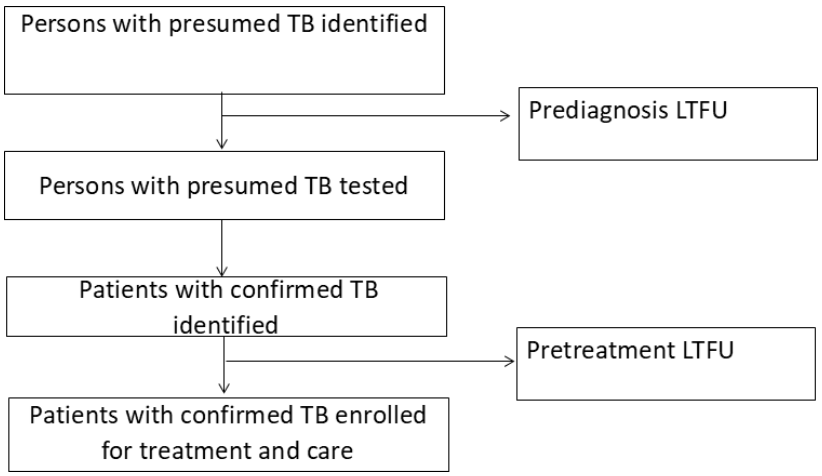
Methods

Study Setting

The study will be conducted in 6 government health facilities in central Uganda: Kiruddu National Referral Hospital, Entebbe Regional Referral Hospital, Mukono General Hospital, Luwero General Hospital, Kawolo General Hospital, and Wakiso Health Centre (HC) IV (a lower-level facility). The selection of these health facilities ensures a mix of urban and rural settings and different administra-tive levels to increase the generalizability of the findings. Uganda's government health system consists of national referral hospitals, regional referral hospitals, and the district health system [28]. The district health system is further divided into district general hospitals; HCs IV, III, and II; and village health teams [28,29]. National referral hospitals provide comprehensive specialist services, while regional referral hospitals have specialists in only some specific fields. District general hospitals and HC IVs have physicians. HCs are graded based on the administrative zone served, popula-tion size, and services offered. HC IVs serve a county or municipality with a population of approximately 100,000 people and provide emergency surgery, blood transfusion, and all general medical services offered at lower-level health facilities. HC IIIs serve a subcounty with a popula-tion of approximately 20,000 people and provide maternity, inpatient, and laboratory services in addition to all health services offered at an HC II. HC IIs provide health services to a parish, ward, or division with a population of approxi-mately 5000 people and offer outpatient care, prenatal care, immunization, and community outreach services [29].

In the study facilities, patients presenting with symp-toms suggestive of TB (eg, cough, fever, weight loss, and night sweats) are identified and their demographic, contact, and clinical details recorded in the registers for persons with presumed TB at the different facility entry points. Patients are evaluated for TB using Xpert MTB/RIF, urine lipoarabinomannan, or chest X-ray depending on their symptoms, with diagnosis primarily conducted via Xpert MTB/RIF as recommended by the Ministry of Health [30]. Persons with presumed TB are offered sputum testing using Xpert MTB/RIF or sputum smear microscopy, while those unable to produce sputum are offered alterna-tive diagnostic tests (eg, chest X-ray, urine lipoarabino-mannan, sonography, tissue biopsy, and cerebrospinal fluid analysis). Details of patients who complete the required investigations are subsequently recorded in the labora-tory or radiology registers. Thereafter, patients confirmed to have TB are started on treatment and recorded in the unit TB register (Figure 1). Ideally, the results of Xpert MTB/RIF tests should be available within 2 hours, allowing persons with presumed TB to receive their results on the same day as sputum submission. However, challenges such as high patient loads, cartridge short-ages, lack of on-site Xpert MTB/RIF equipment, and low staffing levels in laboratories, among others, often prevent same-day completion of the diagnostic process, contribu-ting to a considerable proportion of patients being lost to follow-up [31-33].

Figure 1. Patient flow through the study facilities. LTFU: loss to follow-up; TB: tuberculosis.



Trial Design, Population, and Eligibility

This will be a multicentre individual randomized control-led trial with five arms: (1) SOC (control arm), (2) SMS reminders only, (3) telephone calls only, (4) SMS remind-ers and a transport incentive, and (5) telephone calls and a transport incentive. This intervention was designed and adapted through stakeholder engagements in a co-design workshop. The original design included SMS reminders only and a transport incentive [34]. However, based on stake-holder engagements, telephone calls were added to address the following concerns: (1) the risk of unintentional disclo-sure if someone other than the recipient reads the SMS text message; (2) existing SMS fatigue due to high volume of messages from telecom companies, leading to a likelihood of messages being ignored or deleted; (3) lack of real-time 2-way communication; and (4) lack of usefulness for patients who cannot read. Telephone calls were preferred because they offer privacy and foster 2-way communication in real time .

Intervention Arms

Description of the Study Arms

SOC Arm (Control)

Patients in the SOC arm (control) will continue to receive routine TB care, according to the Uganda Ministry of Health guidelines, including (1) screening individuals for TB, (2) identifying persons with presumed TB and recording their details in the TB register, (3) referring for testing, (4) receiving results, (5) irregular automated SMS text notifica-tion from the Xpert MTB/RIF machine to attending clinicians when results from the tests are ready, (6) irregular telephone calls to patients with positive TB test results to return to the health facility and start treatment, and (7) initiating treatment for patients with confirmed TB. There are irregularities in sending of SMS and making telephone calls due to incon-sistencies in availability of funds, breakdown in the Xpert MTB/RIF server system, and limited human resource to support these processes.

The intervention will comprise 3 enhanced approaches to motivate participants to complete TB diagnosis: SMS reminders, telephone calls, and transport incentives. These interventions will be delivered in four arms: (1) SMS reminders only, (2) telephone calls only, (3) SMS reminders and a transport incentive, and (4) telephone calls and (5) a transport incentive.

SMS Reminders Only

Participants in this arm will receive up to 3 SMS reminders. The first reminder will be sent on day 0, the day of study enrollment. The second reminder will be sent once the patient's results are ready. If the patient does not return to complete the TB diagnostic process (ie, testing and receiving results) within 1 day of the second reminder, a third reminder will be sent. This third reminder will serve as a reinforcement, reminding participants to return and complete diagnosis or initiate treatment if they have not already done so. Standardized SMS reminders will be manually sent by the research team through the telecom service providers MTN and Airtel in either Luganda (the local language) or English, based on the participant's language preference determined at enrollment. The SMS reminders are planned to be 1-way (unidirectional) and the content neutral, excluding any mention of the word "TB" or the patient's name. The specific wording of the SMS reminders will be co-designed with stakeholders including persons with presumed TB and health workers. Quality control officers will verify the SMS reminders sent daily, checking for the correctness of recipient telephone numbers and ensuring that all reminders are sent on time as per the study procedures. Each day, quality control officers will randomly select at least 4 participants from the SMS reminder arm or from among those scheduled to receive the second or third reminder and cross-check their details on the study telephone to confirm that the participant received the appropriate SMS reminder and in the preferred language. They will also cross-check the correctness of the telephone number that received the SMS reminder vis-à-vis the one recorded in the register for persons with presumed TB. Successful transmission of reminders will be checked by requesting sample statements from the telecom companies to confirm SMS dispatch to patients. Moreover, at follow-up,

participants will be asked whether they received either an SMS reminder or a telephone call and a transport incentive, further corroborating whether the participant received the SMS reminder.

Telephone Calls Only

In this arm, participants will receive up to 3 telephone calls as reminders, in addition to the usual SOC. The first telephone call will be made on the day of enrollment (day 0). The second telephone call will be made once the patient's results are ready. If the patient does not return to complete the TB diagnostic process within 1 day of the second call, a third telephone call will be made. The third telephone call will serve as a reinforcement, reminding participants to return and complete diagnosis or initiate treatment if they have not already done so. Telephone calls will be made in either Luganda (the local language) or English, based on the participant's language preference determined at enrollment.

Daily quality checks will be carried out to ensure delivery of the intervention to participants. At least 4 participants from the telephone call arm or from among those scheduled to receive the second or third telephone call will be randomly selected for the quality checks. Participant details will be cross-checked on the study telephone by the quality control officers at each study site to confirm that the participant received the appropriate telephone call. Call logs will also be checked to confirm the language used in the telephone call vis-à-vis the participant's preferred language and the correctness of the telephone number that received the call. Research assistants will continue attempting telephone calls if a patient does not answer the telephone, if another person answers, if it is not convenient for a patient to talk, or if the telephone is switched off until an effective call is made to the intended participant. A successful call will be defined as one in which a patient is reached, and a conversation takes place.

SMS Reminders and a Transport Incentive

Participants in this arm will receive the same SMS reminder package as those in the SMS reminder–only arm, along with a transport incentive of UGX 10,000 (approximately US $3). This transport incentive will be provided either after submitting a sputum sample in case the participant was unable to produce the sputum on the first day of the health facility visit or upon receiving their test results. The transport incentive will be disbursed through a prepaid mobile money system to ensure accountability for both the patient and the study team and to comply with the ongoing government campaign promoting the use of electronic cash [35]. These interventions will be administered in addition to the SOC provided at the health facility.

Telephone Calls and a Transport Incentive

The same telephone call package received by participants in the telephone call–only arm will be offered to those in this arm, along with a transport incentive of UGX 10,000 (approximately US$ 3). This will be in addition to the SOC received at the health facility. This transport incentive will be provided either after submitting a sputum sample in case a participant was unable to produce sputum on the first day of the hospital visit or upon receiving their test results. We will use the prepaid mobile money system to pay the transport incentive to participants in this study arm.

Sample Size Estimation

An estimated sample size of 2389 participants was deter-mined to achieve 80% power at a type I error of 5%, adjusted for multiple comparisons using the Bonferroni correction. Four comparisons were considered according to the study objectives; therefore, the adjusted level of significance is 1.25%, with a corresponding 2-tailed Z value of 2.238. We also adjusted for a 24% LTFU among patients with TB, based on findings from the formative study that informed the design of these interventions. We assumed a 40% reduction in LTFU based on previous similar studies [36,37] for comparisons between SOC and either SMS reminders alone or telephone calls alone, resulting in an assumed proportion of LTFU of 14.4% in both these groups. For comparisons between SOC and combined interventions (SMS reminders or telephone calls with a transport incentive), a 50% reduction will be considered clinically significant, given the expected higher impact of the incentive. The sample size has been further adjusted for clustering using a design effect of 1.5 to account for the clustering anticipated at the health facility level and a postenrollment attrition rate of 20%.

Study Population

The study population will comprise persons with presumed TB who did not complete diagnosis on the same day as their health facility visit. Persons with presumed TB will be defined as those presenting with signs and symptoms suggestive of TB, including cough, fever, night sweats, and unexplained weight loss.

We will include (1) patients referred for Xpert MTB/RIF testing; (2) those aged 18 years or older; (3) those currently residing in the health facility's catchment area; (4) those willing to consent to the study procedures, including follow-ups, and able to sign an informed consent form; (5) those who own a mobile phone and have it in their possession on the day of recruitment; and (6) those able to read (a test SMS text message will be sent to the patient's mobile phone, and they will be asked to read it aloud). Participants planning to move out of the study area within 3 months after enrollment and those participating in other related studies (eg, those involving SMS reminders, telephone calls, or transport incentives) will be excluded.

