Mobile-assisted Medication Adherence Support Intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention

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ABBREVIATIONS AND ACRONYMS

ACTG	AIDS Clinical Trial Group
ART	Antiretroviral Therapy
BCT	Behavioural Change Techniques
CI	Confidence Interval
DOT	Directly observed Treatment
DR TB	Drug-resistant TB
EDHS	Ethiopia Demography and Health Survey
HIV	Human Immunodeficiency Virus
IMB	Information-Motivation-Behavioural skills
INH	Isoniazid
IRB	Institutional Review Board
Ma-MAS	Mobile-assisted Medication adherence support
MDR TB	Multidrug-resistant TB
MEMS	Medication Event Monitoring System
MOH	Ministry of Health
MRC	Medical Research Council
RCT	Randomised Control Trial
RR	Relative Risk
SAT	Self-Administered Treatment
SMS	Short Message Service
TB	Tuberculosis
UTAUT	Unified Theory of Acceptance and Use of Technology
VAS	Visual Analogues scale
VOT	Video Observed Treatment
WHO	World Health Organization

PUBLICATIONS FROM THE THESIS

1. Nezenega ZS, Perimal-Lewis L, Maeder AJ. Factors influencing patient adherence to Tuberculosis treatment in Ethiopia: a literature review. International Journal of Environmental Research and Public Health. 2020 Aug;17(15):5626.[1]

2. Sahile Z, Perimal-Lewis L, Arbon P, Maeder AJ. Protocol of a parallel group Randomised Control Trial (RCT) for Mobile-assisted Medication Adherence Support (Ma-MAS) intervention among Tuberculosis patients. Plos one. 2021 Dec 31;16(12):e0261758.[1]

[1] **NB**: The first author's name listed above as Nezenega ZS and Sahile Z is the same. The author's full name is Zekariyas Sahile Nezenega

CONFERENCE PRESENTATIONS

1. Development and validation of SMS text messages for mobile-assisted medication adherence support intervention for Tuberculosis patients

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2. Mobile-assisted Medication Adherence Support intervention among Tuberculosis Patients: A Parallel Group Randomised Control Trial

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ABSTRACT PUBLICATION

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TRIAL REGISTRATION

The trial has been registered in the Pan-Africa Clinical Trials Registry under the trial identifier PACTR202002831201865. https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=9729

ABSTRACT

Tuberculosis (TB) control programs face serious challenges in resource-limited settings, particularly in Ethiopia, where 20% of TB patients do not adhere to prescribed TB medication. Mobile phone-based adherence interventions can address challenges associated with non-adherence to TB medication because they allow direct communication between providers and patients. However, there is conflicting evidence regarding the efficacy of SMS text message interventions on TB medication adherence. Additionally, most adherence interventions based on mobile phone messaging are not tailored to the local context and needs of the target audience.

A pragmatic mixed-methods evaluation design was employed to systematically develop and evaluate the Mobile-assisted medication adherence support (Ma-MAS) intervention in Addis Ababa, Ethiopia. The Medical Research Council (MRC) framework including the information-motivation-behavioural skills (IMB) model and behavioural change techniques, was employed to develop and validate the Ma-MAS intervention. The feasibility and acceptability of the intended intervention were assessed by a cross-sectional survey. A parallel-group randomised control trial design was used to evaluate the effectiveness of Ma-MAS intervention among a sample of randomly assigned (n=186) participants. Participants in the Ma-MAS group received a daily SMS text message and a weekly phone call regarding their daily medication intake and reminders to attend clinic visits for eight weeks. Participants in the control group did not receive SMS texts or phone calls but received the same routine standard care as the Ma-MAS group. The primary outcome was the proportion of adherence measured by urine tests for isoniazid (INH) metabolites at the end of the fourth and eighth week of follow-up period. A post intervention interpretive study with qualitative descriptive approach and quantitative cross-sectional survey were also employed to inform the study findings on utility and acceptability.

In total, 40 SMS text messages were selected by experts to use for TB medication adherence based on content validity indexes above 0.80. According to a cross-sectional study, 88.5% of TB patients have their own mobile phone, and 93.5% of mobile phone owners were willing to receive SMS text message as reminders for medication intake and 92% were willing to receive SMS text

message as reminder for clinic appointments. Most participants were also willing to receive phone calls as reminders for medication intake (91%) and clinic appointments (93%).

In the experimental study, Ma-MAS significantly improved adherence to TB medications by 15.25% (95%CI: 5.38, 25.12; P-value=0.0065) after eight weeks of the intervention compared to the standard care alone in the control group. At the end of the eight weeks follow-up period, the predicted probability of adherence to TB medication in the Ma-MAS group was 86% (95%CI: 81, 93), and in the control group was 70% (95%CI: 61, 79). Ma-MAS also improved adherence to TB medication by 15.30% (95%CI: 6.68, 23.90; P-value=0.0022) after four weeks of the intervention compared to the control group. Ma-MAS intervention was shown to be useful to improve TB medication adherence as measured by a urine test for isoniazid (INH) metabolites. The Ma-MAS intervention had high acceptance and is a useful for reminder of TB medication, habit formation, awareness creation, motivation, enhancement of perceived professional care, and health consultation. This study therefore provides evidence for the effectiveness of mobile-assisted approaches to medication adherence through a rigorously planned and executed randomised control trial and interpretive study in a particular setting where best practice in medication adherence is critical to health outcomes but difficult to achieve by conventional approaches.

DECLARATION

I certify that this thesis: Mobile-assisted Medication Adherence Support Intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention

1. does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university

2. and the research within will not be submitted for any other future degree or diploma without the permission of Flinders University; and

3. to the best of my knowledge and belief, does not contain any material previously published or written by another person except where due reference is made in the text.

Signed

Zekariyas Sahile Nezenega

Date. January 17, 2024

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CHAPTER 1: INTRODUCTION

1.1. Introduction

This chapter provides the definition of Tuberculosis (TB), the general epidemiology of TB, TB treatment regimen, the crucial role of medication adherence, the risk of non-adherence to TB medication, and the prevalence of non-adherence to TB medication in Ethiopia. Additionally, it discussed the TB treatment administration options and recommendations, explores evidence on the use of mobile health for TB treatment support, and outlines the rationale for the study. The chapter also presented the research aim, objectives, hypotheses, and research questions.

1.2. Background

1.2.1. Overview of Tuberculosis

Tuberculosis (TB) is “an infectious bacterial disease caused by Mycobacterium tuberculosis, which is transmitted between humans through the respiratory route and most commonly affects the lungs, but can damage any tissue.”[1]

Living with TB is a challenging experience that affects the person physically, emotionally, and economically. The impact of TB extends beyond the physiological aspects, as TB patients may face social stigma, discrimination, and psychological distress.[2, 3] The person affected by TB requires a long treatment regimen that necessitates strict adherence for a cure. The TB treatment may have drug side effects, which are additional challenges for the patients. The prolonged treatment regimen is associated with economic losses for the patients and their families due to the cost of food supplements, transportation, and associated medical expenses.[3]

TB is still the biggest infectious cause of mortality worldwide, despite the presence of vaccine and chemotherapy.[1] TB is a major global health problem, accounting for millions of people’s disease each year. According to the 2022 World Health Organization (WHO) global TB report,

in 2021 a TB incidence of 119 per 100,000 population was detected in Ethiopia. The mortality rate of HIV negative TB was 16 per 100,000 population and the mortality rate of HIV plus TB was 1.7 per 100,000 population.[4]

1.2.2. TB Treatment: Why medication adherence is a critical issue

The World Health Organization recommends a six-month treatment regimen for drug-susceptible TB. This treatment regimen involves the administration of rifampicin, isoniazid, pyrazinamide, and ethambutol during the initial phase of two months, followed by a continuation phase consisting of rifampicin and isoniazid for the subsequent four months (2HRZE/4HR).[5]

To be cured of TB, strict adherence to medication for the whole treatment regimen is necessary. The level of adherence to TB medication is defined differently in various studies, but according to the World Health Organization's guidelines for the treatment of drug-susceptible TB and patient care report, patients who take more than 90% of their medications under the observation of another person was considered adherent.[5] Achieving a high level of adherence to TB medication is challenging for many patients due to various complex reasons.[6]

Non - adherence with TB medication increases the risk of additional transmission, treatment failure, relapsed TB, multidrug resistance or extensively drug-resistant TB, and mortality. [7-9] Drug-resistant TB is treatable, but it needs massive use of therapy that is toxic to the patients, too expensive and less effective as compared to drug-sensitive TB.[10] According to one study, non-adherent patients had a longer period until they tested negative to TB (254 versus 64 days), and had a higher risk of developing multi-drug resistance TB, would have an extended treatment regimen (560 versus 324 days) and lower treatment completion rate.[8]

In Ethiopia, TB prevention and control programs are challenged by widespread of non-adherence to TB treatment. One systematic review conducted in Ethiopia indicated that the pooled prevalence of non-adherence to TB medication was 21.3%.[11] In the same geographic

area, other systematic reviews indicated that overall prevalence of non-adherence to TB medication and lost to follow-up rates was 20% and 5%, respectively.[12] The prevalence of non-adherence to TB medication in Addis Ababa, where the current research was undertaken, was 19.5%.[13]

1.2.3. TB treatment administration options and recommendations

The World Health Organization (WHO) recommends Direct Observation of Treatment (DOT) by a trained supervisor to address the problem non-adherence to TB medication over self-Administered Treatment (SAT). In DOT administration, a patient takes medication every day under the observation of a healthcare provider to ensure adherence.[14] While in Self-Administered Treatment (SAT) administration, a patient takes medication without the observation of a healthcare provider.[15] But evidence showed that DOT does not provide an optimal solution to poor adherence in TB treatment.[16] For example, a one systematic review indicated that the difference between DOT and Self-Administered Treatment (SAT) on lost to follow-up, treatment failure, cure, treatment completion, and mortality is small and not statistically significant.[15]

In Ethiopia, implementing DOT is challenging to patients as it requires daily visits to the health facility, which has an undesirable impact on their work, social life and transportation costs.[17, 18] Healthcare professionals highlight the difficulties of implementing a daily DOT at the health facility.[17] Thus, DOT has not been fully implemented throughout the treatment regimen.[17, 18] DOT and non-daily DOT has been implemented in Ethiopia, in which during the first two months of intensive phase of treatment patients take their daily medication with health carer provider observation, and in the continuation of phase treatment, from two to six months, patients take all their medication at home and obtain weekly medication refill at health facilities.[17-19] However, the DOT's standard schedule for both intensive and continuation phase of treatment were interrupted by the COVID-19 pandemic.[20]

The current WHO recommendations are realised using DOT implementation with different treatment administration options. These include Daily DOT, Video Observed Treatment (VOT), and non-daily DOT where not every dose is overseen (overseen weekly or a few times per week).[5] The WHO has also revised the definition of DOT to include patients taking the medication under the observation of any person in real time.

It is desirable to measure and monitor the patient's treatment adherence, identify alternative strategies to DOT [16] and design interventions such as social support including material, food, or financial and transport help; psychological support; tracers through home-to-home visits or digital health interventions such as Short Message Service (SMS) texts and phone calls, to improve TB medication adherence.[5, 21, 22]

The World Health Organization (WHO) has developed a conceptual framework for designing digital health interventions in response to the growing recognition of their benefits.[23] The framework focuses on four key areas: patient care, surveillance and monitoring, program management, and e-learning, all of which can be integrated into the patient pathway of healthcare seeking, diagnosis, treatment, and follow-up.[23] Short Message Service (SMS), Video Observed Treatment (VOT) and Event Monitoring Device for Medication support (EMM) have already been used in TB program in different geographic settings to help to complete treatment and monitor the daily dose of medication.[23] A synthesis of literature reviews showed that one randomised trial of medication monitors and two observational studies of VOT were not found to have a statistical effect on cure or treatment completion.[24] However, the existing evidence supports the use of mobile health intervention to promote medication adherence since these are at least relatively effective as standard care.[24-26] VOT has emerged as an alternative method to DOT, but it is inaccessible to patients in some settings as it requires a smartphone with an internet connection.[27]

1.2.4. Evidence on the use of mobile health interventions

Mobile phones increasingly enable access even for those living on US$1 per day in high TB burden countries.[9] In Ethiopia, access to mobile phones is expanding widely: according to the Ethiopia Demography and Health Survey (EDHS) 2019, 87% of urban households and 59% of rural households had a mobile phone access.[28] This is higher when compared to the EDHS 2011, which showed 65% of urban households and 13% rural households have mobile phone.[29] Mobile health interventions are low cost, easy to use, widely available and use the existing infrastructure including network, internet, and mobile channels.[30]

The increased availability of mobile phones creates opportunities to address the challenges of implementing DOT, as mobile health can facilitate the communication between healthcare providers and TB patients via SMS and voice phone calls, in addition to DOT or non-daily DOT.[22, 27] Digital health interventions through mobile health can create new opportunities for healthcare especially where there is limited infrastructure, expertise, and human resource in the healthcare system.[31-34] Digital adherence technologies including phone-based and smartphone-based technologies are expected to facilitate a more patient-centred approach, although evidence is still limited.[35]

Mobile based SMS text messaging has been used for reminders, awareness creation and behaviour change purposes.[30, 34, 36, 37] Previous SMS text message experiments have proven to be beneficial in helping people quit smoking,[38-43] in the continuation of oral contraception,[44] breastfeeding practice,[45] Antenatal care (ANC) visit,[46, 47] Postnatal care (PNC) visit, [47-49] skilled delivery attendance,[47, 49-52] lower perinatal mortality and stillbirth,[53] self-management of long-term illness,[54] cardiovascular risk factor awareness,[55] diabetes management,[56, 57] systolic blood pleasure management,[58] malaria case management,[59] and medication reminders for chronic disease.[60-62]

Most previous mobile-based SMS text reminder studies in Ethiopia have focussed on maternal and child health services improvement.[47-49, 63-65] An SMS-based intervention was found effective in improving Antenatal Care (ANC) in one randomised trial [47], postnatal care (PNC) in another a randomised control trial and one non-randomised control trial [48, 49] and childbirth attended by a health worker in one randomised and one non-randomised trial.[47, 49]

Making mobile health interventions user-friendly, with good user acceptance and perceived usefulness are important underpinning of success.[66] Previous studies showed that SMS messaging was found acceptable in TB [67-69] and antiretroviral therapy (ART)-medication adherence support,[70-74] self-management of diabetes,[56] maternal health promotion,[52, 63] and had high satisfaction in supporting weight loss, physical activity and dietary behaviour change.[75] Moreover, an SMS-based TB adherence intervention was found to be technically feasible in terms of access to a mobile phone and familiarity with the use of SMS text message, and has a high rate of acceptance.[69]

1.3. The rationale for the study

The design of an adherence intervention needs to address the underlying factors that cause medication non-adherence.[35] Digital health interventions may enhance TB medication adherence and have health benefits to the community by lowering the incidence of disease relapse, acquired drug resistance, and infection transmission. Digital health interventions can be an alternative to observable medication adherence (DOT), and may be more feasible with the expansion and the low cost of technology and because TB treatment is for limited duration as compared to treatment for other chronic diseases.[35]

The Medical Research Council (MRC) framework for complex intervention recommend using appropriate theory and evidence when developing an intervention.[76, 77] However, most adherence interventions were developed without a theoretical base which may be one of the reasons they are sometimes not effective.[78] Literature indicates that ineffectiveness of mobile health SMS-based interventions might be due to the intervention not being developed

systematically [79] and not being customized to the local context and population needs.[30] A mobile-assisted medication adherence support intervention needs to be developed systematically and evaluated for effectiveness through rigorous research design, to provide quality evidence.

The scientific base for designing SMS text and phone call-based adherence intervention is founded in the premise that adherence information, motivation and behavioural skills can make a direct positive effect on adherence,[80] and can be used for awareness creation and behavioural change.[30] There is some evidence that adherence interventions like educating and counselling the patient, medication monitors, and SMS text reminders and tracers can improve treatment adherence and success.[21, 22, 81, 82]

In Ethiopia, for example, a randomised control trial found that psychological counselling and educational intervention can significantly improve a patient's treatment adherence. This intervention combined anxiety and depression counselling along with patient education based on health belief model.[83] However, implementing psychological counselling and educational intervention at health facilities might require high level of expertise and human resources compared to delivering intervention through mobile device. Another trial in the northwest Ethiopia was investigated the effect of a graphic based daily reminder and weekly medication refill reminders on patient's medication adherence reported that the web-based graphic reminder was found to be effective on treatment adherence and patient provider interaction.[84, 85] The graphic-based reminder intervention can be effective in addressing forgetfulness related to medication intake and medication refill reminders, but it might not address other behavioural factors that cause non-adherence to medication such as knowledge, motivation and other barriers.

The current intervention, Ma-MAS, is different from the previous two randomised interventions conducted in Ethiopia in three ways: first, the intervention itself was systematically developed based on evidence from the local context through conducting a

literature review to identify factors affecting TB medication adherence in Ethiopia; second, the intervention was delivered through mobile-based SMS text messages and phone calls, which is feasible to scale up on a large scale; third, the Ma-MAS intervention is designed to serve beyond simple reminders because it developed educational messages based on the factors affecting TB medication adherence. As for this, the combination of SMS text and phone calls intervention using a behavioural change model and techniques has not been previously designed and tested in Ethiopia. Additionally, this study assessed the primary outcome of the intervention trial using the most reliable measurement of adherence (IsoScreen kit) [86-89] Therefore, in this study, a mobile-assisted medication adherence support (Ma-MAS) intervention was systematically designed using the Medical Research Council (MRC) conceptual framework with appropriate behavioural change model and techniques. It was assessed its effectiveness on medication adherence and its acceptance by patients.

For mobile health to achieve its full potential, it must be integrated into the current health care system. In Ethiopia, the existence of national eHealth strategy is an opportunity to conduct a mobile-based adherence intervention trial and to integrate this into the health system. The Ethiopia Ministry of Health (MOH) identified eHealth as one of the top priorities in a five-year health transformation plan, and mobile health is one of the priority areas of the country's eHealth strategy.[90, 91]

Generally, this study may have three positive effects. First, rational [R1] the intervention may supplement the effort of the Ministry of Health by designing mobile-assisted medication adherence support intervention systematically with the local evidence, needs and practices that may promote medication adherence, Second, [R2] the mobile-based SMS text messages and phone calls intervention have been demonstrated in this research to improve the treatment adherence, therefore it may also improve treatment outcome, reduce disease relapse, drug resistance, and infection transmission to others. Third, [R3] the study provides a research question for future studies and can be used as educational material. Thus, this project is believed to make a major potential contribution to the development plan for the health

sector, country and at large globally. The evidence generated from this study is valuable for policymakers, program managers, healthcare providers, education sectors and non-governmental organizations (NGOs) working in Ethiopia and beyond.

1.4. Research aims and objectives

1.4.1. Aims

This study aimed to systematically develop and evaluate a mobile-assisted medication adherence support intervention using SMS and phone calls among TB patients in Addis Ababa, Ethiopia.

1.4.2. Objectives

Objective-1: To systematically develop and validate mobile-assisted medication adherence support intervention for TB patients in Addis Ababa, Ethiopia

Objective-2: To assess the feasibility and acceptability of mobile-assisted medication adherence support intervention among TB patients in Addis Ababa, Ethiopia

Objective-3: To measure the effect of mobile-assisted medication adherence support intervention on treatment adherence among TB patients in Addis Ababa, Ethiopia

Objective-4: To assess perceptions, experiences and intention to adopt mobile-assisted medication adherence support intervention among TB patients in Addis Ababa, Ethiopia

1.5. Hypothesis

1.5.1. Primary hypothesis

Mobile-assisted medication adherence support intervention using mobile SMS text reminders and phone calls improves TB medication adherence in addition to routine standard non-daily DOT care.

1.5.2. Secondary hypothesis

The Unified Theory of Acceptance and Use of Technology (UTAUT) explains and predicts how people adopt and use new technologies. Therefore, the secondary hypothesis of this study examined how factors predict mobile-assisted medication adherence support intervention acceptance (see Table 1). In this study, the term 'Adoption intention' is used synonymously with 'behavioural intention', which is an indicator of acceptance of intervention.

Table 1: Hypothesis on the construct relationships within UTAUT framework

Original UTAUT	**Modified UTAUT**
H1: Performance expectancy has a positive effect on behavioural intention	H1: Performance expectancy has a positive effect on attitude
H2: Effort expectancy has a positive effect on behavioural intention	H2: Performance expectancy has a positive effect on behavioural intention
H3: Social influence has a positive effect on behavioural intention	H3: Effort expectancy has a positive effect on attitude
	H4: Effort expectancy has a positive effect on behavioural intention
	H5: Social influence has a positive effect on attitude
	H6: Social influence has a positive effect on behavioural intention
	H7: Facilitating condition has a positive effect on attitude
	H8: Facilitating condition has a positive effect on behavioural intention

1.6. Research questions

1. What factors affect non-adherence to TB medication in Ethiopia?
2. How can a mobile-assisted medication adherence support intervention be designed to address factors of non-adherence among TB patients in Addis Ababa, Ethiopia?
3. Is a mobile-assisted medication adherence support intervention feasible and acceptable in Addis Ababa, Ethiopia?
4. Is a mobile-assisted medication adherence support intervention effective in improving medication adherence among TB patients in Addis Ababa, Ethiopia?
5. What factors explain the effectiveness of a mobile-assisted medication adherence support intervention among TB patients in Addis Ababa, Ethiopia?
6. How do patients perceive and experience a mobile-assisted medication adherence support intervention in Addis Ababa, Ethiopia?
7. What factors affect the adoption intention of a mobile-assisted medication adherence support intervention among TB patients in Addis Ababa, Ethiopia?

1.7. Overview of the chapters

Chapter one provides an informative introduction to the topic, presenting an overview of TB, TB treatment regimen, the problem of non-adherence to TB medication, the TB treatment administration options, and explores evidence on the use of mobile health interventions for TB treatment support. It explains the rationale behind conducting mobile-assisted medication adherence support intervention study, emphasizing the significance of this research. It also provides an overview of the research aim, objectives, hypothesis, and research questions.[2]

Chapter two provides a comprehensive literature review on adherence to TB medication. It covers factors influencing adherence and explores the use of mobile health (mHealth) interventions. The chapter provides valuable insights into the challenges of adherence to TB medication, interventions, and the potential of mHealth to improve TB medication adherence. The chapter covers the feasibility, acceptability, and effectiveness of mobile-based adherence interventions. The chapter also covers the definition of adherence, various adherence measurements, and the adherence measurements used in the current study.

Chapter three discusses research methodology, a fundamental component of the research. It encompasses essential elements such as the research philosophy, the researcher position, the research paradigm, and the utilization of a mixed methods design. This chapter further presents a comprehensive overview of the study design, including the methods employed for data collection and analysis in both empirical and interpretive research approaches. This chapter provides a comprehensive explanation of the methodology and methods for conducting the research and for generating and analyzing data systematically and rigorously.

Chapter four presents the results of the development and validation of Ma-MAS intervention using Medical Research Council (MRC) framework. This chapter gives general overview of the intervention development and validation process. Each phase of development and

[2] The introduction chapter contains material originally published article of protocol of a parallel group Randomized Control Trial (RCT) for Mobile-assisted Medication Adherence Support (Ma-MAS) intervention among Tuberculosis patients. Plos one. 2021 Dec 31;16(12):e0261758.

validation process is discussed in detail in the method section of the thesis. The purpose of this chapter is to present the key result of Ma-MAS intervention development and validation to establish a solid foundation for understanding its implementation and effectiveness.

Chapter five presents the results of the feasibility and acceptability of the mobile-assisted medication adherence support (Ma-MAS) intervention. The chapter focuses on two key elements: feasibility and acceptability. Feasibility was evaluated by examining participants' access to mobile phones and their level of digital literacy in utilizing SMS text messages and phone calls. The acceptability of Ma-MAS was measured by assessing participants willingness to receive SMS text messages and phone calls as a means of support for their TB medication adherence and clinic appointments. The findings of this evaluation provide insight into the practicality and acceptability of Ma-MAS intervention to enhance medication adherence and clinic attendance for TB patients.

Chapter six presents the results of randomised control trial that aimed to assess the effectiveness of the mobile-assisted adherence support (Ma-MAS) intervention in improving TB medication adherence. The study involved two groups: the Ma-MAS group and the control group. Participants in the Ma-MAS group received daily SMS text messages and weekly phone calls for eight weeks, along with standard care during the continuation phase of treatment. On the other hand, the control group received standard care without Ma-MAS intervention. This chapter will examine the results of this trial, providing valuable insight into the effects of the Ma-MAS intervention on TB medication adherence compared to standard care alone.

Chapter seven presents an overview of patients' perceptions, experiences, and adoption intention regarding the Mobile-assisted Medication Adherence Support (Ma-MAS) intervention. The qualitative analysis of this chapter focuses on patients' perceptions and experiences, while the unified theory of acceptance and use of technology (UTAUT) was used

to identify key factors influencing adoption intentions. This chapter provides valuable insights into patients' experiences and the determinants of Ma-MAS intervention adoption.

Chapter eight provides a discussion and interpretation of the research findings on the effectiveness of the mobile-assisted medication adherence support (Ma-MAS) intervention for TB medication adherence. The chapter discusses factors influencing adherence to TB medication, the intervention development process, acceptability and feasibility assessment. The randomised control trial findings and patients' experiences are discussed in this chapter.

Chapter nine presents the conclusions and recommendations based on the research findings. This chapter presents conclusions about the effectiveness of the mobile-assisted medication adherence support (Ma-MAS) intervention for improving TB medication adherence. This chapter also provides recommendations to improve Ma-MAS intervention implementation, design, and patient engagement. The chapter emphasizes the potential use of mobile technology in supporting TB medication adherence and suggests its integration into healthcare systems for improving health outcomes. The schematic presentation of thesis chapters is presented in Figure 1.