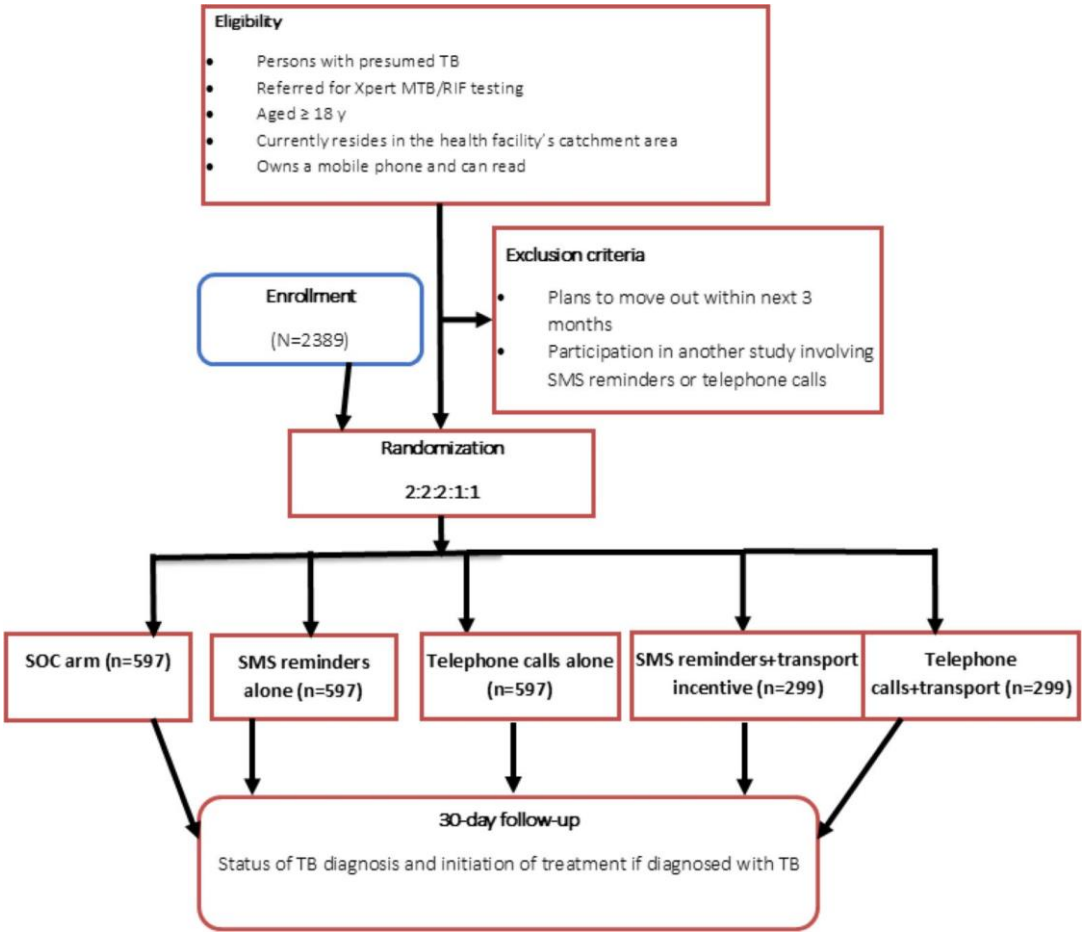
Randomization and Blinding

Eligible participants will be randomly assigned by research assistants to 1 of the 5 study arms using permuted block randomization in a ratio of 2:2:2:1:1 via a predesigned mobile app (Figure 2). The block sizes will be varied to minimize predictability. A computer algorithm will be designed by the biostatistician together with the app designer to generate the allocation sequence in blocks of 8 and 16, assigning their order

randomly. The allocation sequence will then be input

into the predesigned mobile app for automatic randomization once the research assistants input the participant's unique study ID number. Due to the nature of the interventions, participants will not be blinded to their assigned study arm. Research assistants will also not be blinded, given their role in delivering the interventions. However, the outcome assessors and data analyst will remain blinded to the study arms.

Figure 2. Flow diagram for randomization. SOC: standard of care; TB: tuberculosis.



Recruitment Strategies for Study Participants

Two research assistants will be strategically positioned at different potential entry points for persons with presumed TB in each study health facility. The entry points will include the outpatient department, antiretroviral therapy (ART) clinic, prenatal clinic, and TB unit. The inpatient units will be excluded because admitted patients are less likely to be lost to follow-up, as they remain within the health facility throughout the testing process. In each study facility, we will hold entry meetings with health workers from the various departments involved in identifying persons with presumed TB to inform them about the study and solicit their support in referring eligible patients throughout the study period.

Referred patients will be introduced to the study team and asked whether they are interested in participating. Those who express interest will be given a card and requested to return to the study desk once they complete care seeking. The card will serve as a reminder not to leave the health facility before returning to the study desk. Patients who return after completing care seeking will be assessed for eligibility, and

those who meet the criteria will be asked to provide informed consent by signing the consent form. Eligible participants will then be enrolled and randomly assigned to 1 of the 5 study arms using a smartphone preloaded with the randomiza-tion app. All participant details will be recorded in the study registers for persons with presumed TB in both electronic and hard-copy formats for backup.

Participant Follow-Up Procedures

Follow-up interviews will be conducted after 30 days from the day of recruitment for all participants primarily through face to face interviews at the health facility. Home visits will be conducted for patients who fail to turn up at the health facility. If still we can not access the patient, telephone calls will be made by research assistants to conduct the interview over the phone. At follow-up, data will be collected on whether the TB tests had been performed, along with the date of the TB test results, the date of registration for TB treatment, and the TB registration number. If a partici-pant does not submit a sputum sample, receive test results, or initiate treatment after diagnosis, they will be asked to provide reasons for not undergoing testing, receiving results, or starting treatment.

Data Collection Procedures

Participants will be enrolled in the study and assigned a unique ID number, which will be used for randomization using the mobile app. Once the participant has been randomly assigned, baseline measurements and tracking information will be collected and recorded using the Open Data Kit (ODK) platform (Get ODK Inc) and directly uploaded to the server. Data will be collected on age, sex, occupation, date when identified as a person with presumed TB, distance to the health facility of enrollment, test method used (ie, sputum smear microscopy or Xpert MTB/RIF), and knowl-edge and perceptions about the disease and treatment. We will train outcome assessors to objectively conduct inter-views and assess outcomes at follow-up. This approach will minimize any biases associated with the team administering the intervention.

Trial End Points, Outcomes, and Timelines

The primary end point for the trial is completion of the TB diagnosis process within 30 days of being recruited. Completion of TB diagnosis will be defined as submitting a sputum sample for Xpert MTB/RIF testing and receiving test results within 30 days of being identified as a person with presumed TB. The 30-day follow-up period was selected based on previous studies for comparison [25,33]. Comple-tion of TB diagnosis will be measured as the proportion of patients who completed TB diagnosis within 30 days out of all persons with presumed TB recruited into the study.

The secondary outcomes will include (1) TB treatment initiation, which will be defined as starting TB treatment within 30 days of being diagnosed (this will be measured as the proportion of patients diagnosed with TB who initiated treatment out of the total number of patients diagnosed with TB recruited into the study); (2) median turnaround times for TB diagnosis and treatment initiation; and (3) acceptabil-ity and feasibility of the study interventions. The detailed procedures and timelines are indicated in Table 1.

Table 1. Study procedures and timelines.

Study procedure	Screening	Baseline	Day 0	Results available	Day after results reminder	Day 30
Enrollment						
Eligibility screening	✓					
Informed consent	✓					
Allocation	✓					
Sociodemographic information		✓				
Clinical history		✓				
Knowledge of and attitudes regarding TB[a]		✓				
Interventions SMS reminders			✓			
Telephone calls Transport incentives			✓			
Assessments				✓	✓	
Sputum submission Receipt of results Receipt of interventions				✓	✓	
Treatment initiation for those diagnosed Acceptability assessment						✓
Qualitative study on perceptions and experiences of the interventions						✓

[a]TB: tuberculosis.

Data Management and Analysis

Overview

ODK data will be downloaded into Microsoft Excel and transferred to Stata 14 (StataCorp LLC) for cleaning and analysis. The primary analytical approach will follow the intention-to-treat principle, with participants in the interven-tion arm considered exposed to the intervention regardless of whether they received specific intervention services. We will assess for any contamination by conducting and comparing the results of the intention-to-treat and per-protocol analy-ses. Descriptive statistics (means, medians, and proportions) will be used to describe participant characteristics across the study arms. We will control for characteristics that are not balanced across the study arms in the fitted regression models. Chi-square tests will be performed for categorical outcomes. Log-binomial regression models using generalized linear modeling will be applied to assess associations between

each intervention and the outcomes. A *P* value <.05 will be considered statistically significant.

Interim Analysis

Although this trial does not pose a significant risk to participants, we plan to conduct an interim analysis. Findings from the interim analysis will be shared with the data and safety monitoring board (DSMB) to determine whether the trial should continue based on the emerging results.

Ethical Considerations

The study was approved by the Makerere University School of Public Health Research and Ethics Committee (799) and the Uganda National Council of Science and Technology (HS993ES). The study will be conducted in accordance with the World Medical Association Declaration of Helsinki. Written informed consent will be obtained from all partici-pants. Each participant will receive compensation of 10,000 Ugandan shillings (US $3) only for their time in the study at each level of data collection. All hard-copy study materi-als will be stored securely under lock and key, with access restricted to core project staff. Electronic data will be stored on a password-protected server hosted at Verton IT Ltd, with access similarly restricted to core project staff. To minimize the risk of inadvertent disclosure of presumptive TB status through SMS reminders or telephone calls received by unintended recipients, we will ensure that the SMS reminder content is neutral, with no mention of the word “TB,” serving only as a reminder to the patient to return to the health facility. This approach was adopted based on feedback from the co-design workshop with stakeholders, who recommen-ded avoiding the use of the word “TB” in the SMS reminder content. We will also only recruit participants who personally own a mobile phone and do not share it with others. Further-more, at the beginning of each telephone call, participants will be asked to identify themselves to confirm that the data collectors are speaking with the correct individual. All enrolled participants will be assigned a unique ID number at recruitment, which will be used throughout the study period. All data will be deidentified before analysis. The trial has been registered at ClinicalTrials.gov (NCT05964842).

Study Oversight and Monitoring

The study investigators, coordinator, supervisors, and research assistants will meet daily during participant recruitment for quality control purposes. This trial will be monitored by an independent DSMB and a local steer-ing committee (LSC). The DSMB will serve as the core technical team responsible for reviewing cumulative trial data, monitoring adherence to the trial protocol, and ensuring patient safety. It will also review any suggestions for protocol amendments. The DSMB will comprise 3 members (an epidemiologist, a clinical officer, and a senior researcher) and meet every 2 months to assess trial progress. The LSC will provide administrative oversight, ensuring adherence to study procedures, monitoring trial progress, and providing advice and guidance. It will comprise 7 members (a com-munity advisory member, an IT specialist, 2 policymakers, a biostatistician, an epidemiologist, and a social worker) and meet every 6 months.

Adverse Events Monitoring and Reporting

The planned trial interventions pose minimal risk to partici-pants; hence, we do not anticipate serious adverse events. However, we will continually conduct risk assessments to identify any incidents that may occur. The research assistants will be trained to monitor for adverse events, document them accurately, and follow established reporting procedures. All adverse events occurring during the study, whether or not considered related to the study, will be reported in writing to the study team, the LSC, the DSMB, and the Makerere University School of Public Health Research and Ethics Committee for assessment and further review. Each event will be recorded in the study registry, documenting the following information: description of the event, date of occurrence, participant details, onset and end dates, and severity. We will actively follow up each event until resolution or stabilization.

Dissemination Plan for Research Findings

All findings from the trial will be disseminated in workshops and conferences as oral or poster presentations. The target audience will include members of the Uganda National TB and Leprosy Program research forum, policymakers, TB program implementing partners, academic researchers, and the study participants. Policy briefs will be prepared, and a report of the study findings will be submitted to the partici-pating health facilities and to the funder, the European and Developing Countries Clinical Trials Partnership. All findings will be published in open-access, peer-reviewed journals.