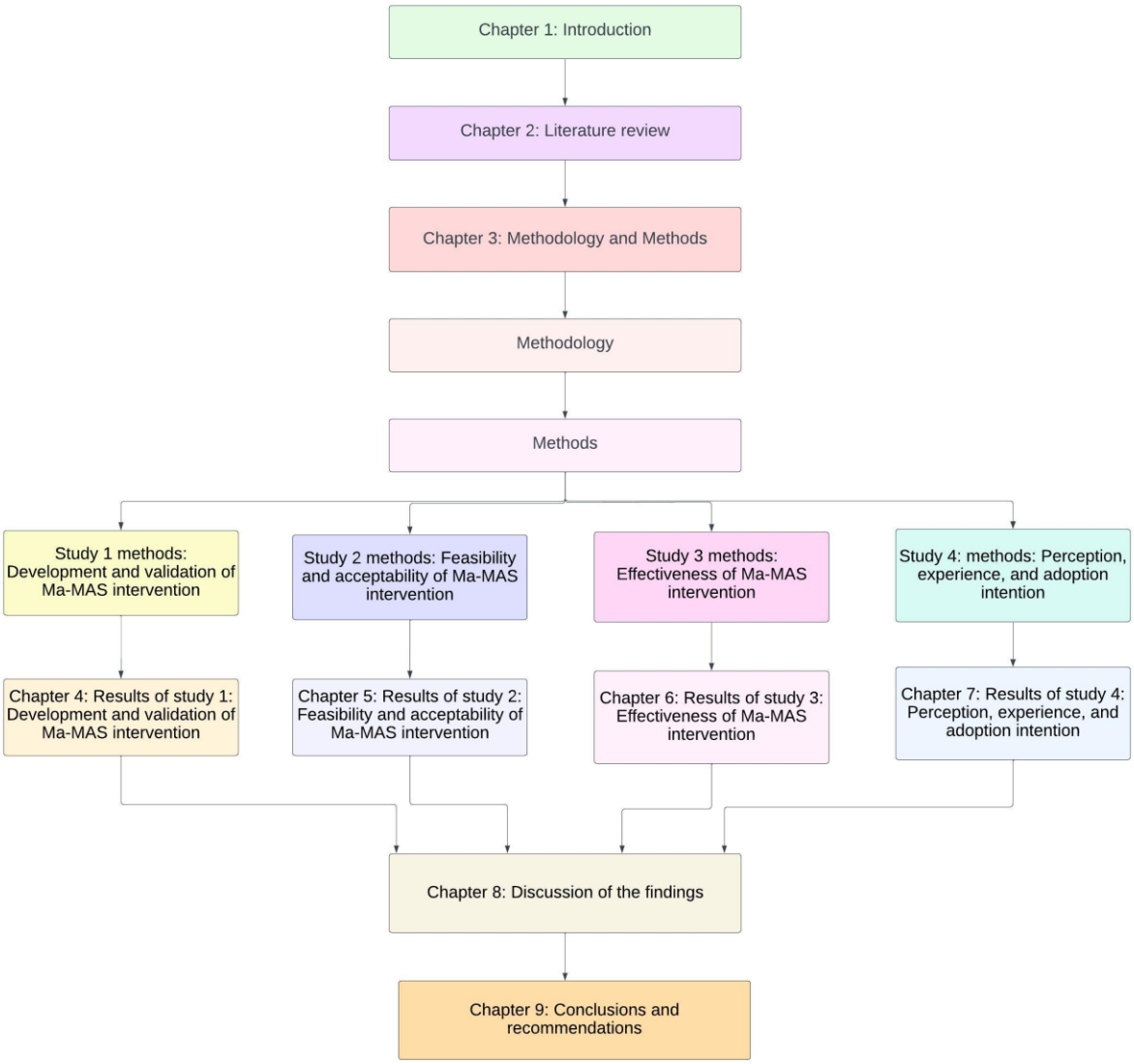

Figure 1: Schematic presentation of the thesis chapters

CHAPTER 2: LITERATURE REVIEW

2.1. Introduction

The literature review section explores various aspects related to adherence to TB medication and interventions aimed at promoting adherence. It begins by discussing the literature review of factors affecting adherence to TB medication in Ethiopia. Next, the review provides an overview of adherence interventions, including the use of mobile health (mHealth) interventions to promote medication adherence. This chapter also discussed the effectiveness, feasibility, and acceptability of mobile health interventions for TB treatment support, drawing on relevant studies in the field. At the end of the chapter, the definition of adherence and the various measures used to assess adherence are discussed.

Overall, the literature review provides a comprehensive understanding of the key issues related to adherence to TB medication, including the challenges faced by patients, the different interventions that have been used to address these challenges, and the potential of mHealth interventions to improve medication adherence.

2.2. Factors associated with non-adherence to TB medication

A literature review was conducted to identify factors influencing non-adherence to TB medication in Ethiopia. Because we develop adherence interventions based on the evidence available locally, the literature review was focused only on Ethiopia. This section contains material originally published article of factors Influencing Patient Adherence to Tuberculosis Treatment in Ethiopia: A Literature Review.[6] The copy of the published article is available in the Appendix Eight.The synthesised findings from both quantitative and qualitative studies are presented below, grouped in seven dimensions of adherence influencing factors based on the Ogundele et al. (2015) classification of adherence influencing factors [92]. The individual studies included in the literature review are found in the Appendix One.

2.2.1. Patient-centred factors

Forgetfulness [19, 93-100] and inadequate knowledge about TB and its treatment regimen [94, 98, 101-104] were the two major patient-centred factors. Three studies conducted in Oromia [105, 106] and Southern region of Ethiopia [100] regions showed that the patient's educational status was associated with non-adherence to TB medication: the more the patient is educated the less likely non-adherence to TB medication. Psychological distress was another factor: two studies conducted in Addis Ababa reported that this indirectly positively influences the non-adherence to TB medication.[13, 107] Another qualitative study conducted in Addis Ababa also stated that poor mental health status of a patient would make them reluctant to regularly attend follow up and clinic appointments.[98]

2.2.2. Social factors

Several studies reported that patients not getting social support from families and neighbours in remembering to take their medication, food and financial assistance was the major social factor that influences non-adherence to TB medication.[18, 98, 99, 103, 105, 108-110] Additionally, one study in Addis Ababa conducted among latent TB-HIV co-infected patients reported that the patient's friends' decision to take the medication would make them less likely to be non-adherent to isoniazid preventive therapy (IPT).[111] Another study among the same subjects and setting found that patients who were comfortable to take IPT in front of other people were less likely to be non-adherent. [112] Busy with work [94] and away from home for work or other social-related activities were also found to influence non-adherence to TB medication.[94-96] Perceived and experienced stigma and discrimination also led the patient to non-adherence. [98, 113-115] These particular factors were highly noted in studies conducted among TB-HIV co-infected patients.[98, 109, 114, 115] As one study indicated, because of fear of stigma and discrimination, the patients were not disclosing their HIV status to their family, which in turn influenced their non-adherence to TB medication.[98]

Beliefs about the disease and treatment, such as perceived wellness or cured, perceived risk, and perceived barriers over the benefits, were influencing factors for non-adherence to TB medication.[13, 93, 105, 107] One study conducted in Addis Ababa reported that a patient's belief in curability and severity of TB in the presence of HIV infection would make them less likely to be non-adherent.[109] Another study in Addis Ababa found that the perceived risk of discontinuing TB medication was the reason for adherence while perceived wellness was the reason for patients have the intention to discontinue TB treatment.[93] One study conducted in Southern region of Ethiopia also reported that belief in traditional healing influenced non-adherence to TB medication.[113]

2.2.3. Economic factors

The patient's economic constraints (which impact the financial burden) were the main economic factor that influences non-adherence to TB medication.[13, 97, 108, 109] Economic constraints limit the patient's ability to have adequate food which influences non-adherence.[109, 113] The cost of medication other than TB medication is also a factor for non-adherence in one study conducted in Southern region of Ethiopia. Another study conducted in Southern region of Ethiopia reported that the patient being not employed was associated with non-adherence.[116]

2.2.4. Health system factors

Poor healthcare provider-patient relationship with communication gaps was a major factor that influences non-adherence to TB medication.[94, 109, 110, 113, 116] For example, one study conducted in Addis Ababa among loss to follow up patients reported that the healthcare providers were seen as disrespectful of their patients and less committed to their profession.[110] The quality of healthcare service and a patient's satisfaction with healthcare service affect non-adherence to TB medication.[96, 108, 116] When patients perceived that they received less professional care, less time spent with the healthcare providers, and waiting a long time to receive the healthcare service, they were more likely to be non-adherent.[96, 110,

[116, 117] Health information/education is also crucial for adherence: a few studies showed that the patients who did not receive health information/education from health facilities were more likely to be non-adherent.[95, 98, 101] Additionally, one study done in Addis Ababa found that lack of cues to action were reported as a factor for non-adherence.[107] Lack of supervision and healthcare provider incapable to manage the patient's illness was also reported as influencing factors for interruption and default from TB treatment.[115]

2.2.5. Therapy factors

Many studies reported that drug side-effects were the major therapy-related reason for non-adherence to TB medication.[95, 96, 102, 103, 105] Pill burden was also reported as a factor for non-adherence to TB medication among active TB and TB-HIV co-infected patients.[109, 113]. The presence of more than one co-morbidity including TB-HIV co-infection was also reported as a factor for non-adherence to TB medication.[19, 94, 96, 105, 114] One study conducted in Addis Ababa also found that being on Antiretroviral Therapy (ART) was a factor for non-adherence to TB medication.[13] Symptom presence after initiation of anti-TB treatment and slow progression of the health status were also found as non-adherence factors.[18, 19, 99, 105] Being in the continuation phase of the treatment (after the initial 2-month clinic-based treatment period) was a factor for non-adherence and default.[19, 94, 103, 111, 118] This might be due to the patient's perceived wellness or cured and because of a daily DOT was not implemented after the first two months of treatment in Ethiopia.

2.2.6. Lifestyle factors

Alcohol consumption was reported as a factor that influences non-adherence to TB medication in three studies.[13, 94, 96, 106] Cigarette smoking [96] and Khat chewing were also found as factors associated with non-adherence.[96, 106]

2.2.7. Geographical access factors

Healthcare inaccessibility from residence location was a major geographical access factor for non-adherence and default from TB treatment.[97, 99, 101, 105, 108, 113, 117] Due to inaccessibility,

patients were unable to keep regular clinic appointments and follow up treatment in two studies, conducted in Addis Ababa and Amhara regions.[96, 112] Distance of the health facility was related to transportation cost, which was also a factor for non-adherence.[18, 100, 101, 104]

2.3. Adherence Interventions

Adherence interventions that enhance medication adherence and treatment outcomes can be categorized as follows: patient education, psychological interventions, reminders and tracers, incentives and enablers, staff education, patient-centred care, and digital health.[5, 21, 119] Adherence interventions and their effectiveness on medication adherence and treatment outcomes are summarised below based on a systematic review and meta-analysis conducted by Alipanah et al. 2018.[21]

2.3.1. Patient education

Patient education and counselling are a recommended adherence intervention to improve medication adherence and treatment outcomes. The counselling here is educational, not psychological.[5] A systematic review showed that patient education and counselling interventions, involving both oral and written educational materials along with counselling, demonstrated positive associations with higher rates of treatment completion, cure, and adherence. However, these interventions did not influence on mortality, treatment success, failure, or loss to follow-up.[21]

2.3.2. Psychological supports

Psychological supports such as counselling for alcohol cessation and establishing a group and clubs as social support network are used to improve adherence and treatment outcomes.[5] A systematic review showed that the utilization of support groups was associated with higher rates of treatment completion and lower rates of treatment failure and loss to follow-up.[21]

2.3.3. Reminders and tracers

Reminders and tracers are also be used to improve mediation adherence and treatment outcomes.[5] A systematic review indicated that the use of reminders and tracers were associated with higher rates of treatment success, cure, medication adherence, and sputum conversion at two months. Additionally, there were lower rates of the development of drug resistance and loss to follow-up with the implementation of reminders and tracers.[21]

2.3.4. Incentives and enablers

Incentives and enablers such as food or financial support are a recommended patient support interventions to improve medication adherence and treatment outcomes.[5] A systematic review found that incentives and enablers were associated with favourable outcomes, including lower rates of mortality, treatment failure, and loss to follow-up, as well as higher rates of treatment success, completion, cure, and sputum conversion at two months.[21]

2.3.5. Staff education

Staff education is also a recommended adherence intervention to enhance medication adherence and treatment outcomes. Staff education such as adherence education for staff, peer training for lay health workers, reminders to initiate adherence discussions, and the provision of educational tools and aids for decision-making.[5] A systematic review showed that staff education interventions were associated with positive outcomes, including higher rates of treatment success and lower rates of loss to follow-up in the studies.[21]

2.3.6. Patient-centred care

Patient-centred care along with DOT was also used as adherence intervention in several studies to enhance medication adherence and treatment outcomes. [21] The interventions compared patient-centred directly observed treatment (DOT) with self-administered treatment (SAT). Patient-centred DOT was demonstrated benefits compared to DOT alone, showing lower rates of loss to follow-up and higher rates of treatment success and cure. When compared with SAT, patient-centred DOT was associated with higher rates of treatment

success, completion, cure, and sputum conversion at two months. However, no studies were found that directly compared patient-centred DOT to patient-centred SAT.[21]

2.3.7. Digital health

Digital health is one of the recommended adherence interventions to improve medication adherence and treatment outcomes.[23] Digital technologies such as daily reminder SMS texts or phone calls, video observed treatment (VOT), wireless pillbox/SMS reminder systems, and electronic medication monitor boxes are used for promoting adherence. A systematic review showed indicated that digital health interventions, such as SMS reminders, wireless pillbox/SMS reminder systems, and electronic medication monitor boxes, were associated with positive outcomes in terms of treatment completion rates, cure rates, and adherence, while VOT did not show a significant impact compared to DOT in treatment completion and mortality rates.[21]

The current research implemented a mobile health intervention by designing a combination of SMS text messages and phone calls. The mobile health intervention designed to have multiple benefits such as facilitate awareness creation through SMS text messaging and phone calls, remind the patient to take their medication and clinic appointment, facilitate the communication between healthcare professionals with patients and enable to reach the service to the patients where they live.

2.4. Mobile health Intervention

2.4.1. Definition of terms

The World Health Organization (2015) defined the following terms as:

mHealth (mobile Health): “the provision of health service and information via mobile technologies such as mobile phones, tablet computers and personal digital assistance (PDAs).”[120]

eHealth (electronic health): “use of information and communication technology (ICT) for health and health-related activities.” [120]

Digital health: “a collective term for eHealth and mHealth technology.”[120]

2.4.2. Effectiveness of mobile health intervention

There is contradictory evidence about the effect of SMS text message interventions on treatment adherence and outcomes. Some studies showed that SMS text messages did not provide an improvement of TB medication adherence [69, 81, 121-123] and treatment outcomes,[69, 121, 122] while other studies found SMS text messages were effective at improving clinic attendance[22, 81] and treatment outcomes.[124, 125]

In four randomised trials conducted in Pakistan,[121] Argentina, [69] China [123] and Cameroon [122] found that the use of SMS text did not show statistically significant improvement in medication adherence. However, one randomised trial in China found that one-way daily SMS text led to a statistically significant lower rate of interrupted treatment and missed does,[125] as well as another trial in China which showed a daily two-way SMS text led to a statistically lower patient lost to follow-up.[123] Medication event monitoring a combination with daily two-way SMS text also showed a statistically significant improvement in medication adherence.[123]

In three randomised trials conducted in Pakistan,[121] Argentina, [69] and Cameron [122] were found that a daily SMS text did not significantly improve treatment outcomes. Conversely, one clustered randomised trial in China and one non-randomised trial in South Africa found that SMS text led respectively to a statistically higher rate of smear conversion and cure rate,[125] and a higher treatment completion rate and a lower interrupted treatment and missed dose.[124] Furtherly, one randomised trial conducted in different geographic settings and one South African non-randomised study found that SMS text along with self-administered therapy did not show a statistically lower effect on completion of treatment [25] and treatment outcomes [26] compared with DOT**.** A phone call reminder was also found effective in improving the TB treatment success rate in one randomised trial study done in Thailand among MDR-TB and

DR-TB patients.[126] The individual studies summary findings are presented in the Table 2. A systematic review found that mobile-based SMS text messaging had a modest effect on TB treatment success rate, but the quality of the evidence was low.[127]

2.4.3. Interactivity of mobile health intervention

Some evidence has shown that an interactive SMS texts may have a better impact than using simple one-way SMS reminders in improving medication adherence [122, 128-130] as it has potential benefits of improving the relationship between patient and healthcare provider.[27, 122] However, there is evidence that two-way SMS reminders are also unable to improve treatment outcomes and adherence to medication [121] [123] [123] [69] and one-way SMS reminders were found to improve treatment adherence [125] and treatment outcomes.[125] [124] The characteristics of SMS interventions are summarised in the Table 3.

It is suggested that a phone call to the patient along with SMS for medication reminders may enhance the healthcare provider and patient relationship, and treatment adherence[121, 122] and thereby improve TB treatment success.[126] The WHO suggests investigating creatively how SMS text messages can influence adherence by combining it with other digital health interventions or blended digital technology such as video, and voice calls.[23] Therefore, it is recommended to use a phone call to improve a patient's treatment adherence, clinic attendance and treatment outcomes, in addition to SMS text messages, and this can make the SMS text messages intervention more interactive.[121, 126]

2.4.4. SMS text messages frequency, time, and duration

Most of the previous interventional studies implemented daily SMS text messages to prompt TB medication adherence and improve treatment outcomes. Most of the studies also implemented the SMS text message intervention throughout the entire six-month period of TB treatment (see Table 3). Two randomised trials explicitly mentioned that the SMS text messages were sent in the morning time. [69, 125] Two randomised trials reported that the SMS text messages were sent based on the patient's preferred time.[121, 123] In one retrospective

analysis study, the SMS text message was sent when the patient did not open the monitoring device (SIMpills) to take the medication.[124] However, one mixed-methods study [26], and two randomised trials did not report the specific times of the SMS text messages.[25, 122, 131]

2.4.5. Feasibility and acceptability of mobile health intervention

On the other hand, SMS based adherence support intervention studies conducted at different geographical settings found that SMS text is acceptable and feasible to support TB medication adherence. The reasons for acceptance of SMS reminders were they feel cared for and supported,[69] and help them to avoid missed medication and remind them to refill their medication.[67, 68, 132] In Tanzania, a real-time medication monitoring study also showed that patients were satisfied with SMS text reminders.[27] SMS intervention was also found as feasible in terms of mobile access and technical familiarity with SMS text messaging. [69, 133] Generally, SMS text messaging is inexpensive, uses existing infrastructure, is easy to use, has high acceptance, satisfaction and is valued by patients and healthcare professionals.[30] The acceptability and feasibility of SMS text intervention studies are summarised in the Table 4.

Table 2: Randomised clinical trials of mobile health interventions for TB extended from Lester et al. 2019 [27] and Nglazi et al. 2013[81]

Trial ID	Location	Sample size	Study design	Population	Intervention	Control	Outcome	Findings
Mohammed 2016 [121]	Pakistan	2207	Individual RCT, open label	Newly diagnosed	Two-way SMS reminders	DOT	Primary outcome: Treatment success-cured (i.e., sputum smear or culture negative in the last month) or treatment completion, death, transferred. Secondary outcome: self-reported adherence	Treatment success ARM1=83% and Control=83% Default; ARM1=10% and control=9% Died; ARM1=2% and control= 2% Treatment failure; ARM1=2% and control=3% Additionally, there was no significant difference on self-report medication difference
Farooqi RJ. Et al. 2017[134]	Pakistan	148	Individual RCT	Newly diagnosed patients	Daily one way SMS reminder	DOT	Primary outcome: default (lost from treatment for 2 consecutive months)	Daily SMS text messages had no significant difference on default of TB patients, but lower number of default cases were reported in the intervention group compared to control group.
Liu 2015 [123]	China	4292	Cluster RCT	Newly diagnosed	Arm1-Two-way SMS reminders Arm2-medication monitor Arm3-SMS reminders plus	Self-administered treatment, family supervision, or DOT	Primary outcome: Poor adherence-at least 20% dose missed. Secondary outcome: Poor adherence-at least 47% dose missed (7/15 doses)	Arm1= 27.3%, Arm2=17.00%, Arm3=13.90 Control=29.90 SMS reminders not only have a statistically significant difference in adherence, but medication monitors and the combination of SMS

					medication monitor			reminders and medication monitors statistically significantly improved medication adherence. However, SMS reminders had a positive effect on lost to follow up. Audio reminded medication monitor box and the combination of medication monitor and text messages had significant improvement on TB medication adherence.
Bediang G. et al. [122, 131]	Cameroon	279	Individual RCT Single-blind of healthcare providers	Active TB	One-way SMS reminders	DOT	Primary outcome: Negative Microscopy at 5 months cured (microscopy) at 6 months. Secondary outcome: Adherence to medication and appointment	Arm1=81% and Control=74.6% SMS reminders did not provide a statistically significant difference in treatment success and adherence to medication and clinic appointments.
Belknap 2017[25]	US, Spain, Hong Kong, and South Africa	964	Individual RCT	Latent TB	Arm1-Weekly SMS Reminders plus self-administered treatment	DOT (monthly)	Primary outcome: Treatment completion -11 or more doses within 16 weeks Secondary outcome: adverse events	Arm1=76.4%, Arm2=74.0% Control=87.2% Self-administered treatment and combination of self-administered treatment and SMS reminders not statistically lower compared to DOT.

					Arm2- self-administered treatment			
Fang 2017[125]	China	350	Cluster RCT	Active TB	One-way SMS reminders	DOT	Primary outcome: Treatment completion Secondary outcome: Missed dose, interrupted treatment, a reexamination of sputum after 2-, 5- and 6-months of treatment	Arm1=96.3% and Control=86.4% A significantly higher treatment completion rate in the SMS intervention group compared to DOT. Both the Interrupted treatment rate and missed dose rate significantly lower in SMS intervention compared with DOT
Hüsler 2005[26]	South Africa		Mixed methods design	Active TB, clinic staff, TB experts	One-way SMS reminders for self-administered patient	DOT	Primary outcome: treatment outcome	Cure rate: Arm1=62.35%, control=66.44% Completion rate: Arm1=10.59%, control=3.0% Treatment success rate: Arm1=72.94%, control=69.4% Daily SMS reminders have similar effect treatment outcome effect with clinic-based DOT
Broomhead 2012 [124]	South Africa	120	Retrospective analysis	Active TB patients	One-way SMS SIMpill	DOT	Primary outcome: smear conversion rate and TB cure rate	Smear conversion rate Arm1=62.5% and control=38.4% Cure rate Arm1=75.0% and control=32.3% Smear conversion rate and cure rate were significantly

								higher among SMSpill based medical adherence support.
Iribarren, 2013[69]	Argentina	37	Mixed method design including RCT	Active TB	Two-way SMS intervention	SAT (monthly)	Primary outcome: Feasibility, acceptability and self-report treatment adherence Secondary outcome: Microscopy test result from positive to negative, treatment outcomes	Arm1=77% Self-reported adherence Arm2=53% calendar-based self-report A similar finding obtained for sputum smear or culture between intervention and control group.
Kunawararak, 2011[126]	Thailand	38 MDR-TB 61 non MDR-TB	Randomised Clinical trial	MDR- TB and non MDR-TB	Daily Phone call reminder	DOT	Primary outcome: Treatment outcomes	In sputum conversion rate at one-month Among MDR-TB Arm1=90% and control group =20% (statistically significant). Among non MDR_TB Arm1 =37% and control group= 52% (not statistically significant). In treatment success Arm1 was a statistically significant higher in both MDR-TB and non MDR-TB (100%) compared with control group (73.7% and 96.7%)

Table 3: The characteristics of SMS text message interventions in randomised control trials extended from Lester et al. 2019[27] and Nglazi et al. 2013[81]

Trial ID	SMS Intervention	Intervention duration (Months)	Message Frequency	Motivational message	Message content	Message time	Follow-up reminder
Mohammed 2016 [121]	Two-way SMS reminders	6	Daily	Yes	"Your health is in your hands. Take your medication and remember to respond by SMS or a missed call."	Reminders sent based on preferred time of patients	A second reminder was sent if the patient did not react within two hours. After two more hours of no answer, a third and final reminder for the day was delivered. Participants who had not responded in seven days were contacted by members of the research team.
Liu 2015[123]	Two-way SMS reminders	6	Daily	No	"Please take the medication on time"	Reminder sent based on preferred time patients	Patients are expected to replay up to three SMS messages, and reminders stop once the patient answers.
Bediang G. et al. [122, 131]	One-way SMS reminders	6	Daily	Yes (every two weeks)	"Good morning it is important to take your drug against TB every day" "Good morning, taking drug daily increases your chance of healing"	Not Reported	--
Belknap 2017[25]	One -way SMS Reminders	4	Weekly	No	Not Reported	Not Reported	--
Hüsler 2005 [26]	One-way SMS reminders	6	Daily	No	Not Reported	Not Reported	
Broomhead 2012 [124]	One-way SMS reminder	6	Daily	NO	Not Reported	Morning	When patient don't take their medication

						When patient did not take their medication	
Fang 2017[125]	One-way SMS reminders	6	Daily	No	Not Reported	Morning	Contained TB-related knowledge for establishing a healthy lifestyle.
Iribarren, 2013[69]	Two-way SMS	2	Daily	Yes (twice weekly)	Not Reported	Morning	Confirmation of message receipt and a reminder sent to the patient if they did not send

Table 4: Acceptability and feasibility of mobile health interventions for TB treatment support

Source	Location	Sample size	Study design	Population	Intervention	Outcome measure	Major findings
Iribarren, 2013 (69)	Argentina	37	Mixed-methods design	Active TB	Two-way SMS intervention	Feasibility, acceptability for treatment adherence	SMS intervention was found feasible as it has high access to mobile phones, patient familiarity with texting, and low refusal. SMS was also found as acceptable as patients had a feeling of care, supported and responsible.
Albino 2014 (67)	Peru	4 FGD	Qualitative	Active TB	One-way SMS	Perception and acceptability for treatment adherence	Patients have positive perception and accept mobile based SMS for improving medication adherence through transmit motivational text and simple reminders.
Nhavoto 2017(68)	Mozambique	140 patients 40 Health professional	Qualitative	Active TB & Healthcare professional	Two-way SMS	Usefulness, perceived benefits, ease of use, Perception satisfaction, risks of the SMS	SMS was found useful and reliable because majorly reduce failure to collect medication and avoiding a missing appointment. Patients were confident on SMS and two-way SMS (questions and appropriate answer) likable features. Unintentional disclosure of health status was the risk in case patient use shared mobile phone.
Hoffman 2010 (133)	Kenya	11 patients 3 Health professionals	Mixed-methods design	Active TB & Healthcare professionals	Mobile Video capture and transmission (Mobile DOT)	Technical feasibility and patient preference and receptivity	Mobile DOT was found to be technically feasible, and both patients and health professionals preferred communicating with one another and were open to remote MDOT and health messaging.
Sumari-de 2016 (135)	Tanzania	10 Patients	Mixed-methods design	Active TB	One-way SMS reminder at	Process measure,	Patients reported that they were satisfied with SMS reminder, but few reported that SMS reminder may be seen by others.

					real-time medication monitoring	adherence, perception	However, patients were disturbed by incorrect SMS reminders.
Mohammed 2012 [132]	Pakistan	30 patients	Qualitative	Active TB	Two-way SMS	Acceptability and engagement	Interactive two-way SMS reminders were acceptable by patients with TB support medication adherence. However, the average response rate for SMS was 57% (62% during the first message of the week and 49% during the last ten days of messaging)

2.5. Adherence definition and measurement

2.5.1. Definition of Adherence

Measuring adherence is a complex task for the TB control program because of the various meanings given for adherence, as well as various methods of measurement. The term 'adherence' is extensively used in the field of psychology and medicine. The very general definition of adherence by Howren (2013) is "the extent to which an individual's behaviour coincides with health-related instructions or recommendations given by a healthcare provider in the context of a specific disease or disorder".[136] The World Health Organization (WHO) defines adherence as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider".[137] Osterberg and Blaschke (2005) define adherence to a treatment program as "the extent to which patients take medication as prescribed by their health care providers".[119]

A review of literature by Valencia (2017)[138] summarised the definition of adherence related to TB treatment at different levels of adherence. Most commonly used definitions of adherence to TB medication are:

- **Lost to follow-up (former called default)-** "treatment interrupted for two consecutive months or more" which measured through direct observation of the patient during treatment regimen.
- **Recent non-adherent**- "missing one dose in the last four days" measured by the number of doses taken through pill count or report.
- **Non-adherent in the last month-** "missing 10% of prescribed doses" measured by the number of doses taken through pill count or report.
- **Adherent-** "all test positive" measured by fluid detection.

- **Adherent-** “attended all visits” measured by the number of visits attended through follow-ups or medication refill visits.
- **Adherent**- “at least taking 70-90% of the prescribed doses” measured through percentage/number of doses taken by pill count or report.

2.5.2. Adherence measurement

Adherence has been measured in a variety of ways in addition to the definition, and there is no gold standard measurement for adherence.[137] The methods of measuring adherence broadly classified into direct and indirect methods.[119] Valencia (2017) summarised these different adherence methods of measurement as below.[138]

2.5.2.1. Direct methods

- **Directly Observed Treatment (DOT)-** Institutional-based DOT (IBDOT) which made at the health facility level is the most commonly used form of DOT. IBDOT is expensive and logistical barriers. Community-based DOT (CBDOT) in which observation performed by family or community members or community health workers. Video Observed Treatment (VOT) has also been implemented in the TB control program which records and transmits medication ingestion video to health care provider so that enable to watch the patient remotely. VOT is not feasible in low resource settings because it requires smartphone and internet accessibility.[138]
- **Detection of drug and metabolites’ concentration in urine –** Urine sample colour change occurs with the presence of rifampicin (RIF). However, it is less effective because of reduction in RIF present in urine a few hours after drug ingestion. The Arkansas and IsoScreen methods detect isoniazid (INH) metabolites in urine. Arkansas and IsoScreen methods are fast, low-cost and easy to interpret, but limited to recent drug use.[138]

- **Ingestible sensor-based system –** This is an ingestible drug sensor, the signal of which is detected by on-body wearable sensor upon ingestion. It can verify the use of pills, but it is expensive especially in high TB burden settings. [138]

2.5.2.2. Indirect methods

- **Patient self-report-** This includes questionnaires, scales, interviews and patient diaries. The most commonly used questionnaire types are; Morisky Medication Adherence Scale (MMAS),[139] Visual Analogue Scale (VAS),[140] Medication Adherence Rating Scale (MARS),[141] and Brief Medication Questionnaire (BMQ).[142] The AIDS Clinical Trial Group adherence questionnaire (ACTG)[143] is also used for TB medication adherence assessment. [144] These approaches can indicate long-term adherence status, but they are unreliable, which is one of the most significant drawbacks of self-reported adherence assessments. Self-report adherence measures are also open to different types of biases such as recall bias, social desirability bias, assuming the patient taking the medication as reported, as well as interviewer skill and construction of questions affecting the adherence measurement.[138]
- **Pill count and refill visit -** If there are any remaining pills in the blister pack of pill bottles, patients bring them to their controller, who compares the total number of pills given with the number of pills left in the blister pack. These methods are less expensive, easy to measure and can show long term adherence. However, it has limitations such as patients may dump their medication deliberately or forget bringing blisters during visits.[119] Recording the patient's appointment attendance for refill medication is therefore not accurate as a measure of ingestion of medication.[119]
- **Electronic pill bottles-** Medication Event Monitoring System (MEMS) are one of the most reliable markers of adherence and can predict long-term adherence. Other adherence methods have been validated using MEMS as a reference. However, MEMS is expensive especially to use in low resource settings and it does not verify the actual medication intake. [119] [108]

2.5.3. Selection of adherence measurement

When testing an intervention with randomised trials, correctly measuring outcomes in the same way for both the experiment and control groups is crucial. For example, in an Argentinian individual randomised study, adherence was measured in flawed way; it was measured differently in the intervention group (measured by replying SMS confirmation) and the control group (measured by calendar diaries and self-report), and a large proportion of patient's information was missed by the calendar diaries. [69] It is therefore important to carefully select the measurement tools based on their pros and cons.

Biochemical analysis of anti-TB drug metabolites in urine is a modern approach, and one method is using the Arkansas method of analysis of isoniazid (INH) metabolites in urine. This is a useful and reliable laboratory-based assay, which has been used in many studies to determine drug treatment adherence.[145] However, the required laboratory equipment and expertise make difficulties for this test. An alternative is to use a point of care test that incorporates the chemicals for the Arkansas method into a simple disposable plastic testing device. [146] The test called IsoScreen which has been used in Tanzania, [144, 147] Brazil [86] and Canada.[87] IsoScreen is a rapid and safe point-of-care test that provides accurate detection of adherence for the patient.[146] The existing evidence shows that Isoscreen has high sensitivity (83%-100%) and specificity (over 95%) in the detection of adherence to TB medication.[86-89] For example, one study indicated that the sensitivity and specificity are very high especially at 12 and 24 hours for purple or blue color change (100% and 99%) and at 48 hours for green color change (78% and 100%). Isoniazid metabolites detection by IsoScreen was not influenced by demographic characteristics, smoking status, alcohol consumption and additional medication uses.[89]

The accuracy of adherence measurement is very crucial to detect the true effect of an intervention on medication adherence. The most commonly used method to measurement adherence is considered to be the indirect method. [148] It is necessary to have a valid and reliable adherence measure with a low cost and acceptable to use in a limited-resource

setting. Indirect measures can be used over a longer period of adherence, but it assumed that the patients are actually taking their medication as they reported.[138, 148] Direct method adherence measures that detect drugs and metabolites concentration in urine are quick, easy, and inexpensive as compared with MEMS. Evidence shows that the IsoScreen NIH metabolites test has been effective in detecting non-adherence [88, 138] and it can also be used to validate the indirect adherence measures in poor resource settings.[88]

In the current study, we choose to use the Isoscreen NIH test over urine color change by the presence of rifampicin (RIF) because evidence showed that the RIF effect is very short-lived (peaking 2-6 hour) and is only seen in <50% of patients.[89] For example, one study found that the sensitivity of RIF was 43.5% compared with 93.2% in INH urine test.[75] The IsoScreen test is easy to use and convenient especially in busy outpatient clinics.

As IsoScreen test only indicates a recent medication adherence, other validated indirect methods were also used for showing long term effects of mobile-assisted adherence intervention. The previous studies showed the four scale Morisky medication adherence was reported as less sensitive among TB patients.[88, 144] The revised eight scales Morisky medication adherence (MMAS-8) has better sensitivity and specificity compared to the four scales but is not licensed to individuals.[139] The AIDS Clinical Trial Group Adherence Questionnaire (ACTG) was validated among TB patients in Tanzania and is recommended for use in adherence interventions, along with other indirect methods of adherence.[144] The Visual Analogue Scale (VAS) is a recommended adherence scale for clinical practice, demonstrating a significant correlation with other methods of adherence measurements.[149] Thus, in the randomised trial, adherence was measured using the combination of direct method of the IsoScreen test and indirect methods: Visual Analogue Scale (VAS),[140] and AIDS Clinical Trial Group adherence questionnaire (ACTG).[143]

CHAPTER 3: METHODOLOGY AND METHODS

3.1. Introduction

This chapter is focused on the research methodology and methods, which is a critical aspect of the research project. The methodology includes various elements, such as the research philosophy, the researcher's position, the research paradigm, and the mixed methods design. Additionally, this chapter provides details of the study design, method of data collection and analysis for each study.

3.2. Research philosophy

3.2.1. Ontology

Ontology deals with the nature of reality. It is the theory of existence or reality.[150, 151] The two major ontological positions are realism and anti-realism. Realism states that reality exists independent of our perceptions or theories. Whereas anti-realism rejects the belief that reality is independent of us or our consciousness.[150] In this study, the realist ontological position was applied in part because the effect of a mobile-assisted medication adherence support (Ma-MAS) intervention on patient's adherence was empirically examined, and the anti-realism ontological position was also applied because the patients' perceptions and experiences of the Ma-MAS intervention were studied with an interpretive research approach.

3.2.2. Epistemology

The concept of epistemology pertains to the meaning and the process of acquiring knowledge. Epistemology is concerned with the nature and justification of knowledge.[150] It asks what knowledge is? What is the justification for knowledge and how are the known and the knower related?[150] The most common epistemological positions raised in the literature are objectivism and constructivism. The Objectivist approaches view the meaning of realist existence as independent of consciousness (objective meaning). Objectivists understand the phenomenon using a positivist research approach with deductive reasoning and empirical

methods.[150] Whereas the constructivist approaches view meaning as socially and experientially constructed by an inductive reasoning and interpretive approach.[150] The constructivist supports the existence of multiple meanings of a phenomenon.

3.2.3. Researcher position

In this research, the phenomenon under investigation is adherence to the prescribed TB medication. An intervention was designed to improve the patients' adherence to medication. The phenomenon of 'adherence' or 'non-adherence' can exist independent of our consciousness or assessment. Adherence is defined as the act of taking the prescribed medication at a consistent time and regularly. In a positivist approach, adherence is measured and analysed statistically to determine whether it has been occurred. For example, adherence can be defined as "a test positive" measured by urine detection, and in self-reported measurement, adherence can be defined as "when a patient is taking 90% and above of the prescribed dose of a medication". The interpretivist would ask why adherence or non-adherence has occurred and what beliefs led to people adhering or not adhering. The interpretivist would also ask what the patients perceived and experienced during the adherence intervention. Thus, both the positivist and the interpretivist approaches can be used depending on the focus of the research questions. In this study, I used truth of knowledge as "what works at the time" and truth of knowledge is relative, not absolute, as indicated in the pragmatism research paradigm. [152] My primary interest is to solve the problem of adherence to TB medication through designing an intervention using a behavioural change model and techniques.

The epistemic questions here are: what is adherence or non-adherence? Is non-adherence to TB medication a problem? What is the justification for that conclusion? What are the causes of non-adherence? Why are people adhering or not adhering? How can resolve the problem of non-adherence to TB medication? How does the intervention improve patient's adherence to TB medication (mechanism of intervention)? What other factors explain the effectiveness of the adherence intervention? What do patients perceive and experience about the

adherence intervention? Some of these questions are answered using objectivist epistemology, others by constructivism, and others by a mixture of both. Therefore, the research is open to different world views, assumptions, and methods of investigation of the problem and focused on identifying a practical solution.

3.2.4. Research paradigm

The current research was conducted using the pragmatic research paradigm. It is important to understand two other research paradigms before explaining pragmatism. The positivist paradigm determines cause-effect relationships. In the positivist research paradigm, hypothesis and research questions are tested through deductive reasoning and statistical methods.[152] The epistemic position of the positivist research paradigm is objectivist. Constructivists hold the assumption that the participant constructs the meanings of the phenomenon being studied. Participants develop a subjective meaning for their experience towards certain object or things. Indeed, there may be multiple meanings given to the phenomenon being studied. Constructivism understands the meaning of the phenomenon through inductive reasoning and an interpretive approach. Thus, constructivism is often combined with interpretivism.[152]

Pragmatism is centred on the problem, the action, and the consequences of the action.[152] In pragmatism, truth is "what works at the time", it is not a dichotomy between a reality independent of the mind or a reality within the mind.[152] Pragmatism accepts both singular and multiple realities that are open to inquiry to solve a problem while avoiding the controversies created by positivism and constructivism.[153] The pragmatist ontological position on reality is close to "existential reality" and refers to an experiential world with elements that are somewhat objective, somewhat subjective, or a mix of both.[153] The pragmatic approach allows for different worldviews, assumptions, and methods that are best suited to solve the problem.[152, 153] In pragmatism, a mixed-methods research approach is dominant, with both quantitative and qualitative research data being used to identify solutions for the problem at

hand and the associated research questions.[152, 153] Thus, pragmatism supports the use of mixed research methods and different methods of analysis to generate socially useful knowledge to identify practical solutions.[153, 154] Pragmatism is an outcome-oriented approach that focuses on finding shared meaning and identifying practical solutions to the problems being investigated using both empirical and interpretive research approaches.[154] In a pragmatist approach, theories can be contextual and generalisable, and support the transferability of results to other situations.[154] In addition, theory can be developed before and after data collection, which is known as abductive reasoning;[154] meaning that the approach uses both inductive and deductive reasoning.

3.3. Mixed methods

3.3.1. Definition of mixed methods

Creswell John and Creswell David's (2018) text on research design, defines qualitative, quantitative, and mixed methods research as follows. Qualitative research is “an approach for exploring and understanding the meaning individuals or groups ascribe to a social or human problem,”[152] quantitative research is “an approach for testing objective theories by examining the relationship among variables,”[152] and mixed-methods research is “an approach of inquiry collecting both quantitative and qualitative data, integrating the two forms of data, and using distinct designs that may involve philosophical assumptions and theoretical frameworks”.[152]

3.3.2. Mixed methods evaluation

In this study, a mixed-methods evaluation design was used to develop and evaluate a mobile-assisted medication adherence support intervention.[152] Mixed-methods design uses both quantitative and qualitative research data to answer the research questions. The mixed-methods design was employed through the Medical Research Council’s (MRC) framework for the development and evaluation of complex interventions.

The Ma-MAS intervention was developed using an exploratory mixed methods design with a literature review and interpretive study using in-depth interviews (qualitative). A Delphi

technique was used to validate the proposed Ma-MAS intervention using expert opinion (qualitative) and a survey (quantitative). The feasibility and acceptability of the Ma-MAS intervention were evaluated through a cross-sectional survey (quantitative) before the Ma-MAS intervention trial. An experimental design with a parallel group randomised control trial employed to evaluate the effectiveness of Ma-MAS intervention. A convergence mixed-methods design, composed of in-depth interviews (qualitative) and cross-sectional survey (quantitative), was used to evaluate the patients' perceptions, experiences, and adoption intention of the Ma-MAS intervention. The data collection, analysis, and interpretation were undertaken separately, but the results were discussed together (see Figure 2).The reasons for using a mixed-methods design with both quantitative and qualitative research approaches are to: describe the change process, explain how the intervention worked, assess whether the intervention was implemented as planned, evaluate the acceptance of the intervention, explain the benefits of the Ma-MAS intervention, receive patient feedback on the intervention design, and examine whether the intervention has a long-term desire.

The methods section presented below in study one and three contains material originally published article of protocol of a parallel group Randomised Control Trial (RCT) for Mobile-assisted Medication Adherence Support intervention.[155] The copy of published article is found in the Appendix Eight.

Figure 2: Schematic presentation of the mixed methods evaluation design

3.4. Study setting and period

The research was carried out in public health institutions in Addis Ababa, the capital city of Ethiopia. Addis Ababa has 10 administrative sub-city regions (see Figure 3). Based on population projections, the total population of Addis Ababa in 2017 was 3,433,999 with 1,624,999 males and 1,809,000 females.[156] In Ethiopia, TB treatment care is provided through direct observed treatment (daily and non-daily DOT). The DOT program has two phases, the intensive and the continuation phase of treatment. In the intensive phase, the patient takes the medication in front of the healthcare worker every day at the health facility. In the continuation phase, the patient is given the responsibility of taking the medication at home, and comes to a health facility at fixed regular intervals (weekly refill visits), which is known as non-daily DOT.[157] However, the daily DOT and non-daily DOT program schedules were disrupted as a result of the emergence of and response to the COVID-19 pandemic.[20] Thus, throughout this research study period, the regular program of daily DOT and non-daily DOT was not implemented; instead, self-administered treatment administration was implemented with irregular medication refill visit schedules. More information is presented in qualitative research findings in the Appendix Two. The research was conducted from August 27, 2020, to October 29, 2021.

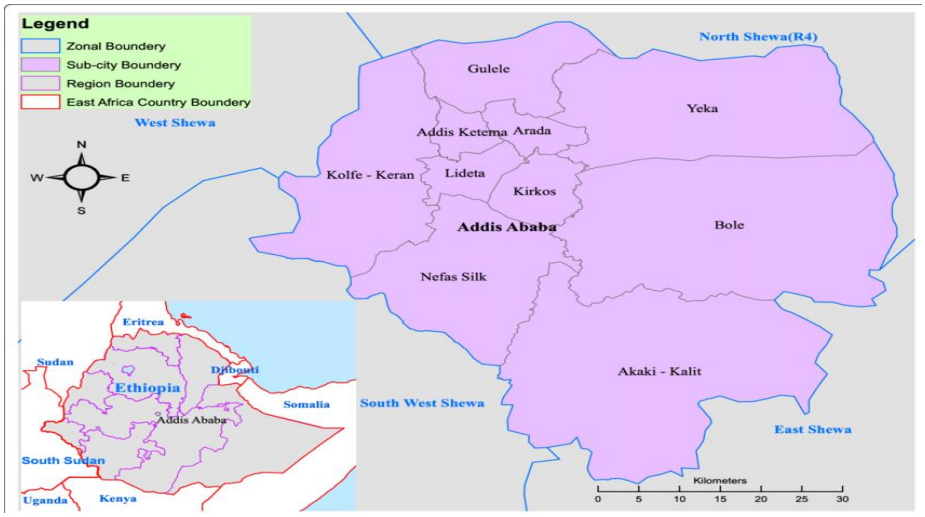

Figure 3: Map of Addis Ababa, Ethiopia (Source: Shapefile from Ethiopian mapping Agency)

3.5. Study one: Development and validation of Ma-MAS intervention: An MRC framework approach

3.5.1. MRC framework for complex interventions

Behavioural interventions involving multiple interacting components are complex, and complex interventions are most commonly used in health research.[76, 158] In 2000, the Medical Research Council (MRC) developed a framework to help the researcher to develop and evaluate complex intervention [159] that was updated in 2008.[76] Complex interventions are commonly described as “interventions that contain several interacting components”. However, complex interventions have also other features.[76] These are: the interconnected components in the intervention and control groups, the target behaviours difficulty, the target groups number in the intervention, the outcomes number and variability, and the flexibility or tailoring of the intervention.

Complex interventions may be effective when it is designed to the home-grown circumstance rather than entirely standardised, and develop systematically using evidence-based and proper behavioural theory and testing in a phased approach before evaluation. [76] The framework has four elements in the development and evaluation process of complex intervention. These are (1) Development; (2) Feasibility and acceptability; (3) Evaluation; and (4) Implementation (see Figure 4). The intervention development process using this framework described in this section.

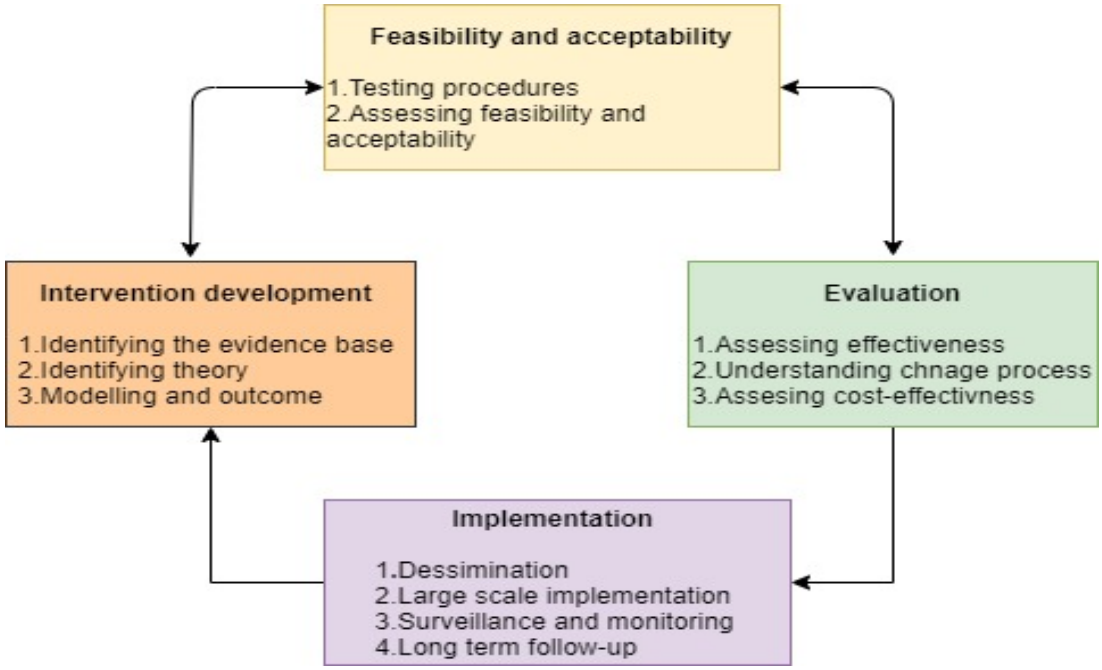

Figure 4: Key element in the development and evaluation process of complex Intervention adapted from Craig P. et al. 2008 [76]

3.5.2. Ma-MAS Intervention development process

To generate quality evidence from the trial of the mobile-assisted medication adherence support (Ma-MAS), the intervention is developed systematically with the best available evidence and using the behavioural model of information-motivation-behavioural skills (IMB)[160] and behavioural change techniques taxonomy.[158] Thus, the Ma-MAS intervention is developed and evaluated based on the Medical Research Council (MRC) framework for complex intervention in health care.[76] The development phase of the framework was adapted from Bleijenberg et al. (2018) to be a more specific to the development of an intervention.[161] The adapted development phase of the MRC framework guideline has seven different phases in a nonlinear iterative process:

1. Phase 1: problem definition (identification and analysis)
2. Phase 2: systematically identifying the evidence
3. Phase 3: identifying and developing a theory
4. Phase 4: determining the needs
5. Phase 5: examining the practice

6. Phase 6: modelling process and outcome and
7. Phase 7: intervention design (see Figure 5).

The development phase of the MRC framework along with the means of evidence collection is summarised in Table 5.