Results

The study was funded in June 2020 and data collection for this RCT started in August 2023. We encountered delays during the COVID-19 period hence the RCT started at a later date than anticipated. The results are not yet availa-ble. Results from the preliminary analysis will be ready by December 2025. As of August 28, 2025, a total of 2355 participants had been recruited, and preliminary analyses are ongoing. The final results are expected to be published by March 2026.

Discussion

Summary

The MILEAGE4TB study is an individual randomized controlled trial to determine the effect of SMS remind-ers, telephone calls, and transport incentives on enhancing completion of TB diagnosis among persons with presumed TB and initiation of treatment for diagnosed patients. The study hypothesizes that, compared to SOC, each individ-ual

intervention—SMS reminders alone, telephone calls alone, or a combined intervention of either SMS reminders

or telephone calls with transport incentives—will reduce prediagnosis LTFU. Some of the factors contributing to patient LTFU are high patient loads, cartridge shortages, and low staffing levels in laboratories [31,32]. In addition, evidence indicates that even with improved diagnostic tools such as Xpert MTB/RIF, same-day results are often not feasible in low- and middle-income countries (LMICs) due to the unavailability of Xpert MTB/RIF equipment and thus the need to refer specimens for testing. These delays prevent same-day result delivery, increasing the likelihood of patient LTFU.

This study will address cascading patient LTFU along the TB care continuum, particularly at 2 time points: before diagnosis and after treatment. Prediagnosis and pretreatment LTFU are important because untreated patients with TB remain infectious and can continue to transmit TB in the community, while failure to initiate treatment results in poor patient outcomes, including death [6,24,38]. Studies have shown that timely diagnosis and treatment improve patient outcomes [39,40]. Effective TB case detection has been reported to lower TB incidence, prevalence, and mortality levels [41]. Therefore, routine follow-up of patients during the process of diagnosis and linkage to treatment is important. This is in line with the targets of the "End TB Strategy" and the United Nations' Sustainable Development Goals [42]. In addition, instances of pretreatment LTFU are not included in routine reporting by national TB programs, leading to an overestimation of program effectiveness [43].

The proposed intervention uses SMS reminders and telephone calls to improve communication between patients and health care providers, while transport incentives address the economic barriers associated with completion of TB diagnosis and treatment initiation. Telephone-based interven-tions such as SMS reminders and telephone calls have successfully improved adherence to TB treatment in Uganda [44-46] and increased the uptake of other health interventions, such as childhood immunization [47]. In addition, incentives have been found to improve health care outcomes [48-50]. However, there is limited data from LMICs on the role of SMS reminders, telephone calls, and transport incentives in interventions seeking to improve completion of TB diagno-sis and initiation of treatment for diagnosed patients. This study will provide evidence on the use of mHealth strategies and incentives to improve completion of TB diagnosis and initiation of treatment for diagnosed patients.

Given that the phase of being presumed for TB offers an opportunity for early diagnosis and treatment initiation [51,52], this study, whose aim is to enhance completion of TB diagnosis and initiation of treatment for diagnosed patients, is critical to achieving the targets of the "End TB Strategy" [2]. In addition, our study will put into practice the "Find. Treat. All." initiative, which seeks to close gaps in TB detection and treatment. This initiative, launched in 2018 by the WHO in collaboration with the Stop TB Partnership and the Global Fund to Fight AIDS and Tuberculosis, focuses on improving the quality of TB services through assessment of the TB care cascade and identification of missing cases [53]. Furthermore, the provision of transport incentives is in line with the principles of social protection for patients and supports the attainment of universal health coverage, as outlined in Sustainable Development Goal 3 and the "End TB Strategy" [42].

Study Strengths and Limitations

This randomized controlled trial is expected to provide one of the highest levels of evidence for ways to enhance com-pletion of the TB diagnostic process and treatment initia-tion. The study will be conducted across different levels of health facilities to enhance representativeness and increase the generalizability of the findings. In addition, we are implementing a multifaceted intervention comprising SMS reminders, telephone calls, and transport incentives, which is an approach that, to the best of our knowledge, has not been previously evaluated among persons with presumptive TB.

However, blinding will not be possible at all levels, particularly for participants, which may introduce some bias. This risk will be minimized through continual clarification of the study goal and methods. Moreover, individuals who share mobile phones will be excluded to avoid inadvertent disclosure of their testing status. This exclusion criterion may limit participation of certain populations that could have benefited from this intervention.

Conclusions

This study will assess the effect of SMS reminders, telephone calls, and transport incentives on enhancing completion of TB diagnosis among persons with presumed TB and treatment initiation for diagnosed patients within Uganda's health care system. The trial will provide evidence that can inform health care practice and policy related to the TB diagnosis process, which could ultimately improve patient care. The use of SMS reminders and telephone calls in the phase of being presumed for TB will provide insights on their effectiveness in this phase, which has not been extensively explored. Moreover, the application of these technologies will add to existing evidence on the effectiveness of mHealth in improving health service delivery.

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Authors' Contributions

RN led the manuscript writing and coordinated the writing process as well as ethical clearance of the protocol. IW, VK, and SK contributed to manuscript writing. RS provided technical support during study conceptualization, protocol development,

and manuscript writing alongside NK, LA, JKN, and VN. EB conceptualized the study and provided overall technical guidance during protocol development and manuscript writing. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

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Abbreviations

DSMB: data and safety monitoring board
HC: health centre
LMICs: low- and middle-income countries
LSC: local steering committee **LTFU:**
loss to follow-up **mHealth:** mobile
health **ODK:** Open Data Kit
SOC: standard of care
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
TB: tuberculosis
WHO: World Health Organization

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Effect of SMS Reminders, Telephone Calls, and Transport Incentives on Enhancing the Completion of Tuberculosis Diagnosis and Initiation of Treatment for Diagnosed Patients: Protocol for a Randomized Controlled Trial

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Appendix 5: Data extraction tool for the cohort analysis of presumptive TB patients

Question	Response
1. HEALTH FACILITY IDENTIFIERS	
Q1. Questionnaire ID *(1st three letters of the facility followed by the number of the entry e.g MUK003)*	
Q2. Data of data collection (dd/mm/yy)	
Q3. Name of Research Assistant	
Q4. Name of health facility	1. Mukono General Hospital 2. Luwero Hospital 3. Wakiso H/C IV 4. Entebbe Regional Referral Hospital 5. Kiruddu National Referral Hospital
Q5a. Ownership of health facility	1. Public (Government owned) 2. Private not for profit (PNFP)
Q5b. Level of health facility	**1.** Hospital **2.** H/C IV
3. IN THIS NEXT SECTION, PLEASE REFER TO THE PRESUMPTIVE TB REGISTER	
Q6a. Date of registration as presumptive TB patient	1. Recorded 2. Not recorded
Q6b. Enter date of registration as presumptive TB patient (dd/mm/yy)	
Q7a. Care entry point of the presumptive register	1. Out Patients Department (OPD) 2. TB unit 3. ART clinic 4. Pedeatric clinic 5. Male ward 6. Female ward 7. Maternity 8. Specialised clinics (Diabetes/ eye etc) 9. Others (specify)
Q7 b. Other entry point	

Q8. Presumptive TB number	
Q9. Initials of the patient	
Q10a. Phone number recorded	1. Yes 2. No 3. Number unreadable
Q10b. Enter phone number	
Q11a. Patient age recorded	1. Yes 2. No
Q11b. Age in complete years	
Q12. Sex	1. Male 2. Female
Q13. Client category	1. National 2. Foreigner 3. Refugee 4. Missing
Q14a. Area of stay recorded	1. Yes 2. No
Q14 b. village	
Q14 c. Sub-county	
Q14 d. District	
Q15. HIV status	1. Positive 2. Negative 3. Unknown
Q16. Criterion for presumptive TB identification	1. Cough of more than 2 weeks 2. Fever 3. Weight loss 4. Excessive night sweats 5. Missing
Q17. Sample collected	1. Yes 2. No
Q18.a What sample was collected?	1. Sputum 2. Urine 3. Chest X-ray 4. Lymphnode Aspirate/ Biopsy 5. Spinal fluid Aspirate 6. Others (specify)

Q18.b Specify other sample collected	
Q19. Type of test taken	1. Gene Xpert 2. TB Lam 3. Microscopy 4. Chest X-ray
Q20a. Date Sample 1 (Gene Xpert) sent to the laboratory recorded	1. Yes 2. No
Q20b. Date Sample (Gene xpert) is sent to the laboratory (dd/mm/yy)	
Q21a. Date sample 1 (microscopy) is sent to the laboratory recorded	1. Yes 2. No
Q21b. Date Sample1 (microscopy) is sent to the laboratory (dd/mm/yy)	
Q22a. Date sample 2 (microscopy) is sent to the laboratory recorded	1. Yes 2. No
Q22b. Date sample 2 (microscopy) is sent to the laboratory (dd/mm/yy)	
Q23a. Date sample from urine (TB LAM) is sent to the laboratory recorded	1. Yes 2. No
Q23b. Date sample from urine (TB LAM) is sent to the laboratory (dd/mm/yy)	
Q24a. Date sample (X-ray) is sent to the laboratory recorded	1. Yes 2. No
Q24b. Date sample (X-ray) is sent to the laboratory recorded (dd/mm/yy)	
Q25. Was TB diagnosed (Patient positive for TB)	1. Yes 2. No
Q25b If yes, how was TB diagnosed?	1. Laboratory 2. Radiology 3. Clinically
Q26a. Date on which diagnosis was done recorded	1. Yes 2. No
Q26b. Date on which diagnosis was done (dd/mm/yy)	

Q27. If Yes in Q25, was the patient started on treatment	1. Yes 2. No
Q27b Write down any comments or issues you noted from this entry of the presumptive book	
4. IN THIS SECTION, REFER TO THE LABORATORY AND GENE X-PERT REGISTER AND TRACK PATIENT AGAINST NAME, SEX AND AGE	
Q28. Laboratory register number	
Q29. Were the patient's results released or recorded within one month?	1. Yes 2. No
Q30a. Type of test taken	1. Gene Xpert 2. Microscopy 3. TB LAM 4. Chest X-ray 5. Others (specify)
Q30b. If others, specify which other test was done	
Q31a. Date on which results from sample (Gene xpert) were received / recorded in the laboratory register recorded	1. Yes 2. No
Q31b. Date results from sample (Gene xpert) were received (recorded in the register)-dd/mm/yy	
Q31c. Test results of Gene X-pert	1. Positive 2. Negative 3. Invalid/ error
Q32a. Date on which results from sample 1 (microscopy) were received / recorded in the laboratory register recorded	1. Yes 2. No
Q32.b Date results from sample 1 (microscopy) were received (recorded in the register)-dd/mm/yy	
Q32c. Test results of microscopy from sample 1	1. Positive 2. Negative 3. Invalid/ error

Q33a. Date on which results from sample 2 (microscopy) were received / recorded in the laboratory register recorded	1. Yes 2. No
Q33b. Date results from sample 2 (microscopy) were received (recorded in the register)- dd/mm/yy	
Q33c. Test results of microscopy from sample 2	1. Positive 2. Negative 3. Invalid/ error
Q34a. Date on which results from TB LAM were received is recorded	1. Yes 2. No
Q34b. Date results from sample (TB LAM)) were received (recorded in the register)- dd/mm/yy	
Q34c. Test results from TB LAM	1. Positive 2. Negative 3. Invalid/ error
Q35a. Date on which results from X-ray were received is recorded	1. Yes 2. No
	3.
Q35b. Date results from sample (X-ray) were received (recorded in the register)- dd/mm/yy	
Q35c. Test results of X-ray	1. Positive 2. Negative 3. Invalid/ error
Q36a. Was TB diagnosed? (Positive for TB)	1. Yes 2. No
Q36b. If Yes, how was TB diagnosed?	1. Laboratory investigation 2. Radilogy 3. Clinically
Q37. Write down any comments or issues you noted from this entry of the laboratory register	
5. FILL IN THE NEXT SECTION FROM THE TREATMENT REGISTER TRACKING THEM AGAINST NAME, AGE AND SEX	
Q38. Was the patient initiated on treatment within one month?	1. Yes 2. No