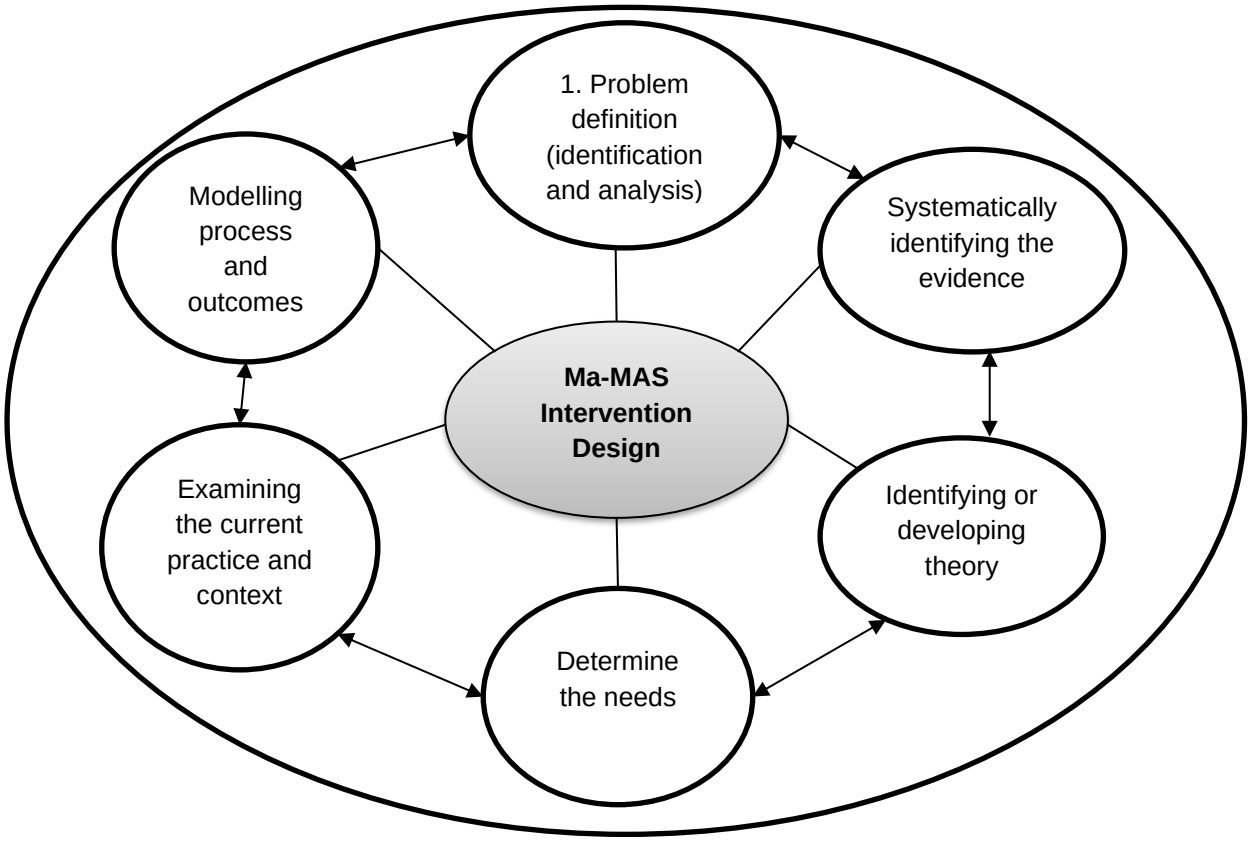

Figure 5: Adapted MRC framework development Phase. Source: Bleijenberg et al. 2018 [161]

Table 5: Mobile-assisted medication adherence support intervention development phases: An adapted MRC framework approach[161]

Development phases	Methods
Phase 1: Problem definition (identification and analysis)	• Review of literature • Qualitative descriptive research
Phase 2: Systematically identifying the evidence	• Review of literature • Qualitative descriptive research • Quantitative survey research
Phase 3: Identifying or developing theory	Review of literature
Phase 4: Determine the needs	• Review of literature • Qualitative descriptive research
Phase 5: Examine the current practice and context	• Qualitative descriptive research
Phase 6: Modelling process and outcome	• Modelling a prototype of intervention components • Identifying interrelation with the outcome • Experts' opinion through Delphi technique
Phase 7: Intervention design	• Experts' opinion • Refine the intervention

3.5.2.1. Phase 1: Problem identification and definition

The problem of non-adherence to TB medication has been identified and defined through a review of the literature conducted in Ethiopia where the study was conducted. The literature review is published under the title of "Factors Influencing Patient Adherence to Tuberculosis Treatment in Ethiopia; A Literature Review" (see Appendix Eight).[6] Along with problem identification and definition, it is recommended to describe the context for an intervention, such as socioeconomic background, the health service system, and the characteristics of the patient and their influence on adherence and the adherence intervention which would benefit the success of the intervention.[79] A further qualitative descriptive research was conducted to extend on the literature review evidence. The qualitative research findings are presented in the Appendix Two. The prototype SMS text messages are developed based on factors influencing adherence to TB medication. The prototype SMS text messages are found in the Appendix Three.

3.5.*2.2. Phase 2: Identifying the evidence base*

Evidence has been collected through a review of literature, to identify the effectiveness of mobile health SMS interventions including acceptability, feasibility, and characteristics of the intervention. A further acceptability and feasibility study was conducted using qualitative descriptive and quantitative survey research before the intended trial was implemented. This phase aimed to identify past interventions and their effectiveness, acceptability and feasibility of the target groups of the interventions, as well as the features of the intervention. In the literature review evidence, there was contradictory evidence regarding the effectiveness of SMS text message interventions on TB medication adherence and treatment outcomes. Nevertheless, the SMS text messages and phone calls intervention for TB medication adherence promotion had high acceptance and was considered feasible to implement. This information is presented in the literature review, in chapter five of study two results and in the Appendix Two.

3.5.2.3. Phase 3: Identifying or developing theory

The behavioural change model that can best explain the proposed intervention's mechanism of action has been identified through the review of literature. This phase of development aims to identify the theory or model that can best explain the intervention mechanism of action. Information, motivation, and behavioural skills model was selected[160], and the relationship between the model constructs with adherence behaviour was logically connected based on factors influencing TB medication non-adherence (see Figure 6).

Information, Motivation and Behavioural Skills (IMB) model

The information, Motivation and Behavioural skills (IMB) model was applied to develop the mobile-assisted medication adherence support intervention (see Figure 6). The IMB model is developed based on the analysis and integration of social and health psychology theories that consider the psychological determinants of adherence, and focuses broadly on information, motivation and behavioural skills factors linked to adherence. [160] The IMB model explains the

relationships between these constructs and adherence. The model's assumption is that adherence related information, motivation and behavioural skill are the major causes for non-adherence. According to this model if a patient is informed, motivated to act and has the required behavioural skills to act, he/she is highly likely to adhere to TB medication and thereby will have a good treatment outcome.[160] This model was used to guide the development of SMS text messages, and phone calls designed to support the SMS text messages in the Ma-MAS intervention.

Information: Information is an antecedent construct for adherence behaviour. Information about TB and its treatment can influence adherence behaviour directly and indirectly mediated through individual motivation and behavioural skills.[160] Information about TB and its treatment regimens, when and how to take their medication, what to do a dose is missed, the link between medication adherence and treatment outcomes, the link between substance use and treatment outcomes, the side effects of the drug, the misconception about TB and its medications and other barriers are the major information required for medication adherence.[6]

Motivation: The IMB model argues that an individual's motivation to adhere is influenced by both personal and social motivations. Personal motivation to adhere to medication includes attitude towards the treatment regimen and beliefs about the consequence of adherence and/or non-adherence to TB medication and the evaluation of these outcomes.[160] Thus, favourable attitudes and beliefs towards the treatment such as perceived curability, severity, risk, and benefit are assumed to be associated with adherence to TB medication. [6] Individual perceptions of social support for adherence from significant others such as families, friends, and healthcare workers, as well as individuals' motivation to comply with the wishes of significant others, are the social motivation.[160] Indeed, the perceived social support and motivation to comply with the wishes of significant others are also associated with adherence to TB medication. The Ma-MAS intervention itself can also be considered as a social support to patients and positively influence adherence to TB medication.

Behavioural skills: The behavioural skills are an antecedent construct for adherence that also determines the success of adequately informed and motivated individuals to adhere to their medication. The activities here include setting goals and perceived abilities and self-management for integrating the treatment regimen into daily life, managing the side effects of the drug, acquiring social and health care support, self-reinforcement, and problem-solving skills. [160] To develop the desired behavioural skills, the information provided through SMS text messages was supported by phone calls.

Moderating factors: Factors other than information, motivation, and behavioural skills are also expected to influence the model and adherence to TB medication. Although patients are properly educated, motivated to act and have the required behavioural skills, they may still not adhere to their medication because of other moderating factors such as economic constraints, inadequate food, co-morbidities, travelling distance, time and cost, social support, stigma and discrimination, psychological distress and others. Thus, moderating factors have a direct and indirect effect, through the influence of the constructs, on adherence to TB medication. However, individuals with a moderate level of moderating factors will theoretically respond to an adherence support intervention.[160] In the Ma-MAS intervention trial, the randomisation of participants into the intervention and control groups is expected to uniformly distribute moderating factors into both groups, ensuring that they do not affect the intervention's effectiveness.

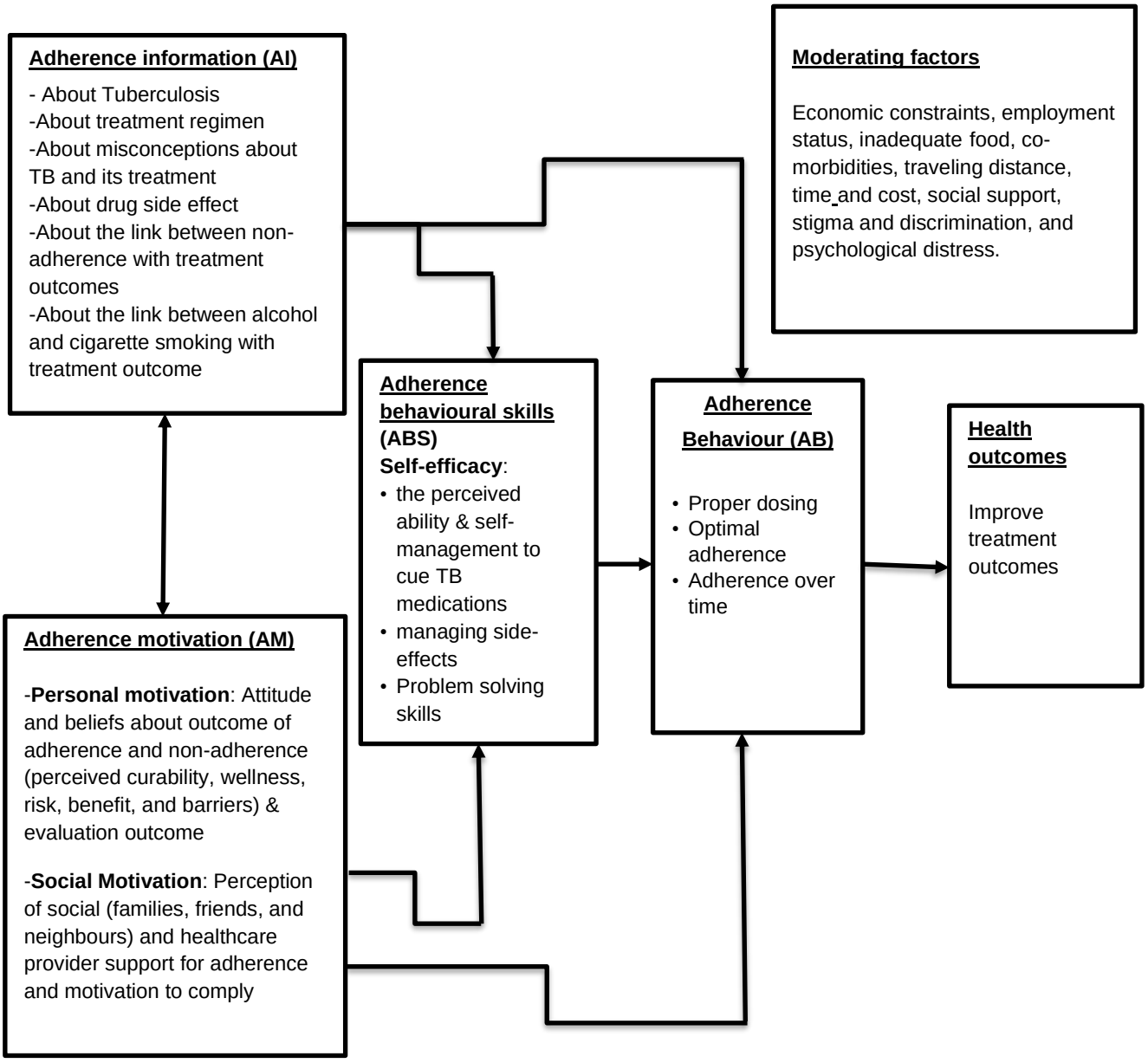

Figure 6: Information, Motivation and Behavioural skills model to TB medication adherence adapted from Fisher et al. 2006 [160]

3.5.*2.4. Phase 4: Determine the needs*

The needs, preferences, perceptions, and capacities of the patient and healthcare providers with the identified problems and proposed solutions were determined through the review of literature and qualitative descriptive research using in-depth interviews. This approach generates information about which characteristics of the intervention are likeable and adaptable, and how the SMS texts and phone calls can be tailored regarding language, content, frequency, length, and time of the day. The frequency of SMS text messages and

phone calls was determined to be daily and weekly respectively based on the need assessment. It was also decided that all SMS text messages, and phone calls would be made in the national language of the country. The content of the SMS text messages suggested by health care providers and patients was included. It was decided that the daily SMS text message and weekly phone call are to be delivered in the morning from 7:30am to 8:00am. The intervention length was agreed to be eight weeks as a first trial to test the effectiveness of the intervention, though most healthcare professionals believed the SMS text messages and phone calls should be used throughout the entire six months of treatment. The details findings of the qualitative research are presented in the Appendix Two.

3.5.2.5. Phase 5: Examine current practice and context

Barriers and facilitators of the mobile assisted adherence support intervention were identified by examining the current practice and context of care from the patient's and healthcare provider's perspectives. This step assures that the functionality of the proposed mobile health intervention best fits with existing practice and the local context. Qualitative descriptive research, using in-depth interviews, was employed to examine the current practice and context. The barriers, facilitators and suggested solutions were considered in the design of the Ma-MAS intervention and some of these are especially useful for future scale-up. The barriers and facilitators of the mobile-assisted adherence support intervention and suggested solutions are presented in the qualitative research findings in the Appendix Two.

3.5.*2.6. Phase 6: Modelling process and outcome*

Modelling the active component of the mobile-assisted adherence intervention and its relationship with outcomes was refined with multidisciplinary team involvement. The initial set of prototype SMS text messages were drafted applying the taxonomy of behaviour change techniques[158] and linked to the constructs of IMB model [160] (see Appendix Three). Factors associated with non-adherence to TB medication were logically connected to the behaviour change technique and IMB model. A Delphi technique was employed to validate the content

of the SMS text messages by senior experts and health professionals who work at ground level.

3.5.2.7. Phase 7: Intervention design

A full mobile-assisted medication adherence support intervention using SMS text messages and phone calls was developed. A total of 40 SMS text messages were selected for the Ma-MAS intervention for eight weeks of intervention (see Appendix Four). The experts gave their comments on the timing, frequency of information, duration of the intervention, and arrangement order of the SMS text messages. Based on the experts' opinions the final mobile-assisted medication adherence support intervention design was prepared and tested.

3.5.3. Study design

To systematically develop and validate the mobile-assisted adherence support intervention, an exploratory mixed-methods approach was employed, together with a review of relevant literature, and qualitative descriptive research. The SMS text messages developed for Ma-MAS intervention were validated using a four round Delphi technique.

3.5.4. Participants

To systematically develop and validate Ma-MAS intervention different groups of participants were utilised. These participants were: (1) Adult TB patients aged 18 years and above involved in qualitative in-depth interviews and (2) Primary healthcare providers at service delivery points and experts at health offices who have experience related to TB prevention and control involved in qualitative in-depth interview (see Figure 7).

For validation of the SMS text messages, experts comprised of professional backgrounds in behavioural science, healthcare systems, pulmonary disease, and digital health were involved in the SMS text messages content validation in the round one to three Delphi technique. In round four, health professionals working as TB experts from health facilities and health offices

in Addis Ababa, Ethiopia were invited to rate the relevance of the proposed SMS text messages.

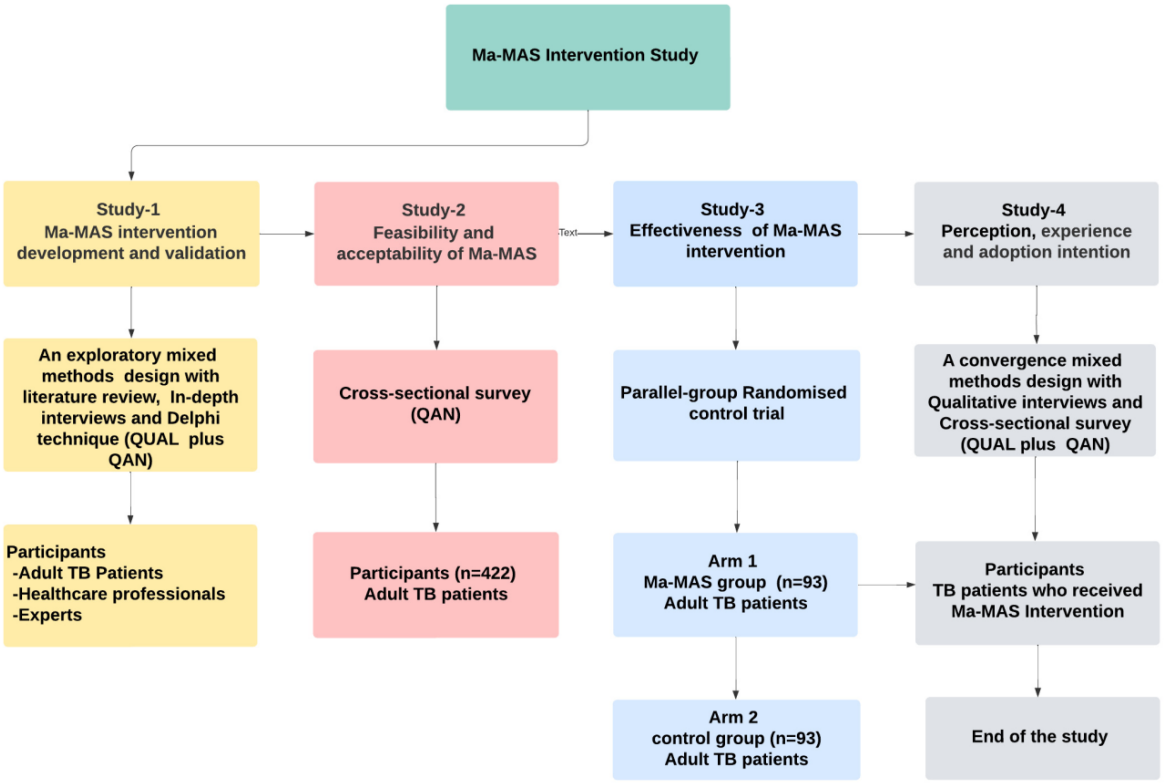

Figure 7: Schematic presentation of study objective, design, and participants

3.5.5. Sample size and technique

The number of qualitative in-depth interviews with patients, healthcare providers and experts were determined based on idea saturation. That means interviews were continued until no further new information was obtained.[162, 163] However, based on the literature review recommendation, the minimum number of interviews was not below 15.[164] Purposive sampling method was employed to select the patients for the in-depth interview.

Eight senior experts involved in the validation process of Delphi technique from rounds one to three. An additional 47 health professionals who work as TB focal person in 36 health facilities and TB prevention and control experts in 11 health offices in Addis Ababa, Ethiopia, were invited for further validation of the SMS text messages in Delphi round four. Both expert

groups were selected purposively based on their professional background, work experience, and geographical location.

3.5.6. Data collection instrument and process

An in-depth interview guide was developed through review of relevant literature and the focus of the research questions, to systematically develop the mobile-assisted adherence support intervention. An open-ended interview guide and audio-recorder were used for qualitative data collection. The qualitative interview audio was recorded using digital recorder. The qualitative data was collected by the principal investigator who has experience with interpretive research and the culture and languages of the location. In-depth interviews with patients and health professionals were conducted at a convenient place and time for discussion and privacy.

To validate the SMS text messages a four round Delphi technique was applied.[165] This are:

Delphi round one: In the first round, the prototype SMS text messages were given to experts who were asked for their opinion about the consistency of the prototype SMS text messages content with the IBM model and behavioural change techniques (BCT), and asked to develop additional SMS text messages according to the IBM model and BCT.

Delphi round two: In the second round, the experts received the modified prototype SMS text messages and were asked to rate the relevance of the SMS text messages for TB medication adherence using a four-point Likert scale. The experts rated the relevance of SMS text messages ranging from 1 to 4, with 1 for "not relevant" to 4 for "highly relevant". The rating criteria were defined and given to experts as seen in the Table 6 below.

Delphi round three: In the third round, the experts received summary statistical reports such as mean, standard deviation (SD), and item-level content validity index (I-CVI) based on the second-round rating. Experts were asked to revise their rating if they would like to change. The experts were also informed about the cut-off point for the I-CVI (0.80) to retain the SMS text message that applied in the third-round rating.

Delphi round four: In the fourth round, the selected SMS text messages in round three were translated to the national language of Amharic and checked the consistency by another professional translator. The translated SMS text messages were given to health professionals to rate the relevance of SMS text messages using the four-point Likert scale. I-CVI above 0.80 was used to retain the SMS text messages for the Ma-MAS intervention.

Table 6: SMS text messages relevance rating description

Scale	Relevance	Description
1	Not relevant	A text message is **not at all important** to promote adherence to TB medication behaviour, and failure to communicate this message to the patient will **not have any** consequence on non-adherence TB medication behaviour.
2	Somewhat relevant	A text message that can be used on **a daily or non-daily basis and has limited importance** to promote adherence to TB medications, and failure to communicate this message to the patient will have **minor consequences** on non-adherence TB medication behaviour.
3	Quite relevant	A text message that can be used on a **non-daily basis and is important to** promote adherence to TB medication, and failure to communicate this message to the patient will have **a major consequence** on TB medication non-adherence.
4	Highly relevant	A text message can be used on **a daily basis and is highly important** to promote adherence to TB medication, and failure to communicate this message to the patient will have **a major consequence** on non-adherence TB medication behaviour.

3.5.7. Data analysis

The qualitative data analysis involves verbatim transcription of in-depth interviews, coding, categorizing themes and sub-themes, and thematic analysis was employed using NVivo software version 12. The detail of the qualitative data analysis process is explained in section 3.8.6. The trustworthiness of qualitative studies is explained in section 3.8.7 in this thesis.

The experts' ratings of SMS text messages data was entered into Microsoft excel and exported to SPSS version 27 for analysis. To retain SMS text messages for the next round of Delphi, the Item level content validity index (I-CVI) of 0.80 was used as the cut-off point.[166]. Consensus on the retained SMS text messages was reached in Delphi rounds three and four. Scale-level content validity index (S-CVI) was calculated in two ways: (I) S-CVI/Ave is the "average of the I-CVIs for all items on the scale" and (II) S-CVI/UA is the "percentage of items on a scale that achieve a relevant rating of 3 or 4 by all experts." This is also known as ‘universal agreement’[166]. To retain the SMS text messages for TB medication adherence intervention, we used 90% for the Scale-level content validity index (S-CVI) for S-CVI/Ave.[166]

3.6. Study two: Feasibility and acceptability of Ma-MAS intervention

3.6.1. Study design

A quantitative cross-sectional survey was used to assess access and use of mobiles for SMS texts and phone calls, and the acceptability of a mobile-assisted medication adherence support intervention.

3.6.2. Participants

To assess the feasibility and acceptability of the mobile-assisted medication adherence support intervention, the participants were adult TB patients receiving anti-tuberculosis medication in 36 primary public health facilities chosen from 10 sub-cities of Addis Ababa, Ethiopia. The eligibility for this study was a diagnosis with TB and commenced on anti-TB treatment at the primary public health facilities, and at least 18 years old. Participants were excluded from this study if their treatment was prescribed for more than six months, or they had been diagnosed with MDR-TB.

3.6.3. Sample size and technique

To assess the feasibility and acceptability of the mobile-assisted medication adherence support intervention, the sample size was determined using Epi Info statistical software and a single population proportion calculation. The proportion of acceptance of mobile-assisted medication adherence intervention was 50%, 95% confidence level (alpha 0.05) and 5% margin of error were used for sample size calculation. The initial sample size calculated was 384, and with a 10% non-response rate, the final sample size was 422. A total of 36 health facilities were randomly selected from 10 sub-cities of Addis Ababa, Ethiopia. The number of participants in each health facility was determined based on the probability proportional to size (PPS) of the patients in the selected 36 health facilities in Addis Ababa, Ethiopia. Eligible participants were sequentially recruited and invited to be a part of the survey when they came to the clinic for medication refill visits (convenience sampling).

3.6.4. Data collection instrument and process

The feasibility and acceptability of the mobile SMS and phone call intervention assessment tool was developed based on the study objective and a review of similar studies.[167][63] The instruments were pretested, and appropriate correction was made during the training of data collectors. The data was collected electronically using Open Data Kit (ODK).

3.6.5. Data analysis

The electronically collected data was cleaned in excel and exported to SPSS version 27 for statistical analysis. To assess the feasibility and acceptability of the Ma-MAS intervention, descriptive statistics with frequency and percentages was employed.

3.7. Study three: Effectiveness of Ma-MAS intervention

3.7.1. Study design

A parallel-group individual randomised controlled trial (RCT) with two groups was employed to investigate the effect of the Ma-MAS intervention on TB medication adherence. Participants were individually randomised into one of the two groups (intervention or control group) in a 1:1 allocation ratio.

3.7.2. Participants

To measure the effect of the mobile-assisted medication adherence support intervention, participants were adult TB patients diagnosed with TB and commenced on anti-tuberculosis treatment at public health facilities of Addis Ababa, Ethiopia. To be included in the randomised control trial (RCT) participants were required to be enrolled in a primary public health facility for anti-TB treatment and have completed their first two months of the intensive phase of treatment, aged at least 18 years, have their own mobile phone, and able to read and understand an SMS text that is written in the national official language (Amharic). Participants who did not have a mobile phone also were included if they could share partner's mobile phone in the household with the collaborative agreement.

Participants were excluded from the randomised trial if they met the following conditions:

1. Patients whose anti-tuberculosis treatment had been prescribed for more than six months. This is because of the need to ensure homogeneity in treatment duration, which could affect adherence.
2. Patients who enrolled or agreed to enrol in any other interventional study at the same time as this study was conducted.