Q39. Give reasons for not initiating treatment if recorded	
Q40a. Where was treatment initiated?	1. Onsite (At the same health facility) 2. Offsite
Q40b. If treatment was initiated offsite, was it a referral?	1. Yes 2. No
Q40c. Give any other comments for this entry	
Q41. Treatment register number	
Q42a. Date started on first line of treatment recorded	1. Yes 2. No
Q42b. Date started on first line of treatment (dd/mm/yy)	
Q43. Type of TB	1. New Case 2. Relapse 3. Treatment after failure 4. Treatment after loss to follow up 5. Treatment history unknown 6. Missing
Q44. HIV Status	1. Positive 2. Negative 3. Unknown
Q.45. If not registered for treatment, was death was documented?	1. Yes 2. No
Q46. Write down any comments or issues you noted from this entry of the treatment register	
Q47. Location of facility (GPS)	

END

Appendix 6: Informed Consent form for In-depth interview participants (Presumptive TB patients LTFU)- Formative phase

Introduction

Hello, my name is _____, a PhD student at Makerere University School of Public Health. I am conducting a research on "Effect and implementation factors of a contextually adapted short message service or phone call intervention to reduce loss to follow-up among presumptive TB patients in Central Uganda" as a requirement for my PhD studies.

Purpose of the Study

The study is about pathways, facilitators and barriers to loss to follow-up for presumptive TB patients and how best to encourage completion of the TB diagnostic process. I invite you to take part in the research study because you were once either presumed with TB or confirmed with TB. You have been identified and asked to voluntarily participate in this study because I believe you will contribute valuable information that we need to design an effective intervention.

Length of your participation in the interview

This interview will last approximately 30 to 40 minutes.

Where the study is being done and number of people participating

This study is taking place in four HCFs in Mukono, Mityana and Buikwe districts. These include St. Francis Hospital Naggalama, Kojja H/C IV, Kawolo Hospital, and Mityana Hospital.

Study procedures

You have been purposively selected to participate in this study. If you consent to participate in the study, you will be asked some questions about your experience at the health facility right from the time when you were presumed to have TB to when you dropped out of the diagnostic process. Notes will be taken during the interview and you will also be audio recorded to ensure we capture all your information correctly without misrepresenting you.

Potential Risks of taking part in this study

There are no anticipated risks to you upon participation in this study. To safeguard against loss of confidentiality, all interview transcripts will use unique study ID numbers instead of personal identifiers. All interviews will be audio recorded and the files will be transcribed into text, and translated into English (if necessary). Electronic audio video files will be kept at Makerere university School of Public Health for purposes of checking accuracy of the data during the transcription phase. We will remove any person identifiers only by code numbers to safeguard confidentiality. After transcription and data verification, audio-video files will be archived in safe locked place and destroyed after the end of the study as per the funder's requirements. To ensure privacy, no information from the focus groups will be kept with your name. You do not have to answer any questions that you do not wish to. You may also find it hard to stay for a 1-hour meeting.

Potential benefits of taking part in this study

There are no direct benefit to your participation in this study. However, information from this study will be used to improve retention of presumptive TB patients till diagnosis and enhance their linkage to care in Uganda. Taking part in this study could make you feel good about helping your community and the health providers as well as the TB program to solve an

important problem.

Participating in this study

If you agree to participate, you will be requested to sign this consent form. You will be given a copy of this form to keep. Your participation in this study is entirely voluntary. You may decide not to answer certain questions that you are not comfortable with or withdraw from the study at any time.

Reimbursement

You will receive Ten thousand Uganda Shillings (10,000) for taking part in this interview/discussion and completing the accompanying questions. This is to reimburse you for time, travel and other expenses you may have from being in this study.

Alternatives to Participation

Your participation in this study is completely voluntary. You may choose to participate in the study or not. Whatever the case, you will still be able to access standard of care from the National TB and Leprosy Program, a private clinic of your choice, or any other public TB control clinics. You are free to withdraw from the study at any time or decline to participate in any or all components of the study (for example, interview, and sample collection) without penalty. If you decide to stop or withdraw from the study, or if the researchers decide to end your participation, the information you have given the researchers up to the time of your withdrawal will be kept as part of the study and will be analyzed unless you request in writing to have it removed.

Confidentiality

The information you provide will be kept confidential. Your name will not appear in any reports or publications.

Problems and questions about the study

If you have any questions related to participation in this study, please contact the team leader, Ms. Rebecca Nuwematsiko, rnuwematsiko@musph.ac.ug, 0781 507 824. If you have questions concerning your rights as a study participant, please contact the Chairperson, Higher Degrees, Research and Ethics Committee of Makerere University School of Public Health; Dr. Joseph Kagaayi, 256-701-888-163/ 256-312-291-397.

Statement of consent

I have been given information on the study and allowed to ask questions. I voluntarily agree to take part in this study. I have received a copy of this consent form to keep for myself and have read and understood all of it.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: _____

I also agree to be audio recorded during the interview for reasons already explained to me.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: ____

Appendix 7: In-depth interview guide for presumptive TB patients who were lost to follow-up from the study facility- Formative phase

*(**Respondents:** Presumptive TB patients who did not finish the screening process)*

Participant socio-demographic characteristics

Variable	Response
Date of Interview	
Interview ID *(IDI_01_MIT_RN)* *Where IDI- Interview type; 01- Number of interview: MIT- First three letters of the facility, Mityana; RN- Initials of the Research Assistant*	
Name of Research Assistant	
Name of Health facility	
Age in complete years	
Sex	
Religion	
Occupation	
Area of Stay	

A. Beginning question

1. What do you know about the disease TB? (***Probe for: how common it is in the respondent's community, How it spreads and How it can be prevented.)***

2. What could be the importance of testing for TB? What problems may arise if one does not test for TB when advised to?

B. Pre-diagnosis loss to follow-up *(For patients who were LTFU before completing diagnosis)*

3. Please tell me a story of your journey from the time you were presumed to have TB in this health facility up to now. (***Probe for: Reactions/ feelings when informed of suspected TB, how they proceeded to test, counselling received, how they obtained their results etc)***

4. I understand that you were presumed to have TB but unfortunately did not finish the screening process. At what point in this diagnosis process did you stop? ***(Probe for I) submit the required sample or do other required investigations for testing and or ii) receive back their results)***

5. Please share with me what could have happened that led you not to **(ask in reference to the answer given in 6 above)**

I) Submit the sample required or do other required investigations ***(Probe for individual, social [social/peer support/stigma influences], community, environmental and health system facilitators [cost of testing, time to test, distance to the facility, availability of the TB testing services, time taken to receive the services, and support from health workers])***

ii) Receive your results? ***(Probe for individual, social [social/peer support/stigma influences], community, environmental and health system facilitators [cost of testing, time to test, distance to the facility, availability of the TB testing services, time taken to receive the services, and support from health workers])***

6. There are some presumed TB patients who manage to submit the samples and receive back their results. From your experience as you went through the diagnostic process what do you think enables those patients to:

i) Submit the samples or do other required investigations? **(Probe *for individual, social, community and health system factors [pay attention to what happens at the points of sample collection, submission of sputum and receipt of results])***

ii) Receiving back their results? **(Probe *for individual, social, community and health system factors [pay attention to what happens at the points of sample collection, submission of sputum and receipt of results])***

7. What do you think can be done to ensure that all presumptive TB patients submit samples, do the required tests and also come back and pick their results? ***Note:*** *Ensure you re-echo to the participant what they mentioned as barriers and facilitators before and ask for solutions for each.* ***(Probe for what can be done at an individual level, family level, societal level, health facility level and policy level)***

C. Pathways following loss to follow up before completing diagnosis

8. Going back to the time when you stopped seeking care for TB from this health facility. Did you continue seeking diagnosis/care for the TB-like symptoms that you had when you first visited this health facility? Yes/ No

<u>If Yes, go to Q9 and if No, go to Q13</u>

9 a) If yes, continued seeking diagnosis, where else did you go to continue seeking care for the symptoms you had at that time?

b) Why did you decide to seek diagnosis/care from this health facility? ***(Probe: personal, social, facility and environmental factors)***

10 a) Besides the facility you have just told me, where elsewhere did you visit before becoming better or getting the diagnosis?

b) Why did you decide to seek diagnosis/care from this health facility? ***(Probe: personal, social, facility and environmental factors)***

11. What could have motivated you to continue seeking care from the facilities you told me above despite being lost from this facility? ***(Probe: personal, social facility and environmental factors)***

12. Did you finally get the diagnosis of the symptoms you had? Yes/No.

a) If Yes, what were the results of this diagnosis and how did you feel about them?

13. If No, did not continue seeking diagnosis and care, are you planning on continuing to do the TB diagnosis? Yes/ No. If No, what are some of the reasons that are still preventing you from completing the diagnosis? ***(Probe: personal, facility and environmental factors)***

D. Concluding question

14. We have now come to the end of this discussion; I appreciate your time in responding to all the questions raised. Is there anything else you would want to share, probably something we have not talked about that would help us understand why some patients do not complete the diagnosis process as well as starting treatment while others do?

THANK YOU

Appendix 8: Informed Consent form for In-depth interview participants (Presumptive TB patients who completed diagnosis)- Formative phase

Introduction

Hello, my name is _____, a PhD student at Makerere University School of Public Health. I am conducting a research on "Effect and implementation factors of a contextually adapated short message service or phone call intervention to reduce loss to follow-up among presumptive TB patients in Central Uganda" as a requirement for my PhD studies.

Purpose of the Study

The study is about facilitators and barriers to completing TB diagnosis and how best to encourage TB presumed patients complete the TB diagnostic process. I invite you to take part in the research study because you were once either presumed with TB or confirmed with TB.

You have been identified and asked to voluntarily participate in this study because I believe you will contribute valuable information that we need to design an effective intervention.

Length of your participation in the interview

This interview will last approximately 30 to 40 minutes.

Where the study is being done and number of people participating

This study is taking place in four HCFs in Mukono, Mityana and Buikwe districts. These include St. Francis Hospital Naggalama, Kojja H/C IV, Kawolo Hospital, and Mityana Hospital.

Study procedures

You have been purposively selected to participate in this study. If you consent to participate in the study, you will be asked some questions about your experience at the health facility right from the time when you were presumed to have TB to when you completed diagnosis. Notes will be taken during the interview and you will also be audio recorded to ensure we capture all your information correctly without misrepresenting you.

Potential Risks of taking part in this study

There are no anticipated risks to you upon participation in this study. To safeguard against loss of confidentiality, all interview transcripts will use unique study ID numbers instead of personal identifiers. All interviews will be audio recorded and the files will be transcribed into text, and translated into English (if necessary). Electronic audio video files will be kept at Makerere university School of Public Health for purposes of checking accuracy of the data during the transcription phase. We will remove any person identifiers only by code numbers to safeguard confidentiality. After transcription and data verification, audio-video files will be archived in safe locked place and destroyed after the end of the study as per the funder's requirements. To ensure privacy, no information from the focus groups will be kept with your name. You do not have to answer any questions that you do not wish to. You may also find it hard to stay for a 1-hour meeting.

Potential benefits of taking part in this study

There are no direct benefits to your participation in this study. However, information from this study will be used to improve retention of presumptive TB patients till diagnosis and enhance their linkage to care in Uganda. Taking part in this study could make you feel good about helping your community and the health providers as well as the TB program to solve

an important problem.

Participating in this study

If you agree to participate, you will be requested to sign this consent form. You will be given a copy of this form to keep. Your participation in this study is entirely voluntary. You may decide not to answer certain questions that you are not comfortable with or withdraw from the study at any time.

Reimbursement

You will receive Ten thousand Uganda Shillings (10,000) for taking part in this interview/discussion and completing the accompanying questions. This is to reimburse you for time, travel and other expenses you may have from being in this study.

Alternatives to Participation

Your participation in this study is completely voluntary. You may choose to participate in the study or not. Whatever the case, you will still be able to access standard of care from the National TB and Leprosy Program, a private clinic of your choice, or any other public TB control clinics. You are free to withdraw from the study at any time or decline to participate in any or all components of the study (for example, interview, and sample collection) without penalty. If you decide to stop or withdraw from the study, or if the researchers decide to end your participation, the information you have given the researchers up to the time of your withdrawal will be kept as part of the study and will be analyzed unless you request in writing to have it removed.

Confidentiality

The information you provide will be kept confidential. Your name will not appear in any reports or publications.

Problems and questions about the study

If you have any questions related to participation in this study, please contact the team leader, Ms. Rebecca Nuwematsiko, rnuwematsiko@musph.ac.ug, 0781 507 824. If you have questions concerning your rights as a study participant, please contact the Chairperson, Higher Degrees, Research and Ethics Committee of Makerere University School of Public Health; Dr. Joseph Kagaayi, 256-701-888-163/ 256-312-291-397.

Statement of consent

I have been given information on the study and allowed to ask questions. I voluntarily agree to take part in this study. I have received a copy of this consent form to keep for myself and have read and understood all of it.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: _____

I also agree to be audio recorded during the interview for reasons already explained to me.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: ____

Appendix 9: **In-depth interview guide for presumptive TB patients who completed diagnosis - Formative phase**

*(**Respondents:** Presumptive TB patients who finished the diagnostic process)*

Participant socio-demographic characteristics

Variable	**Response**
Date of Interview	
Interview ID *(IDI_01_MIT_RN)* *Where IDI- Interview type; 01- Number of interview: MIT- First three letters of the*	

facility, Mityana; RN- Initials of the Research Assistant	
Name of Research Assistant	
Name of Health facility	
Age in complete years	
Sex	
Religion	
Occupation	
Area of Stay	

A. Beginning question

1. What do you know about the disease TB? (***Probe for: how common it is in the respondent's community, How it spreads and How it can be prevented.)***

2. What could be the importance of testing for TB? What problems may arise if one does not test for TB when advised to?

B. Pre-diagnosis loss to follow-up

3. Please tell me a story of your journey from the time you were presumed to have TB up to when you received your results. (***Probe for: Reactions/ feelings when***

informed of suspected TB, how they proceeded to test, counselling received, how they obtained their results etc)

4. I understand that when you were suspected to have TB, you went ahead and submitted the samples for testing/ conducted other investigations required and also received your results. What could have enabled you to;

I) Submit the sample required or do other investigations required? ***(Probe for individual, social, community and health system facilitators [pay attention to what happens at the points of sample collection, and submission of sputum])***

ii) Receive your results? ***(Probe for individual, social, community and health system facilitators [pay attention to what happens at the point of receipt of results])***

iii) Please tell me what the results of your investigations were. Positive or negative?

5. There are some presumed TB patients who don't submit the samples or receive back their results. From your experience as you went through the process what do you think hinders those patients from:

I) submitting the samples? ***(Probe for individual, social, community and health system factors [cost involved, time to visit the health facility, distance to the facility, availability of treatment services, time taken to receive the services, and support from health workers])***

ii) Receiving back their results? ***(Probe for individual, social, community and health system factors [cost involved, time to visit the health facility, distance to the facility, availability of treatment services, time taken to receive the services, and support from health workers])***

6. What do you think can be done to ensure that all presumptive TB patients submit samples, or carryout the required investigations and also come back to receive their results**?** ***(Probe for what can be done at an individual level, family level, societal level, health facility level and policy level)***

C. Concluding question

7. We have now come to the end of this discussion; I appreciate your time in responding to all the questions raised. Is there anything else you would want to share, probably something we have not talked about that would help us understand why some patients complete the diagnosis process as well as starting treatment while others do not?

END

Appendix 10: Informed Consent form for Key Informant Interview participants-Formative phase

Introduction

Hello, my name is _____, a PhD student at Makerere University School of Public Health. I am conducting a research on "Effect and implementation factors of a contextually adapted short message service and phone call intervention to reduce loss to follow-up among presumptive TB patients in Central Uganda" as a requirement for my PhD studies.

Purpose of the Study

The study is about how best to encourage TB presumed patients to complete the TB diagnostic process. We invite you to take part in the research study because you are a key stakeholder in identifying, supporting and treating TB patients at this health facility.

You have been identified and asked to voluntarily participate in this study because we believe you will contribute valuable information that we need to design an effective SMS and phone call intervention.

Length of your participation in the interview

This interview will last approximately 45 minutes to 1 hr.

Where the study is being done and number of people participating

This study is taking place in four HCFs in Mukono, Mityana and Buikwe districts. These include St. Francis Hospital Naggalama, Kojja H/C IV, Kawolo Hospital, and Mityana Hospital.

Study procedures

You have been purposively selected to participate in this study. If you consent to participate in the study, you will be asked some questions about your experience at the health facility right from the time when one is presumed to have TB to when they complete diagnosis or drop out. Notes will be taken during the interview and you will also be audio recorded to ensure we capture all your information correctly without misrepresenting you.

Potential Risks of taking part in this study

There are no anticipated risks to you upon participation in this study. To safeguard against loss of confidentiality, all interview transcripts will use unique study ID numbers instead of personal identifiers. All interviews will be audio recorded and the files will be transcribed into text, and translated into English (if necessary). Electronic audio video files will be kept at Makerere University School of Public Health for purposes of checking accuracy of the data during the transcription phase. We will remove any person identifiers only by code numbers to safeguard confidentiality. After transcription and data verification, audio-video files will be archived in safe locked place and destroyed after the end of the study as per the funder's requirements. To ensure privacy, no information from the focus groups will be kept with your name. You do not have to answer any questions that you do not wish to. You may also find it hard to stay for a 1-hour meeting.

Potential benefits of taking part in this study

There are no direct benefits to your participation in this study. However, information from this study will be used to improve retention of presumptive TB patients till diagnosis and enhance their linkage to care in Uganda. Taking part in this study could make you feel good about helping your community and the health providers as well as the TB program to solve

an important problem.

Participating in this study

If you agree to participate, you will be requested to sign this consent form. You will be given a copy of this form to keep. Your participation in this study is entirely voluntary. You may decide not to answer certain questions that you are not comfortable with or withdraw from the study at any time.

Reimbursement

You will receive Ten thousand Uganda Shillings (10,000) for taking part in this interview/discussion and completing the accompanying questions. This is to reimburse you for time, travel and other expenses you may have from being in this study.

Alternatives to Participation

Your participation in this study is completely voluntary. You may choose to participate in the study or not. You are free to withdraw from the study at any time or decline to participate in any or all components of the study without penalty. If you decide to stop or withdraw from the study, or if the researchers decide to end your participation, the information you have given the researchers up to the time of your withdrawal will be kept as part of the study and will be analyzed unless you request in writing to have it removed.

Confidentiality

The information you provide will be kept confidential. Your name will not appear in any reports or publications.

Problems and questions about the study

If you have any questions related to participation in this study, please contact the team leader, Ms. Rebecca Nuwematsiko, rnuwematsiko@musph.ac.ug, 0781 507 824. If you have questions concerning your rights as a study participant, please contact the Chairperson, Higher Degrees, Research and Ethics Committee of Makerere University School of Public Health; Dr. Joseph Kagaayi, 256-701-888-163/ 256-312-291-397.

Statement of consent

I have been given information on the study and allowed to ask questions. I voluntarily agree to take part in this study. I have received a copy of this consent form to keep for myself and have read and understood all of it.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: _____

I also agree to be audio recorded during the interview for reasons already explained to me.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: ____

Appendix 11: Key Informant interview guide- Formative phase

(***Respondents:*** *In-charges and other key health workers at the out-patient department, TB clinic, ART Clinic and laboratory)*

A. **Participant socio-demographics**

Variable	**Response**
Date of Interview	
Interview ID *(KII_01_KAW_RN)* *Where KII- Interview type; 01- Number of interview: KAW- First three letters of the facility; RN- Initials of the Research Assistant*	
Name of Research Assistant	

Name of Health facility	
Name of facility department where the health worker executes their main duties	
Age of health worker	
Sex of health worker	
Cadre of health worker	
Years in health service	

B. Beginning question

1. In your own view, what do you think of TB occurrence in this health facility? (***Probe for patient and health worker understanding of the disease severity and fatality.)***

C. Pre-diagnosis loss to follow-up

2. Please take me through the screening process for the presumptive TB patients at this health facility. ***(Probe for more information on triage/use of intensified case finding form/ tool; documentation; sample collection; referral for other investigation; and how results are received back by the patients).***

3. In some health facilities in Uganda and elsewhere, a certain percentage of presumptive TB patients get lost to follow up before they are diagnosed with TB. How much of a problem do you think this is here at this facility?

4. We understand there are patients who are presumed to have TB but do not complete the screening process.

   a) In your view, what enables/ facilitates those who complete the screening process? ***(Probe for individual, social, community, environmental and health system facilitators [pay attention to what happens at the points of sample collection, submission of sputum and receipt of results])***

   b) In your view, what hinders others from completing the screening process? ***(Probe for individual, social, community, environmental and health system factors [pay attention to what happens at the points of sample collection, submission of sputum and receipt of results])***

5. What do you think can be done to address these challenges/barriers you mentioned to help presumptive TB patients finish the screening/testing process? *(**Note:** Ensure you re-echo to the participant what they mentioned as barriers before and ask for solutions for each.)*

6. Are there categories of presumptive TB patients at this health facility who are likely to get lost to follow up more than others before they test for TB? Yes/ No Who could those be? ***(Probe: Patients with no telephones, patients who come from far, age of the patient, drug users, etc). Why do you think they are more likely to get lost to follow-up compared to others?***

D. Concluding question

7. We have now come to the end of this discussion; I appreciate your time in responding to all the questions raised. Is there anything else you would want to share, probably something we

have not talked about that would help us understand why some patients complete the diagnosis process as well as starting treatment while others do not?

THANK YOU

Appendix 12: Informed Consent form for In-depth Interview participants- Post-trial evaluation

Introduction

Hello, my name is _____, a PhD student at Makerere University School of Public Health. I am conducting a research on "Effect and implementation factors of a contextually adapted short message service or phone call intervention to reduce loss to follow-up among presumptive TB patients in Central Uganda" as a requirement for my PhD studies.

Purpose of the Study

The study is about evaluating a study you participated in using SMS reminders or phone calls to encourage TB presumed patients to complete the TB diagnostic process. We invite you to take part in the research study because you were one of the participants enrolled in the study. We would like to hear your experiences and perceptions on participating in this study and suggestions for improvement. You have been identified and asked to voluntarily participate because we believe you will contribute valuable information that we need to evaluate this study.

Length of your participation in the interview

This interview will last approximately 45 minutes to 1 hr.