3.7.3. Sample size and techniques

To measure the effect of the mobile-assisted medication adherence support intervention a sample size was calculated using STATA code *power two proportions* considering the primary outcome of TB medication non-adherence. The rate of TB medication non-adherence in Ethiopia varies considerably in the literature ranging from 10% to 26% depending on the patient's treatment phase and different settings.[13, 19, 83, 94, 116, 117] We found the rate of non-adherence was 25.6% (po=0.256%) during the continuation phase of treatment from a previous study conducted at Addis Ababa, Ethiopia in the control group.[83] Previous mobile SMS text interventions in Africa used 15% to 20% differences.[84, 122, 131] Thus, we use a 15% absolute reduction of TB non-adherence due to a mobile SMS text intervention found in a similar study [84] that would yield a non-adherence rate of 10.6% (pa=0.106) in the intervention group. Considering simple randomised controlled trial parallel-group design, 95% confidence level (alpha=0.05), 80% power (beta=0.80) and a one-sided p-value of 0.025 the initial sample size is n=81 participants per arm. Assuming an attrition rate of 15%, the final sample size would become the total n=186 with arm-1 n=93, and arm-2 n=93.

A total of 36 primary public health facilities were included in the trial by random selection with the assumption being that an average of 6 participants would be found in each health facility.

3.7.4. Recruitment

Patients who completed the intensive phase of anti-TB treatment were recruited by the research support team of healthcare professionals from each health facility, based on eligibility and exclusion criteria. The recruitment was continued until the required sample size was achieved. All the recruitment process details were recorded electronically in Open Data Kit (ODK) platform and retained securely by the research team as required approvals.

3.7.5. Randomisation and allocation

Participants who met the selection criteria were centrally randomised into one of the two groups using simple randomisation in a computer-generated algorithm, with an equal allocation ratio (1:1), by member of the research support team, who was not involved in measuring the outcome. The number of participants allocated to each health facility was determined based on the number of patients enrolled in the intensive phase of treatment. The investigators, the data collectors, the intervention administer, and the patients did not know where the next eligible patients would be assigned (Ma-MAS or control group) before randomisation.

3.7.6. Intervention group

Ma-MAS intervention (Arm-1) group participants received a daily SMS text message and weekly phone calls for medication intake and medication refill visit reminders (see Figure 8). All participants received the intervention at a similar time for eight weeks during the continuation phase of the TB treatment. The phone calls information was guided by questions such as ‘Good morning, do you take your daily medication?’ ‘Did you have a question regarding your medication?’ ‘Good morning, this is to remind you of your daily medication intake’ ‘Do you have a question regarding your medication?’, ‘Are you reading and following the SMS text message instructions?’ The phone calls discussions were open and not limited to these questions (see Appendix Five).

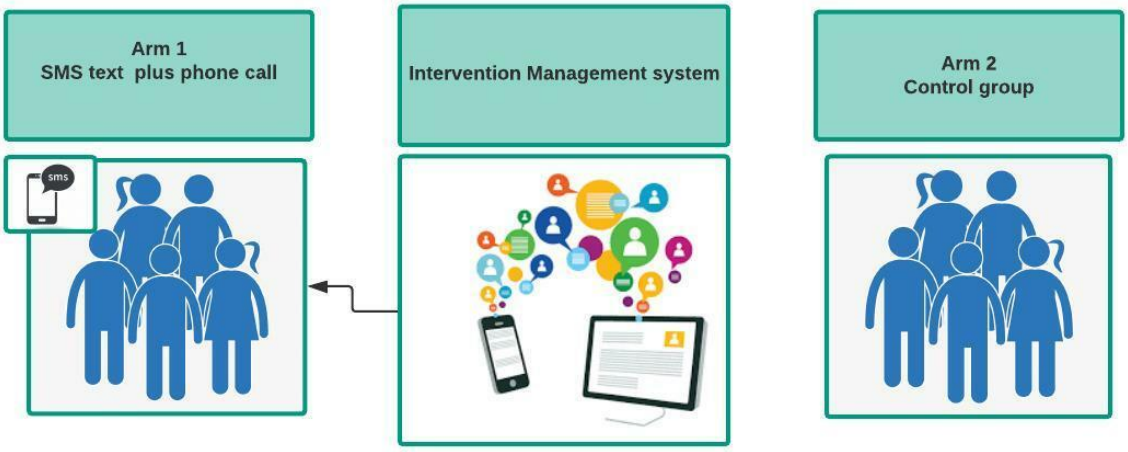

Figure 8: Mobile-assisted Medication Adherence Support (Ma-MAS) intervention trial design diagram

3.7.7. Control group

The control group (Arm-2) participants received the same routine standard treatment care as the intervention group but did not receive the SMS text and phone call intervention. Patients in the control group were followed for the same eight-week period as the intervention group during the continuation phase of the TB treatment (see Figure 8).

3.7.8. Intervention implementation

All patients assigned to any group received the same standard treatment care based on the Ethiopia national TB treatment guideline which is rifampicin, isoniazid, pyrazinamide and ethambutol for two months followed by rifampicin and isoniazid for four months.[168] Patients screening, enrolment, consenting and randomisation were undertaken by the research support team, who have health professional backgrounds. An open SMS automation software platform was used to store, monitor, and send SMS texts. SMS text traffic was managed and monitored in one centralised computer database server by trained IT personnel. The maximum size of an SMS text was not more than 160 characteristics. A weekly phone call was made to the intervention group participants from the health facility by a delegated person from the research team. This person was trained in TB clinical management. A checklist of questions was recorded each time the weekly phone calls were made to the participants. Both the SMS

text and Phone calls intervention were made using the national official language of Amharic. For participants who did not answer the phone calls, three repetitive attempts were made at five-minute intervals. All SMS texts and phone calls were delivered at a similar time between 7:30am to 8:00am at the average medication time. The message delivery reports were continuously monitored to ensure the participants received the SMS texts as planned. Participants were also asked whether they were receiving the SMS texts every week through phone calls and when they came for their medication refill visit. Participants were briefed about the duration, frequency, and timing of the SMS text and phone calls and advised to turn on their mobile phone in the morning. Participants were informed about the intervention and instructed not to tell and/or share the SMS texts or phone calls with other people. For participants who lost or changed their phone numbers, the new phone number was recorded immediately after they informed a support team member. The trial was audited on participant enrolment, consent, allocation, and during the intervention period.

3.7.9. Outcome measurement

The measured outcome of the trial is the medication adherence of the patient, measured by both direct and indirect methods. The primary outcome was measured using an IsoScreen test (GFC Diagnostics Ltd, Bicester, England) for the presence of isoniazid (INH) drug metabolites in urine in accordance with the vendor-supplied user manual. The IsoScreen test result is negative when there is no colour change (i.e., the strip remains yellow) after 5 minutes, and the test result is positive when the colour changes to dark purple, or blue/ green in that time, depending on the concentration of the medication (i.e., if the medication was taken in the last 24 hours or 48 hours respectively). The proportion of adherence measured by the IsoScreen test at the eighth week of the intervention (primary end point) was used as the primary interest of analysis.[88, 89] The proportion of adherence measured by the IsoScreen test at the fourth week of the intervention was used as the secondary interest of analysis.

For the secondary outcome of the trial, indirect methods of self-report medication adherence were used along with direct methods. The AIDS Clinical Trial Group adherence questionnaire (ACTG)[143] and Visual Analogue Scale (VAS) were used.[140] The adapted version of ACTG has three sections: section B (social support), section C (possible reasons for non-adherence) and section D (adherence behaviour). Participant scores less than "somewhat satisfied" to any questions in section B, or other than "never" to any questions in sections C and D were considered as non-adherence.[144] VAS is a single adherence scale that requires a patient to estimate their adherence level from 0% to 100%: 0% means the patient has taken no medication, 50% means the patient has taken half of their prescribed medications, and 100% means the patient has taken all of their prescribed medications, for the last 30 days. Participant scores less than 90% for VAS were considered as non-adherence.[83, 138] The ACTG and VAS questions were asked at the baseline assessment and at the end of eight weeks of intervention (see Figure 9). The difference in proportion of adherence measured by self-report from the baseline to the eighth week of the intervention was used as the secondary interest of analysis.

Study Period					
	Enrolment	**Allocation**	**Post-allocation**		**close-out**
Timeline	- t1	t_0	t_1	t_2	t_3
	Week 1	Week 12	Week 16	Week 20	week 21
Enrolment					
Eligibility screening	X	X			
Informed consent	X	X			
Allocation	X	X			
Intervention					
Daily SMS text			⟷	⟷	
Weekly Phone calls			⟷	⟷	
Assessment					
Baseline					
Socio-demographic	X	X			
Clinical characterstics	X	X			
Substance Use-related information	X	X			
Health Service-related information	X	X			
AIDS Clinical Trial Group adherence questionnaire (ACTG)	X	X			
Adherence measured by Visual Analogue Scales (VAS)	X	X			
Outcome					
Adherence measured by IsoScreen test				X	X
AIDS Clinical Trial Group adherence questionnaire (ACTG)					X
Adherence measured by Visual Analogue Scales (VAS)					X

Figure 9: Timeline for Ma-MAS intervention trial

3.7.10. Blinding

Single blind was applied to avoid bias in outcome measurement by differentiating the person who measures the outcome from the person who randomises and provides the intervention. Thus, in this study, the person who measured the outcome was blind to which group participants were assigned. Participants were not blinded to which group they were assigned, due to the nature of the trial intervention.

3.7.12. Data collection process

The research team was healthcare professionals who have a relevant Diploma and/or above higher degree. The research team were recruited for both data collection and supervision based on their previous experience. The data collectors and supervisors were recruited through the Addis Ababa Health Bureau, and they were responsible for managing any time allocation and remuneration impacts on their staff. The research team (intervention providers, data collectors and supervisors) was trained by the principal investigator for two days on the research procedures of the intervention, data collection, and the quality and security of the data as per the research protocol.

To ensure the quality of the data, the data collection instruments were pre-tested and appropriate corrections were made based on the pre-test result to ensure the accuracy and precision of the measurement.

Data collection was made after the patient received the routine DOT services in a separate room from the TB clinic room to ensure the confidentiality and privacy of the patient's information. The data was collected electronically using a smart mobile app by designing the questionnaire on Open Data Kit (ODK). To assess adherence status using the IsoScreen test a research support team member with a laboratory technology background collected samples of the urine and tested for the presence of Isoniazid metabolites in urine. The Ministry of Health laboratory facilities were used for this adherence assessment.

3.7.13. Data Analysis

The data gathered electronically was cleaned in Excel before being exported to STATA software version 16 for analysis. For continuous variables, descriptive statistics such as mean, standard deviation, median, and range were utilized, whereas for categorical variables, frequency and percentage were used. For binary variables, a chi-square test was employed, and for continuous variables, a student t-test was used to compare the background characteristics between the intervention and control groups participants.

All randomised individuals were subjected to an intention to treat (ITT) analysis based on their group. The intervention effect was analysed using a log binomial regression model with a 95% confidence interval. For primary outcome, multivariable log binomial regression model analysis was employed to adjust confounding factors in the statistical effect. A P-value of less than 0.05 was used as a cut-off point to show a statistically significant association between Ma-MAS intervention and medication adherence with a 95% confidence interval. The predicted probability of TB medication adherence was calculated by the intervention and control group and covariates after multivariable log binomial regression model analysis. For examining the effect of Ma-MAS intervention on self-reported adherence (secondary outcome) difference in difference statistical technique analysis model was used to calculate the difference of proportion of self-reported adherence from the baseline to the end of the intervention, between intervention and control group participants. A sensitivity analysis was performed by including missing and lost to follow-up patients in the analysis as the best and worst scenario cases of the outcome (see Appendix Seven).

3.8. Study four: Perceptions, experiences, and adoption intention

3.8.1. Unified theory acceptance and use of technology

Research has focused on the acceptance of an information system and information technology. There are numerous theoretical models to assess the acceptance and use of information systems/ technology.[169] After reviewing and synthesizing eight theoretical models, Venkatesh et al. (2003) proposed the unified theory acceptance and use of technology (UTAUT). The original constructs of UTAUT are effort expectancy, performance expectancy, social influence, and facilitating conditions (see Figure 10).[170] The Unified theory of acceptance and use of technology was applied to assess doctors' acceptance and usage of electronic medical records and found to be a useful model that predicted 44% variance in behavioural intention.[171] Another similar study found that the explanatory power to predict behavioural intention and usage of electronic medical records was 51.1% and 28.2%, respectively.[172]

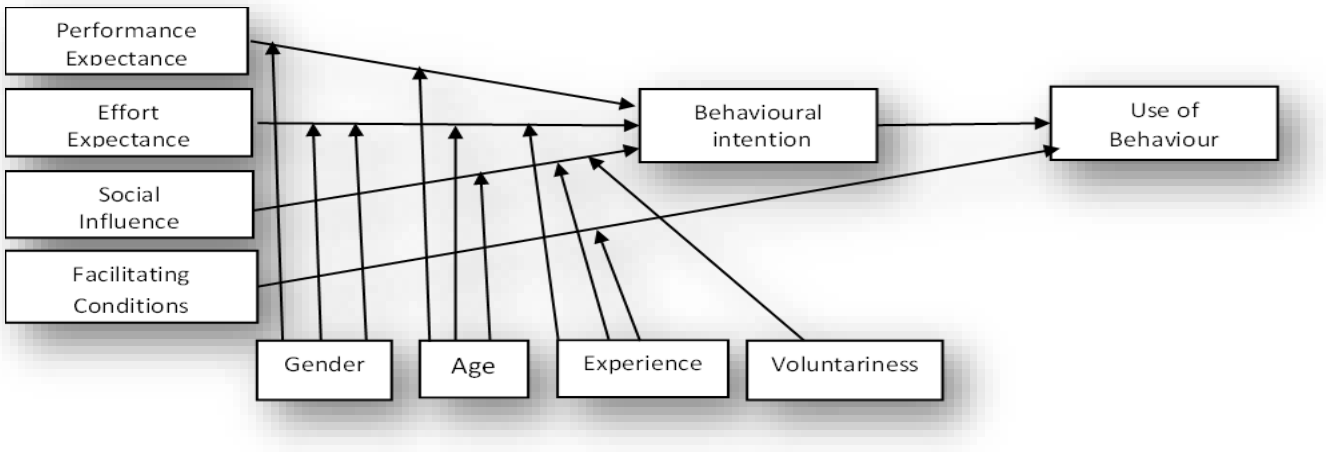

Figure 10: Unified theory of acceptance and use of technology adopted from Venkatesh et al. 2003. [170]

Recently the unified theory of acceptance and use of technology was updated by adding attitude construct into the original UTAUT(see Figure 11).[173] Attitude is included in UTAUT because it is regarded as significantly associated with the behavioural intention and use of information systems or information technology. The explanatory power improved when the attitude construct was added into the model: from 38% to 45% variance in behavioural intention, and from 21% to 27% in usage of behaviour. It was also observed that attitude has a direct effect on the information technology usage.[173] Thus, in this study the patient's intention to adopt mobile-assisted medication adherence intervention was assessed through using both the original and modified version of unified theory of acceptance and use of technology (see Table 7).

The current research utilized both the original and modified Unified Theory of Acceptance and Use of Technology (UTAUT) to assess which factors influence the adoption of the Ma-MAS intervention (see Figure 10 and 11).

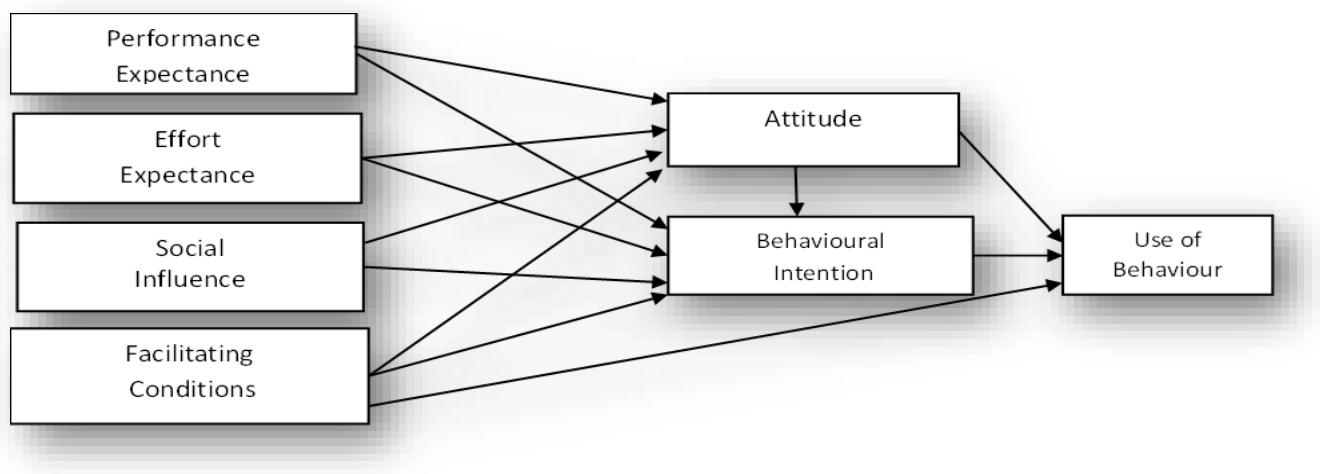

Figure 11: The modified Unified theory of acceptance and use of technology adapted from Venkatesh et al. (2003) and modified by Dwivedi et al. 2019 [173]

Table 7: Definition for UTAUT constructs used in the proposed theoretical model. source: Dwivedi et al. 2019 [173]

Construct	**Definition**
Performance expectancy (PE)	Performance expectancy is defined as “the degree to which an individual believes that using the system will help him or her to attain gains in job performance” (Venkatesh et al. 2003).[170]
Effort Expectancy (EE)	Effort expectancy is defined as “the degree of ease associated with the use of the system” (Venkatesh et al. 2003). [147]
Social influence (SI)	Social influence is defined as “the degree to which an individual perceives that important others believe he or she should use the new system” (Venkatesh et al. 2003). [147]
Facilitating conditions (FC)	Facilitating conditions are defined as “the degree to which an individual believes that an organizational and technical infrastructure exists to support use of the system” (Venkatesh et al. 2003). [147]
Attitude (AT)	Attitude defined as “an individual’s positive or negative feelings about performing the target behaviour” (Davis et al. 1989; Taylor and Todd 1995; Fishbein and Ajzen 1975).[174-178]
Behavioural Intention (BI)	Behavioural intention is defined as “a measure of the strength of one’s intention to perform a specific behaviour” (Fishbein and Ajzen 1975).[178]

3.8.2. Study design

A convergence mixed-methods design was employed to assess patients’ perceptions, experiences, and adoption intention of Ma-MAS intervention. Patients' perceptions, experiences, and adoption intention were assessed interpretively using qualitative descriptive approach. And for the purpose of assessing the factors associated with the intention to adopt the Ma-MAS intervention, a quantitative cross-sectional survey design was used. The data collection, analysis, and interpretation were undertaken separately, and the results were merged into the discussion.

3.8.3. Participants

To assess patients' perceptions, experiences, and intention to adopt mobile-assisted medication adherence support intervention, adult TB patients who received the Ma-MAS intervention for eight weeks were included for both interpretive and survey study. The interpretive and survey studies did not include participants who enrolled in the mobile-assisted adherence intervention but were lost to follow up or discontinued.

3.8.4. Sample size and technique

To assess factors associated with adoption intention (acceptance) of the Ma-MAS intervention, all patients who received daily SMS messages and weekly phone calls for eight weeks were invited to be part of the cross-sectional survey. For the post-intervention qualitative in-depth interviews, participants were randomly selected from each sub-city until idea saturation was reached.

3.8.5. Data collection instrument and process

An in-depth interview guide developed based on the research question, to assess the patients' perceptions, experiences, and intention to adopt mobile-assisted medication adherence support intervention. The in-depth interview guide and audio-recorder were used to collect the qualitative data. The principal investigator was conducted the in-depth interview at the convenient place and time for the patients.

To assess the adoption intention and associated factors, a data collection tool was adapted from similar literature based on the unified theory of acceptance and use of technology.[170, 179-181] It was originally developed in English and then translated into Amharic language by a professional linguist. This questionnaire consists of two sections: background characteristics (age, gender and education level) and items for the unified theory of acceptance and use of technology. In the proposed UTAUT model, 25 items were used to assess six constructs with two endogenous variables, attitude (AT) and behavioural intention (BI), and four exogenous variables namely performance expectancy (PE), effort expectancy (EE), social influence (SI),

and facilitating condition (FC). The construct items were measured using a five-point Likert scale, ranging from 1 for “strongly disagree” to 5 for “strongly agree”. Trained data collectors pretested the data collection instruments, and the data was subsequently gathered electronically using Open Data Kit (ODK).

3.8.6. Data analysis

Thematic analysis approach was employed for qualitative data.[182] First, all the in-depth interviews were transcribed verbatim by a professional translator and the consistency of transcription checked with audio record. The principal investigator read all transcriptions to familiarize themselves with the qualitative data before commencing coding. Nvivo software version 12 was used for coding and analysis of the qualitative data. Coding started with first level coding of broader domains. Under the broader domain an initial deductive coding was made based on the research question and the literature review. The second level domain open coding was done under the broader domain. New emerging concepts from the broader domain were also coded (inductive coding). All codes were reviewed, and similar codes were categorized to form themes and sub-themes. The characteristics of the theme, sub-theme and codes were reviewed. Themes, sub-themes, and codes were compared across all cases to confirm the qualitative data was correctly matched with each theme and sub-theme.[183] An interpretation of the data was made under each theme and sub-theme by the principal investigator and given to three other experts to review if the coding, categorization, analysis, and interpretation were appropriate (see Figure 12). In the report editing in the transcript is indicated by three full stops (…), reported speech indicated by inverted commas (“ ”) and strong feeling indicated by (!).[182]

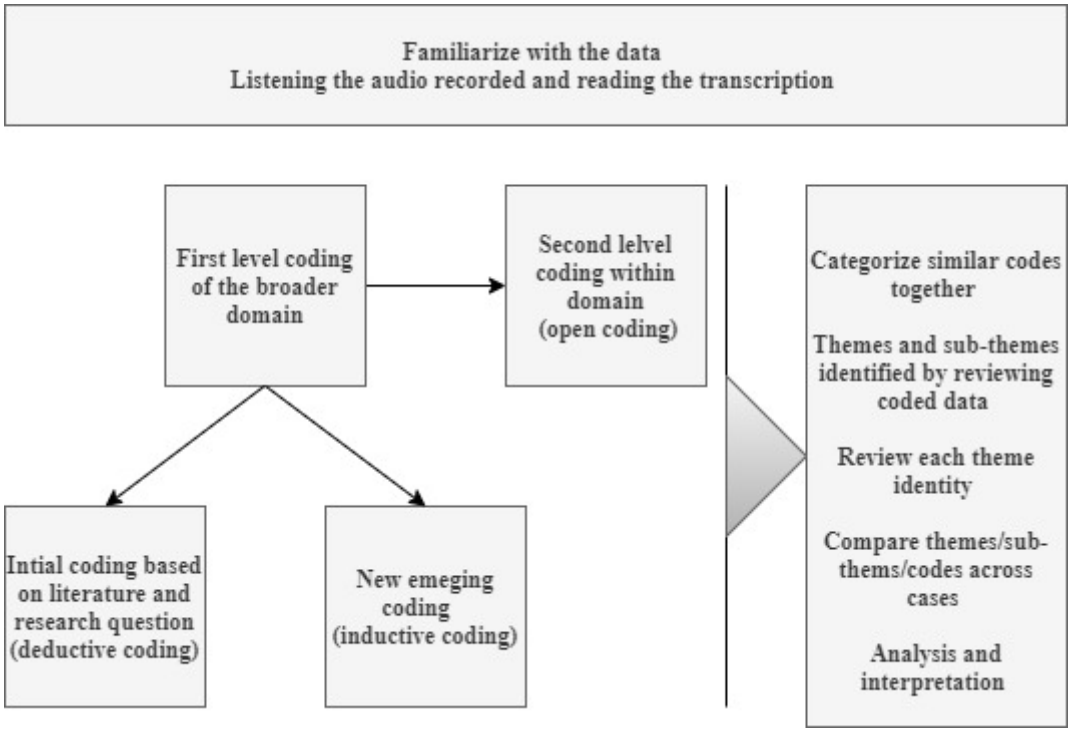

Figure 12: Schematic presentation of qualitative analysis adapted from Raskind et al. 2019[183]

Confirmatory factor analysis and structural equation modelling (SEM) were employed to assess the correlation between behavioural intention with constructs of attitude, performance expectancy, effort expectancy, social influence and facilitating conditions. A structural equation modelling analysis was employed using STATA software version 16. In order to check the construct validity and reliability of the UTAUT measurements model, convergent validity, discriminant validity, and internal reliability were evaluated using a variety of indices including factor loading weight, average variance extracted (AVE), square root of AVE, composite reliability (CR), and Cronbach alpha (α). As a standard criterion, AVE value over 0.5 was considered acceptable for convergent validity, and CR value always greater than over AVE value (AVE>0.5 and CR>AVE).[184, 185] A factor loading value of 0.5 and above was considered as practically significant to remain the item in the construct and is evidence of convergent validity.[186] Pearson correlational analysis was completed to examine the relationship between the constructs of unified theory of acceptance and use of technology and correlation coefficient and a value between 0.10-0.29 was considered week, 0.30-0.49

medium, and 0.5-1 a strong correlation.[185, 187] For acceptable standard of discriminant validity (DV), the square root of AVE of the construct must be greater the value of the correlation coefficient of the same construct with other constructs of UTAUT.[188] For acceptable construct reliability, the composite reliability (CR) and Cronbach alpha (CA) value of 0.70 and above was used as cut off point.[186]

The items under each construct were summed and analysed using structural equation modelling path analysis to test the statistically significant relationship between the constructs of UTAUT. The root mean square error of approximation (RMSEA) and the standardized root mean square residual (SRMR) were used to assess model fitness. RMSEA <0.06 and SRMR<0.08 were used as cut-off values for acceptable goodness of model fit for the standard modeling criteria.[189, 190] Additionally, comparative fit index (CFI) and Tucker–Lewis index (TLI) greater or equal to 0.95 were used as cut off point to accept the model.[186]

3.8.7. Trustworthiness of qualitative research

The trustworthiness refers to the level of confidence in data, interpretation, and methods used to assure the quality of the qualitative research.[191, 192] The trustworthiness of the qualitative research was examined according to Lincoln and Guba's (1985)[193] framework of quality criteria: credibility, dependability, confirmability and transferability. Authenticity, later added as additional criteria by Guba and Lincoln (1994) was also used.[194] These framework of quality criteria are considered a gold standard for quality assessment of interpretive research.[192]

3.8.7.1. Credibility

Credibility refers to the confidence that the findings are truthful and accurate for the participants and the context of the research.[192, 193] An adequate amount of time was allocated for each in-depth interview of participants to ensure the credibility of the qualitative data. Participants were interviewed in Amharic with open-ended guided questions which enabled them to clearly explain their perceptions and experiences. The principal investigator who undertook the interview had experience of qualitative research and the culture and language

of the area. The transcription, codes, analysis, and interpretation of the qualitative data were reviewed with three other experts. Data codes, analyses, and interpretations of qualitative data include both positive and negative findings, which are indicators of credibility. Member checking was not done, and participants were not able to receive verbatim transcriptions due to a shortage of time.