Where the study is being done and number of people participating

This study is taking place in five HCFs in Mukono, Mityana Wakiso, Luwero and Buikwe Kampala districts. These include St. Francis Hospital NaggalamaMukono General Hospital, Kojja Wakiso H/C IV, Kawolo Luwero General Hospital, Entebbe Regional Referral Hospital and Mityana Kiruddu National Referral Hospital. .

Study procedures

You have been purposively selected to participate in this study. If you consent to participate in the study, you will be asked some questions about your experience while participating in the study and perceptions on the SMS reminders and phone calls that you received and how they helped you to either complete TB diagnosis or start treatment in case you tested positive. We would also like to get your suggestions on how best we can improve this study in future. Notes will be taken during the interview and you will also be audio recorded to ensure we capture all your information correctly without misrepresenting you.

Potential Risks of taking part in this study

There are no anticipated risks to you upon participation in this study. To safeguard against loss of confidentiality, all interview transcripts will use unique study ID numbers instead of personal identifiers. All interviews will be audio recorded and the files will be transcribed into text, and translated into English (if necessary). Electronic audio video files will be kept at Makerere University School of Public Health for purposes of checking accuracy of the data during the transcription phase. We will remove any person identifiers only by code numbers to safeguard confidentiality. After transcription and data verification, audio-video files will be archived in safe locked place and destroyed after the end of the study as per the funder's requirements. To ensure privacy, no information from the focus groups will be kept with your name. You do not have to answer any questions that you do not wish to. You may also find it hard to stay for a 1-hour meeting.

Potential benefits of taking part in this study

There are no direct benefits to your participation in this study. However, information from this study will be used to improve retention of presumptive TB patients till diagnosis and

enhance their linkage to care in Uganda. Taking part in this study could make you feel good about helping your community and the health providers as well as the TB program to solve an important problem.

Participating in this study

If you agree to participate, you will be requested to sign this consent form. You will be given a copy of this form to keep. Your participation in this study is entirely voluntary. You may decide not to answer certain questions that you are not comfortable with or withdraw from the study at any time.

Reimbursement

You will receive Ten thousand Uganda Shillings (10,000) for taking part in this interview/discussion and completing the accompanying questions. This is to reimburse you for time, travel and other expenses you may have from being in this study.

Alternatives to Participation

Your participation in this study is completely voluntary. You may choose to participate in the study or not. You are free to withdraw from the study at any time or decline to participate in any or all components of the study without penalty. If you decide to stop or withdraw from the study, or if the researchers decide to end your participation, the information you have given the researchers up to the time of your withdrawal will be kept as part of the study and will be analyzed unless you request in writing to have it removed.

Confidentiality

The information you provide will be kept confidential. Your name will not appear in any reports or publications.

Problems and questions about the study

If you have any questions related to participation in this study, please contact the team leader, Ms. Rebecca Nuwematsiko, rnuwematsiko@musph.ac.ug, 0781 507 824. If you have questions concerning your rights as a study participant, please contact the Chairperson, Higher Degrees, Research and Ethics Committee of Makerere University School of Public Health; Dr. Joseph Kagaayi, 256-701-888-163/ 256-312-291-397.

Statement of consent

I have been given information on the study and allowed to ask questions. I voluntarily agree to take part in this study. I have received a copy of this consent form to keep for myself and have read and understood all of it.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: _____

I also agree to be audio recorded during the interview for reasons already explained to me.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: ____

Appendix 13: **In-depth interview guide for presumptive TB patients who participated in the RCT- Post-trial evaluation**

*(**Respondents:** Presumptive and confirmed TB patients who participated in the RCT regardless of their completion status)*

A. Participant socio-demographic characteristics

Variable	**Response**
Date of Interview	
Interview ID *(IDI_01_MIT_RN)* *Where IDI- Interview type; 01- Number of interview: MIT- First three letters of the facility, Mityana; RN- Initials of the Research Assistant*	
Name of Research Assistant	

Name of Health facility	
Age in complete years	
Sex	
Religion	
Occupation	
Area of Stay	

B. Beginning question

1. I understand that at the time of enrolling in this study, you were presumed to have TB. Please tell me a story of your journey from the time you were presumed to have TB, enrolled in this study up to now. (***Probe for: support received from the study, how the support received enabled them to complete diagnosis, how they proceeded to test, counselling received, how they obtained their results etc)***

2. How exactly did this study assist you or involve you after enrolment? ***(Probe for signing consent, sensitisation on TB, SMS reminders, phone calls, follow-up by health workers etc)***

3. After enrollment into this study, did you go ahead to test for TB? Yes/ No

If Yes, proceed to Qns 4-5. If No, skip to Qns 6-7

C. Pre-diagnosis loss to follow-up

4. So you mentioned that you went ahead and submitted the samples for testing/ conducted other investigations required and also received your results. What could have enabled you to;

I) Submit the sample required or do other investigations required? ***(Probe for individual, social, community and health system facilitators [pay attention to what happens at the points of sample collection, and submission of sputum])***

ii) Receive your results? ***(Probe for individual, social, community and health system facilitators [pay attention to what happens at the point of receipt of results])***

iii) How did the support from this study help you in completing diagnosis? ***(Probe in submitting sample and receiving results, SMS reminders, phone calls, health worker/ staff attitude, sensitization etc)***

iv) Please tell me what the results of your investigations were. Positive or negative?

5. There are some presumed TB patients who were enrolled in this study, supported but still didn't submit the samples or receive back their results. What do you think could have hindered those patients despite the support from:

I) submitting the samples? ***(Probe for individual, social, community and health system factors [cost involved, time to visit the health facility, distance to the facility, availability of treatment services, time taken to receive the services, and support from health workers])***

ii) Receiving back their results? ***(Probe for individual, social, community and health system factors [cost involved, time to visit the health facility, distance to the facility, availability of treatment services, time taken to receive the services, and support from health workers])***

For those who did not complete diagnosis for TB

6.You told me that you did not get tested for TB. What could have hindered you from taking the tests? ***(Probe for individual, social [social/peer support/stigma influences], community and health system facilitators [cost of testing, time to visit the health facility, distance to the facility, availability of treatment services, time taken to receive the services, and support from health workers])***

7. What support did you receive from this study? How did this support help you in this whole process? ***(Probe for SMS reminders, phone calls, sensitization, health worker/ staff attitude, follow-up])***

phone* D. Intervention specific questions *(For participants in the intervention arm only)

Preamble: In this study, we sent out SMS reminders to all presumptive TB patients who were enrolled in the study reminding them to complete diagnosis. For those who did not complete diagnosis after the SMS reminders, we made a up to three phone calls to them after 7 days at day 8, 10 and 12 from enrolement.

8. So which of these components did you receive? What aspects/ components of this study did you like or enjoy the most? Why do you say so?

9. What can you say about the SMS reminders that you received to remind you to complete diagnosis? ***(Probe: timing, frequency, number, content etc)***

10. What effort did you think was required of you regarding receiving the SMS reminder reminding you to complete TB diagnosis? What effort did you actually put in when you received the SMS reminder? Did you receive the SMS, did you think of texting back, what exactly happened?

11. What do you think were the benefits of the SMS reminder in terms of reminding you to complete TB diagnosis?

12. What good or bad things happened to you when you received the SMS reminding you to complete TB diagnosis? Let's start with the good things, what happened? What about the bad things? ***(Probe: on personal, family, social, health facility level)***

13. What can you say about the phone call that was made to you to remind you to complete diagnosis? ***(Probe: timing, frequency, number, content, person calling etc)***

14. What effort did you think was required of you regarding receiving the phone call reminding you to complete TB diagnosis? What effort did you actually put in when you received the phone call? Did you pick the phone call, call back, how was it for you?

15. What do you think were the benefits of the phone call in terms of reminding you to complete TB diagnosis?

16. What good or bad things happened to you when you received the phone call reminding you to complete TB diagnosis? Let's start with the good things, what happened? What about the bad things? ***(Probe: on personal, family, social, health facility level)***

17. Of all the support you received from this study, what can you say helped you more to complete diagnosis. SMS reminder or phone calls? Why do you think this aspect/ component helped you more than the others? How exactly did this component help you?

18. To what extent do you think the SMS or phone call reminders helped you in completing diagnosis? Which one worked more, SMS or phone call? Please explain your answer.

19. What factors enabled your participation in this study? ***(Probe: on personal, family, social, health facility and study staff level)***

20. What factors could have disrupted or hindered your participation in this study? ***(Probe: on personal, family, social, health facility and study staff level)***

E. Concluding question

21. What do you think can be done to improve this study to help presumptive TB patients' complete diagnosis?

22. We have now come to the end of this discussion; I appreciate your time in responding to all the questions raised. Is there anything else you would want to share, probably something we have not talked about that would help us understand what more can be done to help presumptive TB patients complete the diagnosis process?

END

Appendix 14: Informed Consent form for Key informants participants- Post-trial evaluation

Introduction

Hello, my name is _____, a PhD student at Makerere University School of Public Health. I am conducting a research on "Effect and implementation factors of a contextually adapted short message service or phone call intervention to reduce loss to follow-up among presumptive and confirmed TB patients in Central Uganda" as a requirement for my PhD studies.

Purpose of the Study

The study is about evaluating a study you participated in using SMS reminders or phone calls to encourage TB presumed patients to complete the TB diagnostic process and those who test positive start on TB treatment. We invite you to take part in the research study because you were a key implementer in the study. We would like to hear your experiences and perceptions on implementing this study and suggestions for improvement. You have been identified and asked to voluntarily participate because we believe you will contribute valuable information that we need to evaluate this study.

Length of your participation in the interview

This interview will last approximately 50 minutes to 1 hr.

Where the study is being done and number of people participating

This study is taking place in five HCFs in Mukono, Mityana Wakiso, Luwero and Buikwe Kampala districts. These include St. Francis Hospital NaggalamaMukono General Hospital,

Kojja Wakiso H/C IV, Kawolo Luwero General Hospital, Entebbe Regional Referral Hospital and Mityana Kiruddu National Referral Hospital..

Study procedures

You have been purposively selected to participate in this study. If you consent to participate in the study, you will be asked some questions about your experience at the health facility right from when you started supporting this study that was sending SMS reminders and phone calls to presumptive and confirmed TB patients reminding them to complete diagnosis and treatment respectively. Notes will be taken during the interview and you will also be audio recorded to ensure we capture all your information correctly without misrepresenting you.

To gather as many ideas as possible, we are holding small group meetings in form of focus group discussions (FGDs) to hear from the patients their experiencing seeking care for TB. The FGD will have 8-10 members only sharing their experiences. You have been identified and asked to voluntarily participate in this study because we believe you will contribute valuable information that we need to improve this intervention of SMS reminders and phone calls.

Potential Risks of taking part in this study

There are no anticipated risks to you upon participation in this study. To safeguard against loss of confidentiality, all interview transcripts will use unique study ID numbers instead of personal identifiers. All interviews will be audio recorded and the files will be transcribed into text, and translated into English (if necessary). Electronic audio video files will be kept at Makerere University School of Public Health for purposes of checking accuracy of the data during the transcription phase. We will remove any person identifiers only by code numbers to safeguard confidentiality. After transcription and data verification, audio-video files will be

archived in safe locked place and destroyed after the end of the study as per the funder's requirements. To ensure privacy, no information from the focus groups will be kept with your name. You do not have to answer any questions that you do not wish to. You may also find it hard to stay for a 1-hour meeting.

Potential benefits of taking part in this study

There are no direct benefits to your participation in this study. However, information from this study will be used to improve retention of presumptive TB patients till diagnosis and enhance their linkage to care in Uganda. Taking part in this study could make you feel good about helping your community and the health providers as well as the TB program to solve an important problem.

Participating in this study

If you agree to participate, you will be requested to sign this consent form. You will be given a copy of this form to keep. Your participation in this study is entirely voluntary. You may decide not to answer certain questions that you are not comfortable with or withdraw from the study at any time.

Reimbursement

You will receive Ten thousand Ugandan Shillings 10,000 only for taking part in this interview/discussion and completing the accompanying questions. This is to reimburse you for time, travel and other expenses you may have from being in this study.

Alternatives to Participation

Your participation in this study is completely voluntary. You may choose to participate in the

study or not. You are free to withdraw from the study at any time or decline to participate in any or all components of the study without penalty. If you decide to stop or withdraw from the study, or if the researchers decide to end your participation, the information you have given the researchers up to the time of your withdrawal will be kept as part of the study and will be analyzed unless you request in writing to have it removed.

Confidentiality

The information you provide will be kept confidential. Your name will not appear in any reports or publications.

Problems and questions about the study

If you have any questions related to participation in this study, please contact the team leader, Ms. Rebecca Nuwematsiko, rnuwematsiko@musph.ac.ug, 0781 507 824. If you have questions concerning your rights as a study participant, please contact the Chairperson, Higher Degrees, Research and Ethics Committee of Makerere University School of Public Health; Dr. Joseph Kagaayi, 256-701-888-163/ 256-312-291-397.

Statement of consent

I have been given information on the study and allowed to ask questions. I voluntarily agree to take part in this study. I have received a copy of this consent form to keep for myself and have read and understood all of it.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: _____

I also agree to be audio recorded during the interview for reasons already explained to me.

Name of Participant: _____Signature/thumb print: _____ Date: _____

Name of witness: _____Signature/thumb print: _____Date: _____

Name of Research Assistant: _____ Signature: _____Date: ____

Appendix 15: Key informant Guide- Post-trial Evaluation

*(**Respondents:** project staff who implemented the RCT)*

A. Interview identifiers and Participant socio-demographics

Variable	Response
Date of Interview	
Interview ID *(FGD_01_KAW_Male)* *Where FGD- Interview type; 01- Number of interview: KAW- First three letters of the facility; Male- type of the participants*	
Names of facilitator and note taker	
Name of Health facility	
District of the interview	

B. Socio-demographics

No	Name	Age	Sex	Occupation	Area of Stay

C. Beginning questions

Preamble: In this study, we sent out SMS reminders to all presumptive TB patients who were enrolled in the study reminding them to complete diagnosis and if positive to start treatment immediately. For those who did not complete diagnosis or start treatment when positive after the SMS reminder, we made a phone call to them after 3 days and if no response again, we called again after 5 days.

1. Tell us more, what exactly was done while implementing this study to remind presumptive TB patients to complete diagnosis and if positive to start treatment.

2. So what aspects/ components of this study did you like or enjoy implementing the most? Why do you say so?

D. Intervention Specific questions

Questions regarding SMS reminders

1. What can you say about the SMS reminders that participants received to remind them to complete diagnosis and if positive to start treatment?
2. What do you think were the benefits of the SMS reminder in terms of reminding them to complete TB diagnosis and if positive to start treatment? **(*Probe: Proportion that responded and completed diagnosis or initiated treatment)***
3. What good or bad things happened to them when they received the SMS reminding them to complete TB diagnosis and if positive to start treatment? Let's start with the good things, what do you think happened to them? What about the bad things? ***(Probe: on personal, family, social, health facility level)***
4. Tell me more on how these SMS reminders were being sent. ***(Probe: timing, frequency, number, content etc).*** Were they sent as planned? How easy or hard was it to send the SMS reminders. Please explain your answer.
5. Sometimes studies find it necessary and important to adjust implementation details due to several reasons. What adjustments were made to suit implementation sending SMS reminders?***(Probe for adherence or deviations from the planned strategy of implementation and why)***
6. a) What effort did you need to put in regarding sending the SMS reminders reminding participants to complete TB diagnosis or start treatment?

   b) Did the participants receive the SMS reminders, did they attempt to text back, what exactly happened?

   c) How did you balance sending SMS reminders with your daily workload? Would you say it required extra effort? Please explain your answer

Questions regarding phone calls

7. What can you say about the phone calls that were made to remind participants to complete diagnosis and if positive to start treatment?

8. What do you think were the benefits of the phone call in terms of reminding participants to complete TB diagnosis and if positive to start treatment? **(*Probe: Proportion that responded and completed diagnosis or initiated treatment)***

9. What good or bad things do you think happened to them when they received the phone call reminding them to complete TB diagnosis and if positive to start treatment? Let's start with the good things, what do you think happened to them? What about the bad things? ***(Probe: on personal, family, social, health facility level)***

10. Tell me more on how these phone calls were being made. ***(Probe: timing, frequency, number, content, person calling etc).*** Were they made as planned? How easy or hard was it to call the participants. Please explain your answer.

11. Sometimes studies find it necessary and important to adjust implementation details due to several reasons. What adjustments were made to suit implementation of using phone calls?***(Probe for adherence or deviations from the planned strategy of implementation and why)***

12. a) What effort did you need to put in regarding making phone calls reminding participants to complete TB diagnosis or start treatment?

    b) Did the participants receive the phone calls, did they try calling back, what exactly happened?

    c) How did you balance making phone calls with your daily workload? Would you say it required extra effort? Please explain your answer

13. Of the two SMS and phone call, what can you say helped participants more to either complete diagnosis or start treatment if positive for TB. Why do you think this aspect/ component helped them more than the others? How exactly did this component help them?

14. To what extent do you think the SMS or phone call reminders helped them in completing diagnosis or starting treatment if positive for TB? Please explain your answer.
15. What factors enabled you to implement this study to this level? ***(Probe: on personal, family, social, health facility and study staff level)***
16. What factors could have disrupted or hindered the implementation of this study? ***(Probe: on personal, family, social, health facility and study staff level)***

E. Concluding question

17. What do you think can be done to improve this study to help presumptive TB patients' complete diagnosis and those confirmed start treatment?
18. We have now come to the end of this discussion; I appreciate your time in responding to all the questions raised. Is there anything else you would want to share, probably something we have not talked about that would help us understand what more can be done to help presumptive TB patients complete the diagnosis process as well as starting treatment for those confirmed?

END

Appendix 16: Phone call script for the RCT

PHONE CALL SCRIPT (extract from STANDARD OPERATING PROCEDURE: MAKING PHONE CALLS- MILG/21/JULY 2023)

- Ensure a friendly and respectful interaction while making the phone call
- At the start of the call, the caller should introduce themselves to the patient
- Check if the call is being made to the right person-patient's name should be identified before any conversation begins.
- Check with the patient if they are in a private space to have a conversation.
- Give the reason for the phone call making reference to the call script "You are reminded to return to the health facility to complete diagnosis". If it is the 2nd phone call, inform the participant that their results are ready.

***In case results are ready before the participant receives the 1st call, combine the message on the phone call into one by thanking the participant for coming to the facility, let them know their results are ready and remind them to return and complete TB diagnosis.

- Thank them for their time and ask if they have any questions.
- Patients will be welcome to ask other related questions and referrals made to health workers for appropriate responses. DO NOT ATTEMPT to respond to facility/ health unrelated questions.
- Each phone call should not exceed 3 minutes. Devise tactful means to be brief to the point and encourage the patient to come to the health facility for more information.
- If a patient does not answer the phone or another person answers the phone, or it is not convenient for a patient to talk, or the phone is off, the RA shall attempt the call as many times as possible until an effective call is made to the right participant.

***A successful call will be referred to as when a patient was reached and conversation was made.

- All phone calls and relevant conversation should be noted.
- The phone calls shall be made by Research Assistants.
- Phone calls shall be made between 10:00am and 6:00pm. Exceptions are accepted if the participant requested to be called at a time after 6pm.
- Phone calls shall be made only using project phones for identification. Use of personal phones to call is PROHIBITED.

Appendix 17: Search strategy to assess evidence on mHealth interventions have been utilised to reduce pre-diagnosis and pre-treatment loss of presumptive TB patient

Research question: What mHealth interventions have been utilised to reduce pre-diagnosis and pre-treatment loss of presumptive TB patients in LMICs and how effective are they?

P Population or Participants	**I** Intervention(s) or Indicator
-Presumptive TB patients -TB patients -Patients of all ages **NO MESH or MTREE terms** **Brain storming:** TB suspects **Bench marking:** None	Mobile health interventions **MESH AND MTREE term:** telemedicine **Brain storming:** mHealth, ehealth, digital health, SMS, message, phone call, voice call, mobile apps, PDA, mobile phone

	Bench marking: messaging, text, mobile applications, health apps, personal digital assistants, cellular phone, cell phone, smart phones, electronic health, e-health, telemedicine
Comparison or Control Standard of care or any other intervention	**Outcome** What is the impact? Is there a change in knowledge, behaviour, or condition? -Pre-diagnosis loss -Pre-treatment loss **NO MESH or MTREE terms** **Brain storming:** pre-diagnosis, initial-loss, initial loss, pre-diagnostic drop out, pre-treatment, treatment initiation, loss to follow-up, lost-to-follow-up, drop-out, drop out, pre-treatment drop out **Bench marking:** Prediagnosis, prediagnostic drop out, pretreatment, pretreatment drop out, post-diagnosis

PUBMED Search strategy/terms- 27th January 2025 (Rechecked on 5th May 2026)

1. **Population**

#1 Using only the word patients

“tuberculosis patients” OR “TB patients” OR "presumptive tuberculosis patients" OR "presumptive TB patients" OR “suspected TB patients”

#2 Using both words patients and cases

“tuberculosis patients” OR “TB patients” OR "presumptive tuberculosis patients" OR "presumptive TB patients" OR “suspected TB patients” OR “tuberculosis cases” OR “TB cases” OR "presumptive tuberculosis cases" OR “suspected TB cases” OR “TB suspects”

#3 Adding the word tuberculosis to #2

tuberculosis OR TB OR “tuberculosis patients” OR “TB patients” OR "presumptive tuberculosis patients" OR "presumptive TB patients" OR “suspected TB patients” OR “tuberculosis cases” OR “TB cases” OR "presumptive tuberculosis cases" OR “suspected TB cases” OR “TB suspects”

#4 Removing quotation marks from all search terms

tuberculosis OR TB OR tuberculosis patients OR TB patients OR presumptive tuberculosis patients OR presumptive TB patients OR suspected TB patients OR tuberculosis cases OR TB cases OR presumptive tuberculosis cases OR suspected TB cases OR TB suspects

Syntax

((((((((((tuberculosis) OR (TB)) OR (tuberculosis patients)) OR (TB patients)) OR (presumptive tuberculosis patients)) OR (presumptive TB patients)) OR (suspected TB patients)) OR (tuberculosis cases)) OR (TB cases)) OR (presumptive tuberculosis cases)) OR (suspected TB cases)) OR (TB suspects)

2. **Intervention**

#1. Using quotation marks to keep the words together

"mobile health" OR mHealth OR "mobile technology" OR SMS OR “short message service” OR "text messaging" OR “messaging” OR message OR text OR "phone calls" OR “voice call” OR mobile applications OR "mobile apps" OR "health apps" OR “personal digital assistants” OR PDA OR “mobile phone” OR “cell phone” OR “cellular phone” OR “smart phones” OR “electronic health” OR "e-health" OR ehealth OR "digital health" OR "telemedicine"

Syntax

((((((((((((((((((((("mobile health") OR (mHealth)) OR ("mobile technology")) OR (SMS)) OR ("short message service")) OR ("text messaging")) OR ("messaging")) OR (message)) OR (text)) OR ("phone calls")) OR ("voice call")) OR (mobile applications)) OR ("mobile apps")) OR ("health apps")) OR ("personal digital assistants")) OR (PDA)) OR ("mobile phone")) OR ("cell phone")) OR ("cellular phone")) OR ("smart phones")) OR ("electronic health")) OR ("e-health")) OR (ehealth)) OR ("digital health")) OR ("telemedicine")