3.8.7.2. Dependability

Dependability refers to the stability of the data over time and over the phenomenon of the study.[191-193] The principal investigator verified the consistency of the recorded audio with the verbatim transcription in order to ensure the dependability of the qualitative data. For each in-depth interview case, the themes, sub-themes, and categories were cross-checked to ensure they were correctly matched. Additionally, three experts verified the accuracy of coding, analysis, and interpretation of the qualitative data.

3.8.7.3. Confirmability

Confirmability refers to the neutrality of the researcher or the degree to which findings are consistent and could be repeated by two or more independent people.[191-193] Participants' information should be represented in qualitative data, and the data interpretation should be free of researcher bias. In order to ensure the accuracy of qualitative data, an audit trial of the process which includes the verbatim transcription, coding, analysis and interpretation examined by three independent experts, and a review was completed with these experts.

3.8.7.4. Transferability

Transferability refers to the degree to which findings can be transferred to other persons in other settings.[191-193] Participants' characteristics and context can determine whether or not qualitative findings are transferable to other settings and people.[191, 195] In this research, details about the study participants, the study context including the health system and TB treatment care, and the study location are described. It is therefore possible to transfer the findings of the qualitative inquiry to other similar settings and more readily adapt the work to new settings.

3.8.7.5. Authenticity

Authenticity is the extent to which researchers depict the range of different participants' realities completely and fairly.[191, 192, 194] It is possible to ensure the authenticity of the study by selecting appropriate participants and samples, and using tick descriptions.[191] This study therefore draws an adequate sample of participants as recommended in the literature (idea saturation), which can represent a range of different experiences. Additionally, a tick description was made to record and consider the range of participants' experiences.

3.9. Ethical process

Research ethics approval was obtained from the Southern Adelaide Clinical Health Research Ethics committee (SAC HREC) of Flinders University. The proposal was also approved by the Addis Ababa Health Bureau Ethics Committee on August 21, 2020, with reference number A/A/H/930/227, and an official permission letter was provided from Addis Ababa Health Bureau to respective sub-city health facilities (see Appendix Eleven). A change in the trial protocol was submitted to SAC HREC and Addis Ababa Health Bureau ethics committee and was approved on April 7, 2021, before implementing the change. The trial design was modified from three groups to two groups, and the frequency of phone calls was changed from daily to weekly after conducting the needs assessment. This update has been reflected in the trial registration at https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=9729 and in the published trial protocol (see Appendix Eight).[155]

This study had no forms of inducement, or coercion and the study did not bring any risks or incur compensation in cash or kind. Each participant completed a written informed consent after being informed about the research objectives, procedures, anticipated risks, and benefits of the research before the start of data collection. All respondent's information was kept confidential. Participants had the right to withdraw from the study at any time should they feel uncomfortable, concerned or not able to continue.

To safeguard the security of the patient's information, all data was kept in a password protected database. At the completion of the study, the participant's phone numbers, and any other identification of the participants was deleted. Participants were asked clearly at the start of the intervention to report immediately any changes in their phone number and a prompt process was made to unsubscribe and replace the mobile phone numbers. Further detailed information is attached to the participant information sheet and consent form (see Appendix Ten). All data collection was done in accordance with the national Ministry of Health of Ethiopia recommendations for COVID-19 pandemic safety and precautions.

CHAPTER 4: RESULTS OF STUDY ONE: DEVELOPMENT AND VALIDATION OF MA-MAS INTERVENTION: AN MRC FRAMEWORK APPROCH

4.1. Introduction

This chapter presents the results of the systematic development and validation of the mobile-assisted medication adherence support (Ma-MAS) intervention for TB patients. The Ma-MAS intervention is developed using the Medical Research Council (MRC) framework with seven non-linear iterative phases that incorporate literature reviews, interpretive and empirical studies, and Delphi techniques. The details of each phase of intervention development are presented in the method section of this thesis. The Ma-MAS intervention consists of two parts: phone call and SMS text message. The phone call intervention was designed to support the SMS text messages in Ma-MAS intervention. The phone call discussions were based on a guided checklist of questions, which is found in the Appendix Five. This chapter will focus on the final results of the SMS text messages development and validation.

4.2. SMS text messages development

Initially, 57 prototype SMS text messages were drafted using the IMB model and behavioural change techniques. The set of prototype SMS text messages was prepared based on a review of factors that influence TB medication adherence in the local context, a review of relevant facts and guidelines, and the input of experts and patients using behavioural change techniques and the IMB model (see Table 8 and Figure 13).

Table 8: Development and validation process of SMS text messages

	Purpose	**Results**
Drafting SMS text messages	To draft prototype SMS text messages	57 prototype SMS text messages were drafted
Content validation	To validate SMS text messages content	
Delphi round one	To evaluate the content of prototype SMS text messages and prepare additional text messages if necessary	Additional 13 SMS texts were added by senior experts and several SMS text contents was modified as per experts' opinions
Delphi round two	To rate the relevance of the SMS text messages	70 SMS texts were rated by 8 senior experts, and low rated SMS text messages were improved but no SMS message was dropped in this round
Delphi round three	To reach on consensus on qualified SMS text messages rating	70 SMS texts rated by 8 senior experts the second time and 40 SMS texts messages were qualified to next round
Delphi round four	To evaluate the SMS text messages at the ground level	40 SMS texts messages were evaluated by 44 health professionals and all SMS texts messages were qualified

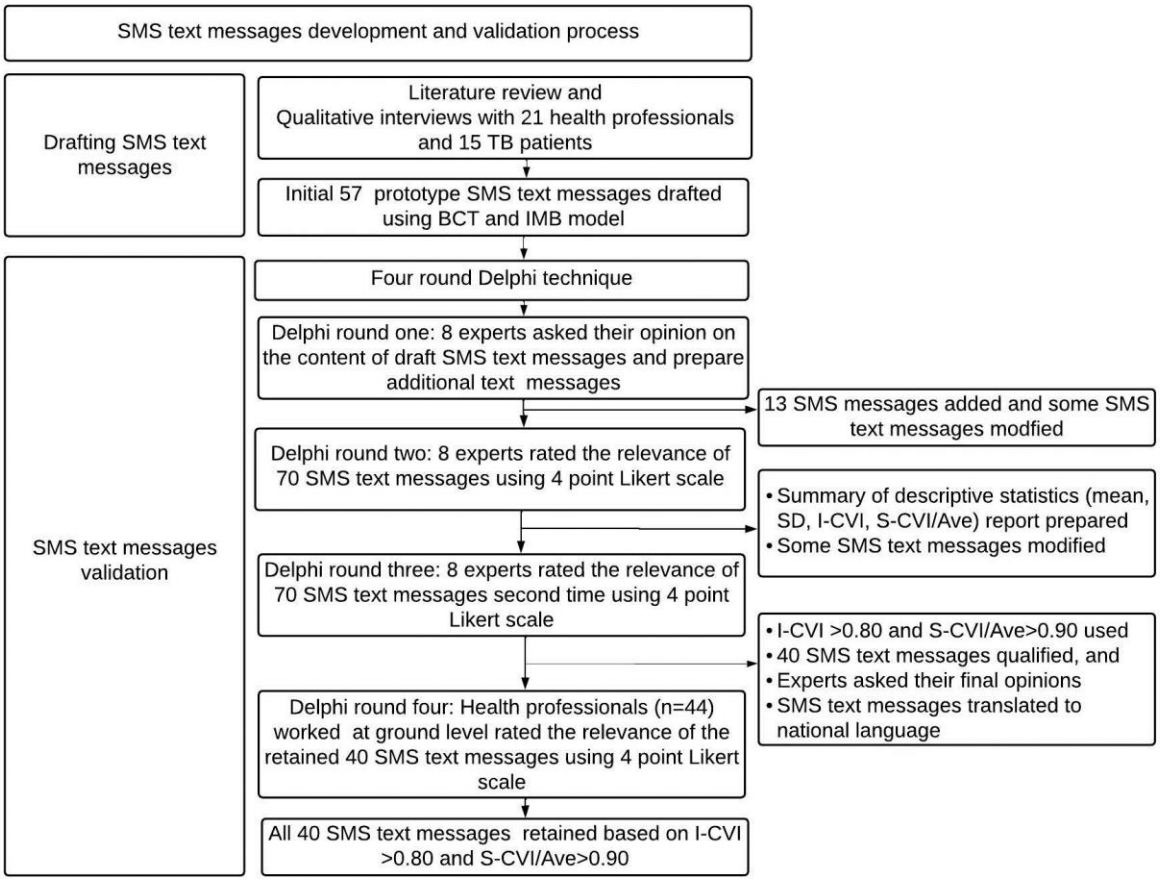

Figure 13: SMS text messages development and validation process

4.3. Demographic characteristics

Eight senior experts (1 female and 7 males) with expertise in behavioural science, health care systems, digital health, information technology, public health and pulmonary diseases participated in the SMS text message validation.

A total of 44 health professionals working at the health facility and health office completed the relevance rating for SMS text messages, with a response rate of 93.6% (44/47). The majority of respondents (61.4%) were females. The health professionals' age was between 18 and 35 years. Three quarters of the health professionals worked as TB focal person in the service delivery point of a health facility (See Table 9).

Table 9: Demographic characteristics of health professionals participated in SMS text messages validation, Addis Ababa, Ethiopia

Variables	Frequency	Percentage
Gender	**n=44**	**n=44**
Male	17	38.6%
Female	27	61.4%
Age (year)	**n=44**	**n=44**
18-35	29	66%
36-55	14	31,8%
Above 55 years	1	2.2%
Job position	**n=44**	**n=44**
TB focal person	33	75%
TB experts	11	25%
Institution	**n=44**	**n=44**
Health facility	33	75%
Health Office	11	25%
Education level	**n=44**	**n=44**
Diploma	8	18.2%
Bachelor's Degree	30	68.2%
Master's degree	6	13.6%

4.4. SMS text messages validation

In the first round of Delphi, 7 of 8 senior experts completed the tasks of qualitative evaluation of the prototype SMS text messages which was 88% of response rate. The experts prepared 13 additional text messages, adding to the first draft text messages. The experts also gave their opinions to improve several of the prototype the SMS text messages in accordance with the behavioural change techniques definition and IBM model. Thus, the SMS text messages were modified according to the experts' suggestions before the second-round quantitative rating.

Eight senior experts rated the relevance of 70 SMS text messages in the second Delphi round, and 38 (54.3%) SMS text messages were rated as 3 'quite relevant' or 4 'highly relevant' by more than 88% of the experts (I-CVI=0.88). A scale-level content validity index (S-CVI/Ave) of 81.6% was obtained for an overall score and all experts (n=8) agreed that 19 text messages contained relevant information based on the scale-level content validity index of expert agreement (S-CVI/UA) which was 27% of the total SMS text messages. Thirty-two (45.7%) SMS text messages were below the minimum acceptable item-level content validity index (I-

CVI<0.80), but no SMS text message was dropped in the second round Delphi. The low-rated I-CVI SMS text messages were modified before the third round (See Appendix Three).

In the third Delphi, 8 senior experts reviewed the summary statistics report of the second round. The individual expert's rating was not included in the summary report (anonymous). The experts rated the SMS text messages for the second time with the same rating criteria. In this round, 88% of experts (I-CVI=0.88) rated 40 SMS texts (57%) as 3 'quite relevant' or 4 'highly relevant'. Based on the acceptable standard content validity index (I-CVI≥0.80), decision was made to retain 40 SMS text messages for the next round. The scale level content validity index (S-CV/Ave) for these 40 SMS texts was 94.6%, which was higher than the minimum suggested score of 90%. A scale level content validation index of universal agreement (S-CV/UA) of 21 (52.5%) was obtained for the retained SMS text messages, indicating that all experts (100%) agreed that the 21 SMS texts were relevant for TB medication adherence promotion, as they were rated 3 'quite relevant' or 4 'highly relevant' (Table 10). Experts were informed of the final retained SMS text messages and final quality improvements were made.

In the fourth round Delphi, 44 of 47 invited health professionals rated the relevance of 40 SMS text messages. The item-level content validity for 40 SMS text messages was over 0.84, meaning that the item-level content validity fulfills the acceptable standard of 80%. Based on these 40 SMS texts, the scale level content validity index was 94.3%. According to the S-CV/UA index of universal agreement (S-CV/UA), 17.5% (7/40) of the retained SMS text messages were rated as relevant for TB medication adherence promotion by all experts (n=44). These SMS texts were rated 3 'quite relevant' or 4 'highly relevant' by all experts (see Table 10).

Table 10: Validated SMS text messages for promoting TB medication adherence

S.NO	BCT	SMS text messages English Version	Experts rating at the 3rd round (n=8)			Health professionals rating at the 4th round (n=44)		
			No. of agreement	CVI	UA	No. of agreement	CVI	UA
1	Goal setting (Behaviour)	A person infected with TB must take their medications every day at a regular time for at least six months to be cured. Please plan to take all your medications with no interruptions.	7	0.88	0	44	1	1
2	Problem-solving	Why do some patients forget to refill their medication? You can come to refill any time before you run out of medications. Keep your calendar card in a place where you can see it.	7	0.88	0	43	0.98	0
3	Problem-solving	Please ask your family member to pick up your medications for you if you are not able to come to the clinic to refill your medications.	8	1	1	42	0.95	0
4	Goal setting (outcomes)	If you want to be fully cured from TB, you must take all your medications for at least six months. Please do not forget to come to refill your medication supply.	8	1	1	44	1	1
5	Discrepancy between current behaviour and goal	Consider some form of self-tracking such as a medication calendar to mark the number of consecutive days that you are adhering. How many days in a row have you taken your medication as prescribed?	7	0.88	0	37	0.84	0
6	Behavioural contract	Every day when you wake up in the morning, remember to take your medication before your breakfast. Consider asking a family member to remind you.	7	0.88	0	41	0.93	0
7	Commitment	For how many days have you correctly taken your medication as prescribed? To be cured from TB, you must take all your medications for at least six months.	7	0.88	0	42	0.95	0
8	Feedback and monitoring	Thank you for picking up your medication as per your scheduled date. Keep it up, and take your daily medication as directed.	8	1	1	42	0.95	0

9	Self-monitoring of behaviour	Plan ahead to visit the health facility to refill your medication supply. Use a calendar card to check off the days when you have taken your medicine.	8	1	1	37	0.84	0
10	Feedback on outcome(s) of behaviour	Do you know that those who adhere will have a better chance to be cured? If you missed any dose of TB medications, please tell the healthcare provider.	8	1	1	41	0.93	0
11	Practical	Please tell the healthcare provider if you are traveling somewhere away from home. They can give you extra medications or link you with another healthcare worker, so you will not run out of medications	8	1	1	44	1	1
12	Practical	Please tell us if you are feeling ill while you are on your medications. Ask the healthcare provider about the common side effects.	7	0.88	0	44	1	1
13	Emotional	Your health status is our priority. Please Keep in touch with your healthcare provider and family support team for help when needed.	7	0.88	0	39	0.88	0
14	Instruction on how to perform a behaviour	It is common to experience some side effects while you are taking TB medication. Please tell to your healthcare provider if you experience mild side effects.	8	1	1	41	0.93	0
15	Information about Antecedents	People tend to forget to take their medications when they are away from home. Please remember to have an adequate amount of medications with you when you are away from home.	8	1	1	43	0.98	0
16	Information about Antecedents	TB can be cured in almost all cases by taking the medications as prescribed without interruption.	8	1	1	42	0.95	0
17	Information about Antecedents	Some patients will stop taking TB medications when they experience side effects. Please tell the health care provider if you have any side effects.	8	1	1	42	0.95	0

18	Reattribution	Please remember that TB bacteria die very slowly. Simply because you are feeling well does not mean you have been cured. You must maintain regular treatment for at least 6 months to be cured.	8	1	1	44	1	1
19	Information about Health consequences	Be aware that if you are unable to adhere to TB medication regularly as directed, this can lead to failed treatment, relapse, and multidrug resistance.	8	1	1	42	0.95	0
20	Salience of consequences	A person with TB who takes all the medications as directed will be cured and will not be a risk of TB transmission to his/her family and other communities.	8	1	1	42	0.95	0
21	Information about social and environmental consequences	Untreated TB can be transmitted to close family members, friends and other people. Please take your medications until the end of the treatment period as per prescription.	8	1	1	43	0.98	0
22	Monitoring of Emotional consequences	Did you take your medications at the same time every day? If you did, congratulations! If you didn't adhere, try again, but tell your healthcare provider the doses that you missed.	8	1	1	40	0.91	0
23	Anticipated regret	Do you know that if TB treatment fails, you will become sick again, and you may transmit TB to loved family members and friends? Treatment fails if a patient is not adhering to medications.	8	1	1	40	0.91	0
24	Self-assessment of affective consequences	Imagine what you would feel if you had a multi-drug resistant TB because of non-adherence to medications. It would need long-term treatment and may not ever be cured.	7	0.88	0	41	0.93	0
25	Demonstration of the behaviour	Consider using a strategy like setting an alarm in your mobile phone, or tell a family member to remember your daily TB medication and refill visit schedule.	8	1	0	42	0.95	0
26	Prompts/Cues	You must decide the first task in the morning is always to take your daily medication. Keep taking your daily medications at the same time every day as directed.	8	1	1	41	0.93	0

27	Cue signalling reward	Good morning! Before you eat your breakfast, please take your daily medication.	8	1	1	42	0.95	0
28	Remove access to the reward	Cigarette smoking during TB treatment can lower your treatment success. Avoid people or places that make you want to smoke as much as possible.	7	0.88	0	44	1	1
29	Associative learning	Some patients take their medication in the morning immediately after they wash their faces. Keep taking your daily medication.	7	0.88	0	37	0.84	0
30	Behavioural practice/rehearsal	Please remember to take your medication regularly every day at the same time. Please keep your medications in a safe place where you can see it.	7	0.88	0	42	0.95	0
31	Habit formation	Please take your medications every day at the same time in the morning. This helps you to remember to take your medications regularly.	7	0.88	0	40	0.91	0
32	Generalization of target behaviour	Please keep taking your daily medications regularly until the end of your treatment. TB is a curable disease if you are fully adhering to treatment.	7	0.88	0	39	0.89	0
33	Social reward	Thank you for picking up your medications. Please remember to take your daily medications at the same time every day.	7	0.88	0	43	0.98	0
34	Future punishment	Do you know that non-adherence to medications may cause multi-drug resistant TB that may need complex treatment for a long time, has more side effects, and may not work or allow you to be cured	8	1	1	42	0.95	0
35	Avoidance/reducing exposure to cues for the behaviour	Please remember to keep your medications with you anytime when you are away from home.	8	1	1	43	0.98	0
36	Avoidance/reducing exposure to cues for the behaviour	Please remember to avoid alcohol and smoking that will affect your TB treatment success.	8	1	1	44	1	1
37	Body changes	You will gain body weight and become healthy if you appropriately adhere to your TB medications and lead a healthy lifestyle.	7	0.88	0	42	0.95	0

38	Identification of self as role model	Be a role model and save others from TB transmission by fully adhering to your TB medications regularly to the end of treatment.	7	0.88	0	41	0.93	0
39	Verbal persuasion about capability	You have the capacity to fully adhere to all your TB medications every day to be cured. Yes, you can do it!	7	0.88	0	40	0.91	0
40	Mental rehearsal of successful performance	Imagine that you can remember to take your daily TB medications to the end of treatment. Your imagination will become true!	7	0.88	0	39	0.89	0
S-CVI/Ave by expert rating (n=8) = 0.946 S-CVI/UA by experts (n=8)=0.525 S-CVI/Ave by Health professionals rating (n=44) =0.943 S-CVI/UA by Health professionals rating (n=44) =0.175								

BCT: Behaviour change technique[158], CVI: content validity index , UA: Universal agreement

CHAPTER 5: RESULTS OF STUDY TWO: FEASIBILITY AND ACCEPTABILITY OF Ma-MAS INTERVENTION

5.1. Introduction

In this chapter, the results of a cross-sectional survey evaluating the feasibility and acceptability of mobile-assisted medication adherence support (Ma-MAS) intervention for TB patients are presented. To determine the feasibility of Ma-MAS intervention, participants' access to mobile phones and their digital literacy for using SMS text messages and phone calls was assessed. Additionally, the acceptability of Ma-MAS was evaluated by asking participants whether they would be willing to receive SMS text message and phone call to support their TB medication adherence and routine attendance at clinic appointments.

5.2. Demographic characteristics

In total, 416 participants participated in the study, with 98.6% responding. More than half (54.3%) were males. The median age of the participants was 30 years old. Among the participants, 199 (47.8%) were never married, while 187 (45.0%) were married. Most participants were educated, only 15% of participants did not have a formal education. Occupationally, participants were daily laborers (20.4%), government employees (13.2%), unemployed (13%), merchants (12.5%), and housewives (11.8%). The median number of family members in the household was 3, and 19% of participants lived alone. At the time of the study, 176 (42.3%) participants had a monthly income below the poverty level, which was 2373 Ethiopian Birr, or less than 57 US dollars. The majority of participants (53.8%) walked to the health institution for treatment and medication refills (see Table 11).

Table 11: Socio-demographic characteristics of adult TB patients, Addis Ababa, Ethiopia

Variables	**Frequency (percent)**
Gender	**n=416**
Male	226 (54.3%)
Female	190 (45.7%)
Marital status	**n=416**
Never married	199 (47.8%)
Married	187 (45.0%)
Divorced	19 (4.6%)
Widowed	11 (2.6%)
Educational level	**n=416**
No formal education	62 (14.9%)
Primary education (1-8 grade)	123 (29.6%)
Secondary education (9-10 grade)	86 (20.7%)
Technical/Vocational education (11-12 grade)	48 (11.5%)
Higher education (above 12 grade)	97 (23.3%)
Occupational status	**n=416**
Daily laborer	85 (20.4%)
Governmental employee	55 (13.2%)
Unemployment	54 (13.0%)
Merchant	52 (12.5%)
Housewife	49 (11.8%)
Student	41 (9.9%)
Driver	20 (4.8%)
Private employee	18 (4.3%)
Pensioner	12 (2.9%)
Guard	10 (2.4%)
Other*	20 (4.8%)
Family size	**n=416**
Living alone	79 (19.0%)
2-3 people	155 (37.3%)
4-5 people	120 (28.8%)
6 and above people	62 (14.9%)
Monthly income in ETB (USD)	**n=416**
Less than 2373 (57$)	176 (42.3%)
2373 (57$) and above	240 (57.7%)
Transportation used to reach the health facility	**n=416**
Walk	224 (53.8%)
Taxi	148 (35.6%)
Bajaj	32 (7.7%)
Bus/Public transport	9 (2.2)
Other**	3 (0.7%)

*Farmer, House Servant, Cleaner, Mechanics, Non-governmental employee, Barberry, Volunteer worker
**Personal care, Bicycle/Motor bicycle
ETB: Ethiopia Birr, USD: United States Dollar, ETB to USD exchange was made based on the data collection time conversion rate.

5.3. Clinical characteristics

A total of 254 (61%) participants had pulmonary TB, with 176 (42.3%) participants having smear-positive pulmonary TB and 78 (18.8%) participants having smear-negative pulmonary TB. Overall, 371 (89.2%) of the participants were newly diagnosed with TB, and 10% had relapsed TB. Among the total participants, 78 (18.8%) had TB-HIV co-infection, 11 (2.6%) had TB-diabetes, and 12 (2.9%) had TB-hypertension (see Table 12).

Table 12: Clinical characteristics of adult TB patients, Addis Ababa, Ethiopia

Variables	**Frequency (percent)**
Type of TB and AFB sputum smear positivity	**n=416**
Smear positive pulmonary TB	176 (42.3%)
Smear negative pulmonary TB	78 (18.8%)
Extra pulmonary TB	162 (38.9%)
History of TB	**n=416**
New case	371 (89.2%)
Relapsed	42 (10.1%)
Treatment failure	3 (0.7%)
TB-HIV co-infected	78 (18.8%)
Non-communicable disease	**n=416**
Diabetes	11 (2.6%)
Hypertension	12 (2.9%)
Other*	22 (5.3%)

*Allergic, Asthma, Gastritis, mental illness, Anemia, Liver disease, and kidney disease, AFB: Acid-Fast Bacillus tests

5.4. Feasibility of Ma-MAS intervention

In total, 368 (88.5%) of the participants had their own mobile phones. Two hundred (54.3%) of the participants with their own mobile phones have smartphones that can install and run applications. Of the total participants, 368 (76.4%) had a trusted family member or caregiver in the household with access to a mobile phone. Of the participants who did not have their own mobile phones, 30 (62.5%) had access to a mobile phone through a family member or caregiver in the household. Only 18 (4.3%) of the participants did not have their own mobile phone and did not have access to a mobile phone through a family member or caregiver in the household. The demographic characteristics of participants who did not have their own mobile phone is presented in the Appendix Six.

Participants were confident in their ability to receive and open (81.3%), read (82.7%), and send (80.0%) SMS text messages using their mobile phones. Three hundred and seventy-three (89.7%), 341(82.0%), and 329(79.1%) were likewise confident in using a mobile phone to make a phone call, please call me and set a reminder, respectively (see Table 13).

Table 13: Feasibility of mobile-assisted medication adherence support among adult TB patients, Addis Ababa, Ethiopia

Variables	Response	Frequency (percent)
Having own mobile phone (n=416)	Yes	368 (88.5%)
	No	48 (11.5%)
Type of mobile phone (n=368)	Smart phone (can install and use applications)	200 (54.3%)
	Basic phone (can only use for voice and text message)	168 (45.7%)
A trusted family or caregiver have mobile phone (n=416)	Yes	318 (76.4%)
	No	98 (23.6%)
Confident to use a mobile phone (n=416)	to receive and open an SMS text message	388 (81.3%)
	to read an SMS text message	344 (82.7%)
	to send an SMS text message	333 (80.0%)
	to make a phone call	373 (89.7%)
	to set a reminder	329 (79.1%)
	to send a “please call me”	341 (82.0%)

5.5. Acceptability of Ma-MAS intervention

Among those with their own mobile phones, 344 (93.5%) participants had a willingness to receive SMS text messages for medication reminders, and 339 (92.1%) participants had also willingness to receive SMS text messages for clinic appointments. Also, the majority of participants with their own mobile phones were willing to receive a phone call reminding them to take their medication (90.8%) and attend clinic appointments (93.25%).

Two hundred eighty-five (89.6%) and 287 (90.3%) participants were willing to receive SMS text messages for medication intake and clinic appointments reminders, respectively, through family member's or caregiver's mobile phone. Through a family member’s or caregiver’s mobile phone, participants were willing to receive phone calls for medication intake (89.3%) and clinic appointments (89.9%) reminders (see Table 14).

Of the participants who did not have their own mobile phones but had access to a mobile phone through a family member or caregiver in the household (n=30), 26 (86.7%) and 28 (93.3%) were willing to receive SMS text messages for medication intake and clinic appointment reminders, respectively, through a family member's or caregiver's mobile phone. Similarly, of the participants who did not have their own mobile phones but had access to a mobile phone through a family member or caregiver in the household (n=30), 27 (93.0%) of participants were willing to receive phone calls for medication intake and clinic appointment reminders.

Table 14: Acceptability of mobile-assisted medication adherence support (Ma-MAS) among adult TB patients, Addis Ababa, Ethiopia

Variables	**Response**	**Frequency (percent)**
Willing to receive SMS reminder (n=368)	for medication intake	344 (93.5%)
	for clinic appointments	339 (92.1%)
Willing to receive a phone call reminder (n=368)	for medication intake	334 (90.8%)
	for clinic appointments	343 (93.2%)
Willing to receive SMS reminder on shared trusted family member's mobile phone (n=318)	for medication intake	285 (89.6%)
	for clinic appointments	287 (90.3%)
Willing to receive a phone call reminder on shared trusted family member's mobile phone (n=318)	for medication intake	284 (89.3%)
	for clinic appointments	286 (89.9%)

CHAPTER 6: RESULTS OF STUDY THREE: EFFECTIVENESS OF Ma-MAS INTERVENTION

6.1. Introduction

In this chapter, the results of a randomised controlled trial evaluating the effectiveness of a mobile-assisted adherence support (Ma-MAS) intervention for TB medication adherence are presented. The study included two groups of participants: the Ma-MAS group and the control group. Participants in the Ma-MAS group received daily SMS text messages and weekly phone calls for eight weeks during the continuation phase of TB treatment, in addition to standard care. The control group received only the standard care for TB treatment, without the Ma-MAS intervention.

6.2. Background

A total of 206 adult TB patients were screened using the eligibility criteria to obtain 186 eligible participants. Twenty participants were dropped from the study; 18 did not meet the eligibility requirements, and two patients declined to participate. The 186 eligible individuals were randomly assigned to one of the two groups: Ma-MAS group or control group, with 93 participants in each group. Two participants from the Ma-MAS and control groups were lost to follow-up before the fourth week because their treatment care was transferred to other healthcare facilities, and in the same follow-up period one additional participant from the Ma-MAS group was discontinued because of death. Two participants from the Ma-MAS group and one from the control group were lost from the follow-up because they were unable to travel to the clinic for IsoScreen urine test at the end of eighth week of follow-up. The resulting loss to follow-up rate was 5.4% and 3.2% in the Ma-MAS and control groups, respectively. After eight weeks of follow-up, a total of 88 participants in the Ma-MAS group and 90 participants in the control group completed the study (see Figure 14).

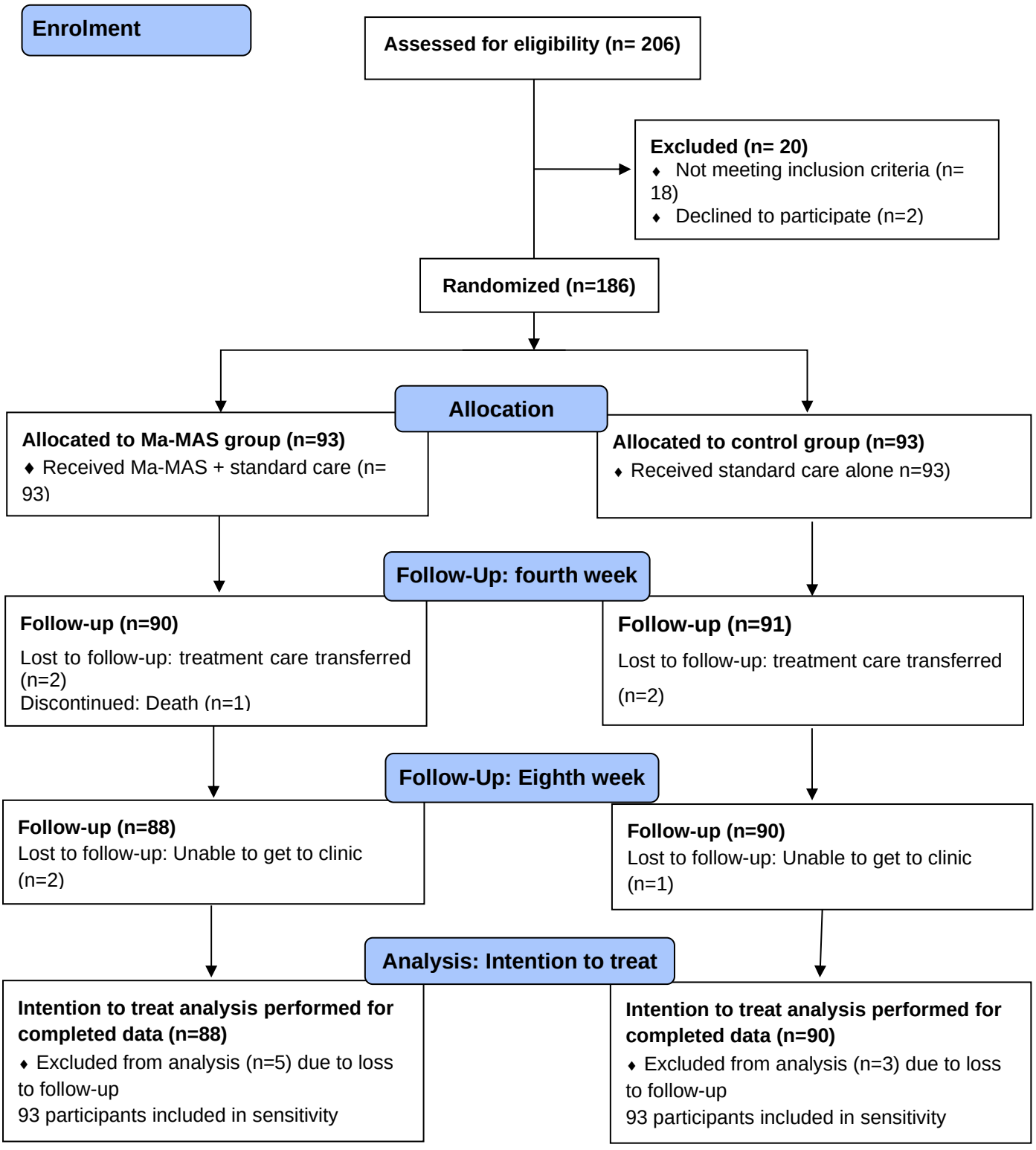

Figure 14: Ma-MAS trial flow diagram (adapted from CONSORT 2010)[196]

A total of 56 SMS text messages and 8 phone call reminders were sent to the participant during 8 weeks of Ma-MAs intervention. Of the total 5,208 SMS texts sent and 744 phone calls made for participants of intervention group during 8 weeks, 99% of the SMS text and 85.4% of the phone calls were successfully delivered to the recipients.

6.3. Demographic characteristics

Fifty-five (59.14%) of the Ma-MAS and 51 (54.84%) of the control group were males. The median age of patients in both Ma-MAS and control group was 28. Forty-four (47.3%) of the Ma-MAS group and 54 (58.0%) of the control group patients had never married. Thirty-nine (41.9%) of the Ma-MAS and 21 (22.5%) of the control group patients had attended elementary school (1–8), whereas 9 (9.6%) of the Ma-MAS and 17(18.2%) of the control group patients had attended secondary school (11-12 grade) (see Table 15).

Table 15: Demographic characteristics of adult TB patients enrolled in Ma-MAS trial, Addis Ababa, Ethiopia

Variables	**Ma-MAS group n=93**	**Control group n=93**	**P value**
Gender			
Male	55 (59.14%)	51 (54.84%)	0.554
Female	38 (40.86%)	42 (45.16%)	
Age in years			
Mean (Sd)	32.11 (11.24)	31.26 (11.07%)	0.6045
Median (IQR)	28 (14)	28 (15)	
Marital status			
Never Married	44 (47.31%)	54 (58.06%)	0.165
Married	40 (43.01%)	35 (37.63%)	
Divorced/separated	8 (8.60%)	3 (3.23%)	
Widowed*	1 (1.08%)	1 (1.08%)	
Educational status			
No formal Education	3 (3.23%)	7 (7.53%)	0.043**
1-8 grade	39 (41.94%)	21 (22.58%)	
9-10 grade	17 (18.28%)	19 (20.43%)	
11-12 grade	9 (9.68%)	17 (18.28%)	
Above 12 grades	25 (26.88%)	29 (31.18%)	

*Widowed merged with divorced/separated for chi square test. ** P value statistically significant (P value<0.05), sd: standard deviation IQR: Interquartile range

6.4. Socio-economic characteristics

Nineteen (20.4%) patients in both Ma-MAS and control groups worked in a government organization, whereas 14 (15.0%) of the Ma-MAS and 17 (18.2%) of the control group patients were unemployed. Thirty-five (37.63%) patients in both Ma-MAS and control groups were identified as living below the poverty level ($57 or 2738 ETB). The majority of patients, 78 (83.87%) of the Ma-MAS and 76(81.72%) of the control group, reported they had access to adequate food. Seventeen (18.2%) of the Ma-MAS and 9 (9.6%) of the control group patients had received food support from any sources. More than three-fourths of patients in both Ma-MAS and control groups had received a reminder from families or caregivers for medication intake and clinic appointments. A few patients, 10(10.7%) of the Ma-MAS and 12(12.90%) of the control group, had experienced stigma and discrimination related to their disease diagnosis (see Table 16).

Table 16: Social and economic characteristics of adult TB patients enrolled in Ma-MAS trial, Addis Ababa, Ethiopia

Variables	Ma-MAS group (n=93)	Control group (n=93)	P value
Occupation			
Governmental	19 (20.43%)	19 (20.43%)	0.826
Daily laborer	19 (20.43%)	15 (16.13%)	
Housewife	14 (15.05%)	10 (10.75%)	
Merchant	11 (11.83%)	8 (8.60%)	
Student	6 (6.45%)	8 (8.60%)	
Unemployment	14 (15.05%)	17 (18.28%)	
Other*	6 (6.45%)	10 (10.75%)	
Monthly family Income ETB (USD)			
Less than 2738 (57$)	35 (37.63%)	35 (37.63%)	1.0
2738 (57$) and above	58 (62.37%)	58 (62.37%)	
Mean (Sd)	3900 (3266.49)	4090.32 (3341.14)	0.6949
Median (IQR)	3000 (3000)	3000 (3000)	
Access to adequate food			
Yes	78 (83.87%)	76 (81.72%)	0.698
No	15 (16.13%)	17 (18.27%)	
Food support (any source)			
Yes	17 (18.27%)	9 (9.68%)	0.091
No	76 (81.72%)	84 (90.32%)	
Financial support (any source)			
Yes	14 (15.05%)	11 (11.83%)	0.519
No	79 (84.95%)	82 (88.17%)	
Family number per household			
Living alone	15 (16.13%)	27 (29.03%)	0.123
2-3	42 (45.16%)	30 (32.26%)	
4-5	30 (32.26%0	28 (30.11%)	
6 and above	6 (6.45%)	8 (8.60%)	
Family or caregivers remind to take the medication			
Yes	75 (80.65%)	71 (76.34%)	0.475
No	18 (19.35%)	22 (23.66%)	
Family or caregivers remind to clinic appointments			
Yes	77 (82.80%)	73 (78.49%)	0.458
No	16 (16.20%)	20 (21.51%)	
Stigma and discrimination			
Yes	10 (10.75%)	12 (12.90%)	0.650
No	83 (89.25%)	81 (87.10%)	

*Guard, self-employment, Barbery, House renter, and Farmer

ETB: Ethiopia Birr, USD: United States Dollar, ETB to USD exchange was made based on the data collection time conversion rate, sd: standard deviation, IQR: Interquartile range

6.5. Substance use chracteristics

Twenty-one (22.5 %) of the Ma-MAS and 26 (27.9%) of the control group patients had ever consumed alcohol. Few patients, 7.53% of the Ma-MAS and 6.45% of the control group, had ever smoked. When compared to the control group, the proportion of ever khat chewing in the Ma-MAS group (10.7%) was lower (27.9%), which was statistically significant. There was also a statistically significant difference between Ma-MAS and control groups in the proportion currently chewing khat (see Table 17).

Table 17: Substance use characteristics of adult TB patients enrolled in Ma-MAS trial, Addis Ababa, Ethiopia

Variables	**Ma-MAS group n=93**	**Control group n=93**	**P value**
Ever drank alcohol			
Yes	21 (22.58%)	26 (27.96%)	0.399
No	72 (77.42%)	67 (72.04%)	
Current drink alcohol			
Yes	10 (10.75%)	14 (15.05%)	0.382
No	83 (89.25%)	79 (84.955)	
Ever smoke cigarette			
Yes	7 (7.53%)	6 (6.45%)	0.774
No	86 (92.47%)	87 (93.55%)	
Current smoke cigarettes			
Yes	1 (1.1%)	4 (4.3%)	NA
No	92 (98.9%)	89 (95.7%)	
Ever chewing khat			
Yes	10 (10.75%)	26 (27.96%)	0.003*
No	83 (89.25%)	67 (72.04%)	
Current chewing khat			
Yes	5 (5.4%)	14 (15.0%)	0.029*
No	88 (94.6%)	79 (85.0%)	
Ever use of shisha, ganja, or other substances			
Yes**	2 (2.15%)	0	NA
No	91 (97.85%)	93 (100%)	

*P value statistically significant (P value <0.05)

** There was no current user of shisha, ganja, or other substances

6.6. Health service and geographic access characteristics

Most patients believed the waiting time to get treatment care was acceptable; 93.5% in the Ma-MAS group and 94.4% in the control group. Sixty-seven (72.0%) in the Ma-MAS and 76(81.7%) in the control group believed their relationship with the healthcare provider was very good. In both the Ma-MAS and control groups, more than three-quarters (76.3%) of patients believed the quality of treatment they received was very good. Nearly half of the patients, 46.4% in the Ma-MAS and 43.4% in the control group, walked to reach the health facility. The median transportation cost to reach the health facility was 4 and 5 Ethiopia Birr (ETB) for the Ma-MAS and control groups, respectively (see Table 18).

Table 18: Health service and geographic access characteristics of adult TB patients enrolled in Ma-MAS trial, Addis Ababa, Ethiopia

Variables	**Ma-MAS group n=93**	**Control group n=93**	**P value**
The Perceived waiting time			
Acceptable	87 (93.55%)	88 (94.62%)	0.757
Unacceptable	6 (6.45%)	5 (5.38%)	
The Perceived relationship with healthcare provider*			
Good	26 (27.96%)	17 (18.28%)	0.118
Very good	67 (72.04%)	76 (81.72%)	
The Perceived quality of care*			
Good	22 (23.66%)	22 (23.66%)	1
Very good	71 (76.34%)	71 (76.34%)	
Means of transportation			
Walk	46 (49.46%)	43 (46.24%)	0.904
Car	37 (39.78%)	39 (41.94%)	
Bajaj	10 (10.75%)	11 (11.83%)	
Travel cost (ETB)			
Mean (Sd)	6.04 (8.75)	8.96 (11.97)	0.058
Median (IQR)	4 (6)	5 (7)	
Travel time to reach health facility (minutes)			
Mean (Sd)	21.21 (12.57)	21.53 (13.74%)	0.867
Median (IQR)	20 (20)	20 (20)	

*poor and very poor options were zero reponse, ETB: Ethiopian Birr

6.7. Clinical characteristics

Smear positive pulmonary TB was found in 44 (47.3%) patients in the Ma-MAS group and in 39 (41.9%) patients in the control group. Most patients were newly diagnosed; 91.4 % in the Ma-MAS group and 89.2% in the control group. A total of 11.8% of the Ma-MAS and 15.1% of control group patients had co-infections with TB and HIV (see Table 19).

Table 19: Clinical characteristics of adult TB patients enrolled in Ma-MAS trial, Addis Ababa, Ethiopia

Variables	Ma-MAS group n=93	Control group n=93	P value
TB diagnosis category			
Smear positive pulmonary TB	44 (47.31%)	39 (41.94%	0.518
Smear negative pulmonary TB	15 (16.13%)	21 (22.58%)	
Extra pulmonary TB	34 (36.56%)	33 (35.48%)	
History of TB			
New	85 (91.40)	83 (89.25%)	0.620
Relapsed	7 (7.53%)	9 (9.68%)	
Treatment failure*	1 (1.08%)	1 (1.08%)	
TB-HIV co-infection			
Yes	11 (11.83%)	14 (15.17%)	0.519
No	82 (88.17%)	79 (84.95%)	
Any other non-communicable disease			
Yes**	5 (5.38%)	6 (6.45%)	0.756
No	88 (94.62%)	87 (93.55%)	

*Treatment failure was merged with relapsed case for chi square test, ** Diabetes and Hypertension

6.8. Effectiveness of Ma-Mas intervention

6.8.1. Effectiveness of Ma-Mas intervention on primary ouctome

The mobile-assisted medication adherence support intervention significantly improved TB medication adherence by 15.25% (95%CI: 5.38, 25.12; P-value=0.0065) after eight weeks compared to the standard care provided to the control group. Ma-MAS also improved TB medication adherence by 15.30% (95%CI: 6.68, 23.90; P-value=0.0022) after four weeks of intervention compared to the control group. Although the proportion of adherence decreased by 5.86% in the Ma-MAS group and by 5.81% in the control group from week four to eight, the Ma-MAS intervention remained effective in improving TB medication adherence (see Table 20).

Table 20: Ma-MAS intervention effect on TB medication adherence measured by IsoScreen urine test, Addis Ababa, Ethiopia

Primary outcomes	**Adherence measured by IsoScreen test**	**95% CI**	**P value, 1-tailed**
After 8 weeks of follow-up			
Ma-MAS group (n=88)	86.36%	[79.19, 93.53]	
Control group (n=90)	71.11%	[61.74, 80.47]	
Absolute Difference (AD)	15.25%	[5.38, 25.12]	0.0065
After 4 weekss of follow-up			
Ma-MAS group (n=90)	92.22%	[86.68, 97.75]	
Control group (n=91)	76.92%	[68.26, 85.57]	
Absolute Difference (AD)	15.30%	[6.68, 23.90]	0.0022

Absolute Difference (AD) is calculated Ma-MAS group- control group with 95% confidence interval (CI)

6.8.2. Effectiveness of Ma-Mas intervention in multivariable analysis

In a multivariable analysis, mobile-assisted medication adherence support had a statistically significant association with higher TB medication adherence compared to the standard care after controlling for TB/HIV co-infection, reminders from family or caregivers for clinic appointments, monthly household income, and financial support. When compared to patients who only received the standard care, those who received mobile-assisted medication adherence support had 1.21 times higher adherence to TB medication (95% CI: 1.07, 1.36). After adjustment, none of the co-variates demonstrated a statistically significant association with TB medication adherence (see Table 21).

Table 21: Multivariable analysis of covariates in Ma-MAS intervention effectiveness after eight weeks of follow-up, Addis Ababa, Ethiopia

Variables	Adherence	Risk Ratio [95%CI]	Adjusted Risk Ratio [95%CI]	P value
Randomisation group				
Ma-MAS group	86.36%	1.21 [1.05, 1.37] *	1.21 [1.07, 1.36] *	0.0035*
Control group	71.11%	1	1	
TB/HIV co-infection				
Yes	60.86%	0.74 [0.53, 1.04]	0.77 [0.54, 1.08]	0.140
No	81.29%	1	1	
Family or caregivers remind to clinic appointments				
Yes	80.82%	1.17 [0.91, 1.50]	1.17 [0.93, 1.46]	0.178
No	68.75%	1	1	
Monthly family income (ETB)				
<2738	69.69%	1	1	
2738 and above	83.92%	1.20 [1.01, 1.43] **	1.06 [0.92, 1.23]	0.380
Financial support				
Yes	63.63	0.778 [0.56, 1.09]	0.82 [0.62, 1.09]	0.184
No	80.76%	1	1	

*One sided tailed used since it is a superiority trial; **P value=0.004, ETB: Ethiopian Birr

After eight weeks of follow-up, the predicted probability of adherence to TB medication in the Ma-MAS group participants was 86% (95%CI: 81, 93), while the predicted probability of adherence to TB medication in the control group participants was 70% (95%CI: 61, 79), after controlling for TB/HIV, family monthly income, financial support, and reminders from family or care givers for clinic appointments (see Figure 15).[3]

After four weeks of follow-up, the predictive probability of adherence to TB medication in the Ma-MAS group participants was 93% (95%CI: 89, 98), while the predicted probability of adherence to TB medication in the control group participants was 77% (95% CI: 70, 84) after controlling for TB/HIV, TB diagnosis category, access to adequate food, mode of transportation to health facility, and relationship with healthcare provider (see Figure 15).[3]

[3] This section contain material originally published abstract conference of Mobile-assisted medication adherence support intervention among tuberculosis patients: a parallel group randomized control trial. Population Medicine. 2023;5(Supplement):A585.

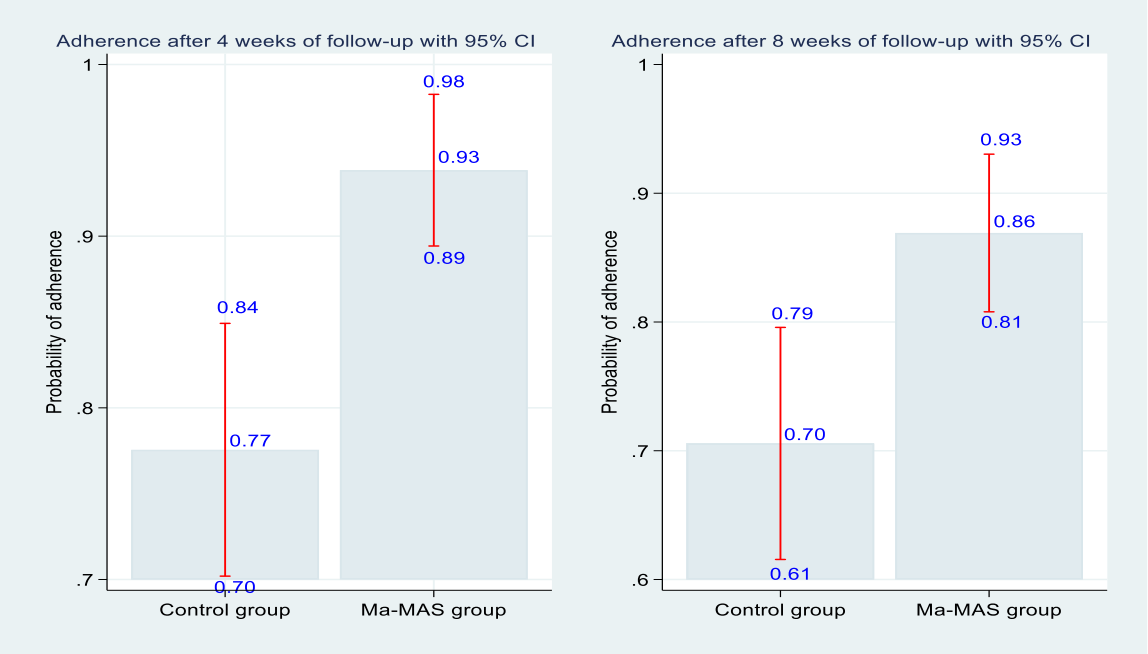

Figure 15: The predictive probability of adherence to TB medication after four weeks and eight weeks of follow-up in Ma-MAS trial, Addis Ababa, Ethiopia

6.8.3. Effectiveness of Ma-Mas intervention on secondary outcomes

The mobile assisted medication adherence support intervention had no statistically significant positive effect on self-reported TB medication adherence as measured by ACTG and VAS (P value >0.05) (see Table 22).