#2. Without using the quotation marks

mobile health OR mHealth OR mobile technology OR SMS OR short message service OR text messaging OR messaging OR message OR text OR phone calls OR voice call OR mobile applications OR mobile apps OR health apps OR personal digital assistants OR PDA OR mobile phone OR cellular phone OR cell phone OR smart phones OR electronic health OR e-health OR ehealth OR digital health OR telemedicine

3. **Comparator**

None for the search, will extract it from each article

4. **Outcome**

- **Pre-diagnosis and pre-treatment loss**

"pre-diagnosis" OR “prediagnosis” OR “initial-loss” OR “initial loss” OR “pre-diagnostic drop out” OR “prediagnostic drop out” OR "pre-treatment" OR pretreatment OR “post-diagnosis” OR “treatment initiation” OR “loss to follow-up” OR “lost-to-follow-up” OR “drop-out” OR “pre-treatment drop out” OR “pretreatment drop out”

FINAL SEARCH STRING FOR PUBMED

((((((((((((tuberculosis) OR (TB)) OR (tuberculosis patients)) OR (TB patients)) OR (presumptive tuberculosis patients)) OR (presumptive TB patients)) OR (suspected TB patients)) OR (tuberculosis cases)) OR (TB cases)) OR (presumptive tuberculosis cases)) OR (suspected TB cases)) OR (TB suspects)) AND ((((((((((((((((((((((("mobile health") OR (mHealth)) OR ("mobile technology")) OR (SMS)) OR ("short message service")) OR ("text messaging")) OR ("messaging")) OR (message)) OR (text)) OR ("phone calls")) OR ("voice call")) OR (mobile applications)) OR ("mobile apps")) OR ("health apps")) OR ("personal digital assistants")) OR (PDA)) OR ("mobile phone")) OR ("cell phone")) OR ("cellular phone")) OR ("smart phones")) OR ("electronic health")) OR ("e-health")) OR (ehealth)) OR ("digital health")) OR ("telemedicine"))) AND ((((((((((((((("pre-diagnosis") OR ("prediagnosis")) OR ("initial-loss")) OR ("initial loss")) OR ("pre-diagnostic drop out")) OR ("prediagnostic drop out")) OR ("pre-treatment")) OR (pretreatment)) OR ("post-diagnosis")) OR ("treatment initiation")) OR ("loss to follow-up")) OR ("lost-to-follow-up")) OR ("drop-out")) OR ("drop out")) OR ("pre-treatment drop out")) OR ("pretreatment drop out")))

114 results

Appendix 18: Descriptive summary of the 12 studies included in the systematic review

Authors	Country	Objective (s)	Study design	Setting	Study population	Age	Sample size	Intervention	Comparison	Function of mhealth	Follow-up period (days)	Effect
Meehan, 2023 (Meehan et al., 2023)	South Africa	To investigate the ef- fect of (1) a hospital-based recording interventio n that linked PWTB to standard hospital manageme nt and referral processes and (2) an alert-and-response patient manageme nt interven-	quasi-experime ntal	Urba n and rural	Persons routinely diagnosed by Xpert MTB/RIF patients eligible to link but with no evidence of linkage	Not specif ied	16,75 7	SMS and Phone call and home visit	Hospital-recording interventi on	To facilitate linkage to TB treatmen t	30	The relative reduction in ILTFU appeared greater in subdistricts where the alert-and-response patient manageme nt intervention was implemente d compared with subdistricts where only the hospital-recording intervention was implemente d. The relative

		tion to reduce ILTFU among individuals routinely diagnosed with TB.										reduction in KZN was 49.3% (95% CI, 32.4%–62.0%) vs 32.2% (95% CI, 5.4%–51.4%), and in the WC, it was 34.2% (95% CI, 20.9%–45.3%) vs 13.4% (95% CI, 0.7%–24.4%). In Gauteng, there was no relative reduction in ILTFU
Mwansa-Kambafwile, 2022 (Mwansa-Kambafwile et al., 2022)	South Africa	To evaluate the effectiveness of the SMS technology and WBOTs in	Randomised controlled trial	Urban	Newly diagnosed TB patients	18 years and above	314	SMS technology and ward-based outreach teams	Standard of care	Reminder	28	More patients in the SMS group (92/105; 88%) initiated treatment

		increasing the proportion who initiated treatment and in reducing the time to treat-ment initiation among TB patients						(WBOTs)				than in the SOC group (81/104; 78%), although this difference did not reach statisti- cal significance (P = 0.062). The time to treatment initiation was significantly shorter in the SMS group than in the SOC group (P < 0.001).
Wagstaff, 2019 (Wagstaff et al., 2019)	South Africa	To see the effects of SMS on whether people returned to clinic, and	Randomised controlled trial	Urban	Presumptive patients not already being treated for TB	18 years and above	649	SMS	Standard of care	Reminder	2,5,10,20	SMS recipients were more likely to return to clinic in the requested two days

		how quickly.										than the control group. The effect was smaller in the intent-to-treat analysis (52/101 or 51.5% vs. 251/405 or 62.0%, p = 0.05) than in the per-protocol analysis (50/97 or 51.5% vs. 204/318 or 64.2%, p = 0.03). The effects of SMS messages diminished as the interval increased

Maraba, 2018 (Maraba et al., 2018a)	South Africa	To determine if support from a case manager would assist adults being investigated for tuberculosis (TB) to link into TB and HIV care	Cohort	Urban and peri-urban	Adults being investigated for tuberculosis	18 years and above	585	Phone call (Case manager)	None	Results alert	28	35 TB treatment linkage only; 22 both). Of 555 attempts to contact these 189 participants, 407 were to facilitate HIV care linkage, 78 for TB treatment linkage and 70 for both. 4 of the 35 (11.4%) needing to start on TB treatment only and 7 of the 22 (31.8%) needing both).

Maraba, 2018 (Maraba et al., 2018b)	South Africa	To assess, using mixed methods, the feasibility, acceptability, and potential for addressing TB ILFU of a mHealth application to support and improve the TB care continuum	Quasi-experimental	Urban	Adults who had been referred for TB investigation including sputum testing.	18 and above	319	SMS	None	Results notification	28	Time to TB treatment was decreased from 4 days (IQR 2–6) in the pre-implementation period to 3 days(IQR 2–5) in the implementation period; this was not statistically significant (p = 0.5)
Farley, 2019 (Farley et al., 2019)	South Africa	To evaluate the time from clinical presumption of TB to RR-TB treatment initiation after	Quasi-experimental	Peri-urban	Newly diagnosed patients with RR-TB	N/I	6341	Mobile App and SMS	None	Tracking	1 year	The mean time from RR-TB laboratory diagnosis to linkage to care via telephone linkage officer contact with

		implementation of miLINC with the support of a linkage officer.										the patient for appointment scheduling was 10 h 14 min (standard deviation [SD] 11 h 8 min; interquartile range [IQR] 14 h 22 min) and from that contact with the patient to treatment initiation, 2 days 11 h 31 min (SD 3 days 7 h 10 min; IQR 2 days 19 h 26 min). Among 36 (88%)

												patients found to have a RR-TB sputum diagnosis based on RMP resistance results, and linked to care, the mean time from their initial clinic enrollment to RR-TB treatment initiation was 3 days, 21 h, 17 min (SD 3 days 15 h 21 min; IQR 3 days 3 h 2 min) (Figure 2).

Choun, 2017 (Choun et al., 2017)	Cambodia	We aimed to assess if tracking of TB patients referred to peripheral health facilities using mobile phone tech-nology can reduce loss to follow-up	Quasi-experimental	N/I	All TB patients diagnosed in SHCH and referred to other peripheral health facilities for initiation or continuation of TB treatment	N/I	109	Phone call	None	Tracking	Not indicated	87/92 (94.6%) were initiated on treatment
Chadha, 2017 (Chadha et al., 2017)	India	To determine the feasibility and yield of pre-sumptive TB case referrals by RHCPs using mHealth	Quasi-experimental	Rural	Presumptive TB patients	N/I	1578	Mobile App and SMS	N/A	Referrals	7	During the study period, there were 1578 referrals, 1056 of which came from the mRHCPs (i.e., 35 referrals per

		technology										RHCP) and 522 were referred by oRHCPs (4 referrals per RHCP). Of the total 194 TB cases diagnosed, the number of mRHCP refer- rals was 127 (4 TB cases per RHCP), while oRHCPs contributed 67 (0.5 TB cases per RHCP). The number of TB patients diagnosed on day 1 (day of referral) was

												158/194 (82%); 99/194 (51%) were re- ferred by mRHCPs (3.3/mRHCP and 0.4/oRHCP). All 194 cases di- agnosed were started on treatment.
Majella, 2021 (Majella et al., 2021)	India	To assess whether mobile voice call reminders to TB patients diagnosed at a tertiary care centre and referred to PHIs decrease the	RCT	N/I	All newly diagnosed TB patients, both pulmonary and extrapulmonary, who were referred for treatment from this tertiary care hospital	N/I	310	Phone call	Conventional paper-based	Reminder	14	In the intervention arm, 14 (9%) out of 155 were PTLFU compared with 28 (18%) of the 155 patients in the control arm. The absolute risk difference

		proportion of PTLFU compared with the conventional paper-based referral			(DMC) and who possessed a mobile phone, were eligible to participate in the trial.							was 9% (95% CI [1.5, 16.6], P = 0.01)
Bassett, 2019 (Bassett et al., 2019)	South Africa	To evaluate the yield of GeneXpert MTB/RIF on a mobile HIV testing unit	RCT	N/1	Adults voluntarily undergoing HIV testingand not known previously to be HIV-infected	18 years and above	4815	SMS	SOC	Relay TB results	21	Seven participants tested GeneXpert +, six in the intervention (3%, 95% CI 1%,5%) and one in usual care (1%, 95% CI 0%, 6%). Ofsix participants who tested GeneXpert-positive in the inter-vention, three (50%, 95% CI 36%, 88%) linked to the TB

												clinic within 3 weeks.
Marx, 2022 (Marx et al., 2022)	South Africa	To investigate the uptake and usage of aWhatsApp-based interactive communication strategy to avert pre-diagnosis loss to follow-up (LTFU) from TBcare in a high-incidence settin	Quasi-experimental	N/I	Presumptive TB patients who underwent routine sputum testing for TB b	18	103	Whatsup message and Phone call	None	Reminder for appointment	10	Of the 103 participants, 73 (70.9%) returned on (or before) the day of the scheduled appointment; 23 (22.3%) returned within 10 days and seven (6.8%) were lost to follow-up (Figure 4). There was no association between failure to

												respond to WhatsApp prompts and LTFU.
Stalin, 2020 (Stalin et al., 2020)	India	To measure the effectiveness of the new intervention package, developed based on qualitative study in reducing pretreatment loss to follow-up (PTLFU) of all TB patients diagnosed and referred for treatment from medical colleges to PHIs	Quasi-experimental	N/I	TB patients diagnosed and referred for treatment from medical colleges to PHIs,	N/I	618	Phone call	Home visit	Tracking	14	Out of 618 TB patients referred from medical colleges to PHIs for treatment, feedback was received for 282 (46%) TB patients at baseline. After the initiation of interventions, the proportion of feedback received from four medical colleges

												increased to 61% and 66|% in the first and second quarters of 2017, respectively .This difference was statistically significant ($P < 0.05$). It clearly showed that our intervention s were effective. According to the project data, a total of 520 (99%) of 525 TB patients diagnosed at four

												medical colleges were referred for treatment to PHIs. Eighty seven percentage of them reported within 1 week to the PHIs.