Table 22: Ma-MAS intervention effect on self reported TB medication adherence, Addis Ababa, Ethiopia

Secondary outcomes	**Adherence measured by ACTG [95%CI]**	**P value, 2-tailed**	**Adherence measured by VAS [95%CI]**	**P value, 2-tailed**
Before intervention				
Ma-MAS group (n=93)	70.97% [61.74, 80.19]		91.40% [85.69, 97.09]	
Control group (n=93)	79.57% [71.37, 87.76]		92.47% [87.11, 97.83]	
Absolute Difference (AD)	-8.6% [- 20.9, 3.7]	0.174	-1.0% [-8.8, 6.7]	0.787
After intervention		**P value 1-tailed**		**P value 1-tailed**
Ma-MAS group (n=86)	83.72% [75.91, 91.52]		96.51% [92.63, 100]	
Control group (n=88)	82.95% [75.09, 90.81]		92.05% [86.39, 97.69]	
Absolute Difference (AD)	0.8% [-8.4, 9.9]	0.446	4.5% [-1.2, 10.2]	0.1028
DIFF	-9.4% [-23.3, 4.5]	0.137	-5.5% [-14.3, 3.3]	0.1515

Absolute Difference (AD) calculated Ma-MAS group- control group with 95% confidence interval (CI).
DIFF-Difference in difference, AIDS Clinical Trial Group adherence questionnaire, VAS: Visual Analogue Scale

CHAPTER 7: RESULTS OF STUDY FOUR: PERCEPTIONS, EXPERIENCES AND ADOPTION INTENTION

7.1. Introduction

This chapter presents the interpretive and cross-sectional survey studies assessing the patients' perceptions, experiences, and adoption intention of mobile-assisted medication adherence support (Ma-MAS) intervention, which involves daily SMS messages and weekly phone calls for eight weeks. The first section of the chapter presents the interpretive study results of patients' perceptions, experiences, and adoption intention of the Ma-MAS intervention. The second section presents the cross-sectional survey results of factors influencing patients' adoption intention of Ma-MAS intervention using the Unified Theory of Acceptance and Use of Technology (UTAUT). The model identified four key factors that affect patients' adoption intention of a technology-based intervention: performance expectancy, effort expectancy, social influence, and facilitating conditions. These factors were analysed to its influence in the context of Ma-MAS intervention.

7.2. Background

7.2.1. Demographic characteristics

Twenty TB patients (15 males and 5 females) who received the Ma-MAS intervention were interviewed to assess their perceptions and experiences regarding the adherence intervention. The participants' ages were uniformly distributed, ranging from 21 to 60 years. There were nine participants who had attended education above grade 12, five who had attended grade 9 to 12, and six who had attended grade 1 to 8. Most participants either worked in private organizations (n=9), were employed by government organizations (n=5) or were unemployed (n=3) (see Table 24).

Table 23: Demographic characteristics of adult TB patients, Addis Ababa, Ethiopia

Background	n	Participants																			
		A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
Gender																					
Male	15	M		M		M	M	M	M			M	M	M	M	M		M	M	M	M
Female	5		F		F					F	F						F				
Age group																					
20-24 years	3									21				22							22
25-29 years	5		29			28		27				27						27			
30-34 years	4				30		30		32							30					
35-39 years	4	38											35				38		35		
40+ years	4			49							60				53					60	
Educational status																					
Grade 1-8	6	5				8			8		8			8					8		
Grade 9-12	5			12	10			10				10			10						
Grade 12+	9		B				B			B			B			M*	M*	D		D	B
Employment status																					
Self-employed (SE)	1				SE																
Private organization employed (POE)	9	POE				POE		POE	POE			POE	POE		POE			POE		POE	
Government employed (GE)	5		GE				GE				GE*					GE	GE				
Unemployed (UE)	3			UE										UE					UE		
Student (S)	2									S											S

GE* is Pensioner, Education: D is Diploma, B is bachelor's degree, M is master's degree

Private organization employed (POE) are includes merchants, daily labour employees and other workers in private organization.

7.2.2. Theme, sub-theme, and categories

Based on the thematic analysis of the qualitative data, three overarching themes were identified: acceptance, benefits, and convenience. The theme of acceptance refers to the patients' willingness to adopt and use a particular Ma-MAS intervention. The theme of benefits includes the perceived benefits of Ma-MAS intervention. The theme of convenience relates to the ease and practicability of using the Ma-MAS intervention (see Table 24).

Table 24: Theme, sub-theme, and categories

Theme	**Sub-theme**	**Categories and sub-categories**
Acceptance: Attitude and adoption intention	Attitude	
	Adoption intention	
Benefits: The perceived benefits of adherence intervention	Awareness of the disease and its treatment	A. Awareness of TB medication and the consequence of discontinuing B. Awareness of precautions while taking TB medications C. Awareness creation through asking questions
	A reminder of TB medication	
	Habit formation	
	Motivation and adherence	
	Sense of professional care	
	General health consultation	
Convenience: Experience of adherence intervention design	Content of the messages	I. Evaluation of the content of the messages II. Suggested contents A. Cause and prevention of TB B. TB diagnosis categories and related symptoms C. TB treatment and its side-effects D. Food and nutrition E. Substance use F. Question and answer G. Courage to talk and psychological advice
	Comprehension	
	Time of delivery	A. Evaluation of the time of delivery B. Suggested time of delivery
	Frequency of SMS text messages and phone calls	A. Evaluation of the frequency of SMS text messages and phone calls B. Suggested frequency
	Adherence intervention period	
	Privacy and confidentiality	A. Confidence in the intervention B. Fear of stigma and risks

7.3. Theme 1: Acceptance: Attitude and adoption intention

7.3.1. Attitude

Most participants had a positive attitude towards the SMS text messages and phone calls intervention implemented to improve their TB medication adherence. In agreement with this point a 60-year-old male participant stated that

> *"Yes! I am very interested in the support. I have good appreciation. It is such great work to reach all the clients and contribute to their health recovery by providing advice. It is a great job and I appreciate your efforts."*

Another 22-year-old male TB patient said that the adherence support intervention was not only useful for him, but was also useful for supporting other patients,

> *"I have been reading all the texts and obtained the lessons. Not only for ourselves, but the messages also gave us lessons that we can support other victims. It is my first time to use such a service. And it has been very useful to me. I have got it is critically important to me."*

However, some participants preferred SMS text messages more than phone calls while others preferred the phone calls. Participants who liked the SMS text messages reported that the phone calls did not go beyond asking a few questions, nor did they encourage the patients to talk more about their issues. The phone call would end abruptly when the patient had no more questions. For example, the 35-year-old male participant stated that

> *"The text messages are so good especially for reminding me of my medication. That is very good because I receive them in the morning. It helps me not to be reckless. The phone call is just, "are you taking your medication?" It has nothing else, as to me. Except for this, the text message is very good... It contributes a lot to reminding them of their medication."*

Another 38-year-old male participant added that *"I take out and read the text right away it reaches me. I got everything useful, and I followed it happily." On the other hand,* one 21-year-old female participant reported that phone communication was more beneficial than SMS text messages, because the text messages provided no added information on what she already knew, *"the phone calls have been better. I have been asking the health worker about any issue I face, and they have been responding to me adequately. It was good."*

7.3.2. Adoption intention

Most of the participants had a willingness to adopt the mobile-assisted medication adherence support intervention not only for their TB treatment, but also for other healthcare services. Most of the participants believed that the intervention had a positive effect on their TB medication adherence. The 35-year male participant reported that the adherence intervention was beneficial and should be continued,

> *"It was a very beneficial follow up. I would like to say that it shall be kept up. I am also grateful to you. I appreciate you, really! It is very vital to follow up the conditions of patients like that of people who support them at home. I am very happy about your support. Keep it up."*

The 29-year female participant also suggested that this type of intervention was

> *"Not only about TB treatment, but it is also good if such an opportunity of having close talk between the patients and physicians is practiced. It opens path to use to consult our physicians regarding our health progress and issues. Let it be applied in other ill cases as well. It is a good start.*"

Some participants were also willing to continue the Ma-MAS intervention because they found it useful for reminders and for assistance in avoiding undesirable behaviours related to TB treatment. The 53-year-old male participant said that

"The text messages were more useful for reminding purpose for they were received on daily basis. The phone call got me encouraged additionally. I am very grateful! ... I have benefited from your intervention. The service will be better if continued. It should be kept up because it will help in preventing undesirable conditions and behaviour in taking the medication."

7.4. Theme 2: Benefits: Perceived benefits of adherence intervention

7.4.1. Awareness of the disease and its treatment

7.4.1.1. Awareness of the TB medication and the consequence of discontinuing

The SMS text messages were considered useful for promoting awareness of the importance of taking TB medication as directed by the physician, and the consequences of discontinuing the medication. *A* female participant aged 60 years stated that

"I have obtained good awareness from your messages; for example, the harm that is embraced if one quits the TB medication, and the improvements that I will get if I take the medication accordingly."

Another 53-year-old male participant reported that the Ma-MAS intervention enabled him to continue the TB medication as directed,

"You are writing us educative lessons. For example, it makes people aware that quitting the medication unduly will cause illness or body adaptation to the medication. And it has helped me to continue taking the medication so far and will continue to the end…. It will even create awareness for more people if enhanced … It enabled me not to quit taking the medication for I got explanation of the effects if I quit it. They supported me not to quit taking the medication, not to be reckless, and to apply the prescriptions …"

Another male participant who was 35 years old also said that

> *"They give good awareness of how to take them, if side effects, stuff that we should not intake and others. Indeed, there was a certain repetition after some time. It has been good beyond that."*

The advice from the phone calls was also found to be useful to patients for helping them to continue taking their TB medication as directed by the physician. The 22-year-old male participant reported that, at first, his intention was to discontinue his TB medication, but he later changed his mind after discussing the issue with his healthcare provider, particularly on the potential consequences of discontinuing the medication.

> *"It has benefited me a lot. Every message teaches you a lesson. I was faced with some boredom and intent to quit the TB medication in the beginning days. On the first few days, for example, the health worker advised me on the consequence of the illness. He notified me that the illness may spread to family members, friends, and other community members if I quit the medication. I decided to continue it not to be a source of health problems for other people. I was reckless on the first days. I began to pay attention when the healthcare professional continued to call and give me information."*

Another 28-year-old male participant also reported that the phone communication had helped him to take the TB medication properly, stating that

> *"I am taking the medication properly. The healthcare provider gives me useful information on how to follow my medication. And I can forward any point I have to them."*

7.4.1.2. Awareness of precautions while taking TB medication

One of the benefits of the SMS text messages was the promotion of awareness about the precautions needed while taking TB medication. A 27-year-old male participant said that

"It is greatly beneficial to me by noting me about foods and drinks that should not be taken and things that are forbidden to do while taking the medication. The messages incorporated in the text are so vital. The messages have enabled me to stay away from things that are forbidden when one is taking the medication."

The 60-year male participant also reported that the messages raised awareness about the negative effects and consequences of substance use while taking TB medication,

"They were very important, because some people are reckless, and some other people may engage in drug addiction. The information beware the people how much drug addiction will affect them and the likelihood of getting heal will decline steeply if taking the medication is quit. It was very important."

This participant also explained how the messages made him aware of the effects of substance use while taking TB medication, stating that

"Yes! For example, it deals with the gradual harm of substance abuse while taking the TB medication may result resistance, and problems resulted from poor adherence. Generally, they were educative."

7.4.1.3. Awareness creation through asking questions

The regular phone calls created an opportunity to ask questions and helped the patients to better understand TB treatment-related issues. The 27-year-old male reported that the phone calls were good for gaining greater awareness, stating that *"You can ask the health worker whatever your concern is. There was a question that I asked and got an explanation. I believe that is good …".* Another 38-year female participant also mentioned that she was able to ask questions and understand more about the TB medication, *"The phone call has supported me a lot. I have been asking if taking the medication is associated with one or another condition. It has supported me better."* The 32-year-old male participant added that, *"It aimed at*

educating. Similarly, the checking out via the weekly phone call was good. I also have got clarity by asking different things."

7.4.2. A reminder of TB medication

The SMS text messages served to remind patients to take their TB medication if they forgot to do so. The 27-year-old male participant reported that the daily SMS text messages helped him to confirm if he had taken his TB medication,

> "R*egarding reminding me to take my medication, it has been good for me. I should take my medication at 07:00am. Sometimes, I forget to do that on time. The text reaches me at about 07:30am. Thus, it reminds me if I have forgotten till 07:30am. That has been very vital to me. For the text message reminds me every day, there is no possibility for me to forget to take my medication currently ..."*

Another 38-year-old female participant reported that the SMS text messages were useful for reminding her about her TB medication, despite it not being a real-time reminder,

> *"It is beneficial. Of course, I take the medication early because I leave for work earlier. I accept that the text message is good although it was not alerting enough to me. It is not as reminding as an alarm that is set for waking from sleep. Still, it has supported me to cross-check that I have taken my medication. It has been supporting me to remember and get sure whether I have taken the medication or not. I get a click and take a moment to remember if I have taken my medication, because I take the medication before the text comes."*

The SMS text messages were found to be useful for avoiding forgetfulness related to being busy with work and other social activities. The 53-year-old male participant reported that the demands of his job could result in him forgetting to take his TB medication if he had not received a daily SMS text message reminder, *"Really, it has supported me a lot. Because of*

the nature of my work, it was a good reminder to me. I am glad about it!" The 22-year-old male participant also said that *"there are days on which you may forget to take the medication because of several factors. For example, there was a day that I took it at about 10:00am after seeing the message."* Another 35-year-old male participant reported that he once forgot to take his TB medication, but he remembered because of the SMS text message,

> *"The text messages are so good, especially for reminding me of my medication. That is very good because I receive them in the morning. It helps me not to be reckless. It supports the people who are outside the health field of study. It contributes a lot to reminding them of their medication. There were such days. I forgot on some days and reminded by the text message. I faced that overwhelmed with work."*

The phone calls also proved to be useful for helping the patients remember when they forgot to take their TB medication. There were instances where patients forgot to take their TB medication and remembered as a result of the phone calls. The 22-year-old male participant stated that

> *"I took the medication an hour late after a phone call was given to me. The benefit has been significant to me. Unfortunately, I forgot to take it on the day. I did not see the text message either because I was sleeping. It was the call ring that woke me. I meant that the benefit is significant."*

Another 53-year-old male participant added that *"It had similar support with the text message. There were times that it woke me up in the morning. I could not hear the text message if I was sleeping."*

7.4.3. Habit formation

The daily SMS text messages were also found to be useful for developing the habit of taking their TB medication at a regular consistent time. A 29-year-old female participant reported that

she was not taking the TB medication consistently at the same time before the start of the daily SMS text messages, stating that,

> *"Previously, sometimes, I had been taking the medication on undue time. After I began to use the messages, I have become able to keep the timing. It supported me in that aspect. I used to stay as late as 09:00am. I have improved it to 08:00-08:30am with the support of the reminder of the messages. I did not stay as late as 09:00 after I began to receive the SMS text messages reminder ..."*

Another 22-year-old male participant stated that,

> *"Very much! It makes you alerted about taking the medication for you receive it on daily basis. The reminder teaches you the habit of waking up early, taking medication 30 minutes before having breakfast. Even, a message is received at 04:00pm in the afternoon will contribute to remember that he/she should take the medication in the next morning. It gives a responsibility. That has been very important to me."*

7.4.4. Motivation and adherence

The daily SMS text messages were found to be useful to motivate patients and enhance their commitment to properly adhere to their TB medication. The 53-year-old male participant reported that he read the daily SMS text message and complied with the advice, *"Currently, I have been taking the medication according to the advice that you have been giving me, by adhering to the timing you advise me."* The 32-year-old male participant also said that *"I have been taking the medication properly. I have not made a quit. I have been taking it on time ... I am taking it properly. There has been no gap with my medication."*

Participants also reported that getting a phone call and being asked about their issues by a healthcare professional gave them hope and motivation. The 49-year-old male participant

reported that the phone calls were helpful for taking the medication properly, even if the TB medication was strong and had side-effects,

> *"It (phone calls) was very good. It was constructive. The medication was also good, although it is difficult for the patients who are physically weaker. It is painful because the pill is very powerful. Nevertheless, it is impossible to heal without the pills. On my part, I have been taking the medication with great attention and commitment. I will complete that accordingly.*"

Another 22-year-old male participant added that, *"Talking through the phone is very important for some people even under normal circumstances, let alone for patients. It gives them hope and motivation for them."*

Daily SMS text message was also useful for preventing negligence and to ensure adherence to the TB medication. The 60-year-old female participant said that *"I took the medication duly in the morning. It (SMS) has supported me that I should not be reckless about my medication."* Another 60-year-old male participant also mentioned that the daily SMS text message was very helpful for alerting him to the TB medication, *"Very much! The text messages give us advice to be in conditions conducive to taking our medication on time. I follow it attentively."* Another 30-year-old female participant added that,

> *"They are good. I follow such things attentively. I take the medication carefully indeed. The information is useful for those who do not have good adherence. They (SMS text messages) are good reminders to them.*"

The phone discussions were also useful and encouraging for adhering to the TB medication. The 28-year-old male participant reported that he was taking the TB medication according to the phone advice and stated that *"I am taking the medication properly. The healthcare professional gave me useful information on how to follow my medication. And I can forward any point I have to them."* Another 27-year-old male participant added that, *"Its benefit was to*

promote adherence. They give you different advice, I mean the health workers. That is good because it encourages you to take the medication properly."

7.4.5. Sense of professional care

The SMS text message and phone call intervention to improve TB medication adherence also proved useful for enhancing patients' feelings towards professional care. The 60-year female participant was happy with the professional healthcare, stating that

> *"I understand how much you are concerned about our health, although it is the responsibility of the person to take care of I. Even, I have not ever expected that there is such kind of support. It is very good."*

Another 22-year-old male participant also expressed his feelings about the professional care, *"It is my first time to use such a service! And it has been very useful to me."* Another 35-year-old male participant added that *"… In addition to the text message, the healthcare professional was following me up by giving me a phone call. Giving attention to the patients that much itself is very good. I am happy about it!"*

Participants were happy with the health advice on the phone calls because they were able to ask questions and get explanations from healthcare professionals. The 21-year-old female participant stated that, *"I have been asking the health workers about any issue I face, and they have been adequately responding to me. It was good."* Another 29-year-old female participant had experienced what she considered to be good professional care, because she had the opportunity to ask questions, *"It was very good in giving us the opportunity to ask if we face any concern in our medication. The physicians encourage us to call them any time and ask if we have any concerns. It was so good."*

Participants also felt that the professional care was good because the healthcare professional made the phone calls and asked them about their health status. The 27-year-old male participant stated that

> *"The phone calls also have been very good communication. They have been asking about my progress and if I have been getting better or not from time to time. They have been asking me about my progress when I took the medication. I consider that it has been so good."*

Another 28-year-old male participant expressed his feelings about the care, *"They asked me if I was taking the medication properly and if there was any new problem with my health. I told them accordingly."* The 22-year-old male participant added that

> *"The phone call that you gave us is important in case there is certain concern. They were calling and asking me if I had an illness or any problem. I think that the communications were useful in this regard as well.*"

How the healthcare professional communicated through the phone calls was important for the patients' perceptions of their professional care. The 32-year-old male participant reported that he was happy with the communication of the healthcare professional and how they answered his questions, *"They were good. They asked me and had a good conversation with me. They also gave me good explanations for my questions. It was good."* A 30-year-old female participant also expressed her feelings about the professional care of the healthcare professional, *"They have been giving me a call. They have been asking me if I would have experience of different illness."*

The healthcare professionals' efforts to improve medication adherence enhanced the positive perceptions of the professional care, and the patients' commitment to adhering to their TB medication. The 60-year-old male participant shared his feelings of appreciation for the professional care team,

> *"Here one thing that I want to assure you is that I appreciate the struggles of your health team in supporting people. I am happy as an Ethiopian and about your health principles when I see the efforts exerted to support others.*"

A 27-year-old male participant also said that *"the health workers are doing well in giving us important advice and reminding us to take the medication properly. They are good".*

7.4.6. General health consultation

Having a health consultation through a phone call was one of the benefits of the Ma-MAS intervention. Patients could have a consultation on their health issues through a phone call without needing to attend the health facility. The 27-year-old male participant explained how the phone calls helped him in relation to his health consultation,

> *"I explain to them when they call and ask me about my health progress. Last time, for illustration, I moved to a certain area that has cold weather. I had some difficulty, perhaps because of the cold. As a result, I asked them on the phone about it. I told them about the bad sensation I experienced. And they advised me to visit my physician by guessing that it may be because of the cold weather. Accordingly, I visited my physicians and they explained to me that such sensations develop because of the cold weather. Finally, my health condition got back to good status after I returned to my original place."*

The 21-year-old female participant also reported that she received a health consultation without needing to go to the health facility,

> *"I could get explanations on phone by asking the workers without going to a health facility. It was good to ask if I have any concerns. That has been helpful … I had a cough in between and asked the health care professional at the health facility if it was among the side effects. She told me to wait sometime till I take a certain amount of the medication instead of giving me answers. I asked your healthcare professional through phone, and he advised me to have a Medical examination and I did so. Say to me thank you to him."*

Another 22-year-old male participant also shared his experience, *"I consulted him through phone when I got swelling on my body. He told me to visit a health facility ... To talk about the case itself is something."* Another 32-year-old male participant added that *"… I also have got clarity asking different things. For example, they supported me when I could not find vitamins because it was not available at the health center."*

7.5. Theme 3: Convenience: Experience of adherence intervention design

7.5.1. Evaluation of the contents of the messages

Most participants believed that the content of the SMS text messages was appropriate and useful for promoting TB medication adherence. The 38-year-old female participant reported that the information included in the SMS text messages was good for promoting TB medication adherence,

> *"It gives good notification to hold the medication along us if we move to another area, not to forget it. The messages also include the risks associated with failing to follow the prescription medication accordingly. It is not something that we can undertake recklessly. It also results that our body may adapting to the medication and that it may not be easily treated and cured. It is forbidden to drink alcohol. The messages tell us about all these issues."*

Another 38-year-old male participant stated that

> *"The messages to take the medication properly and not to drink alcohol are very good. There was also the message of not to forget to grab the medication if we move away from home for some days, be aware not to forget to do this. That was very useful."*

Participants also reported that the overall content of the SMS texts was useful for awareness and promoting TB medication adherence but recommended that repeated SMS text messages should be avoided. The 22-year-old male participant stated that

> *"I have not seen a defect in the messages. I read and got awareness. There has been some repetition of course. If possible, it would be good if that was reduced. I am satisfied with the messages beyond that. The text messages give good lessons every day. It gives us information about what to do when we move to another place, to take medication from other health facilities for example. I have been reading all the texts and obtained lessons."*

Another 35-year-old male participant added that

> *"They are very good. They (SMS text messages) give you good awareness of how to take them, if side effects, stuff that we should not intake and others during the medication, the conditions that make people forget taking their medication, for example. Indeed, there was a certain repetition after some time. It has been good beyond that. I properly read them daily."*

Similarly, most participants reported that the information from the phone calls was also useful because open questions were asked of the patients, which made it a two-way form of communication. The 27-year-old male participant said that

> *"This one (phone call) is open. You can ask the health worker whatever your concern is. There was a question that I asked and got an explanation. I believe that is good. It depends on the service seekers. It is good to me because I have got explanation when I asked about my concern."*

Another 30-year-old female participant stated that the phone communication included open questions that asked the patient about any challenges they had encountered, *"They are questions if we are taking the medication properly and if there is any challenge. And they are*

good. They also advise us to visit our physicians if there is any concern. That was good." Another 30-year-old male participant added that,

> *"Yes! I am happy about the question they ask, "is there any challenge you faced?". I have not faced any challenges. Yet, the question is very important for others. I believe that asking that question and inviting the patients to have explanation on their concern is good opportunity.*"

7.5.2. Suggested content of messages

7.5.2.1. Cause and prevention of TB

It was suggested that information about the causes and prevention of TB should be included in the SMS text messages. The 38-year-old female participant stated that

> *"It is good if awareness is created for us regarding the causes behind the health problem. Nobody has explained that to us. Additionally, awareness is good for us to have regarding how it can be prevented."*

Another 60-year-old female participant also suggested the inclusion of information about the causes and prevention of TB, and the precautions to be taken once a person developed the disease, *"It is good if the contents include information about the causes of the illness, how to protect oneself from it, and the cautions that we should take after contracting the illness."* The 30-year male participant also suggested that information about the risk factors for TB and prevention methods should be included,

> *"Yes, with respect to vulnerability, it is better if the information of how people become bound to the illness, so that they can refrain from the exposure. In addition to educating the people who have contracted the illness about the disease conditions, and there shall be some contents about how people can protect themselves from contracting the illness."*

Some participants also suggested that information about the causes and prevention of TB should be included in the phone discussions. According to the 60-year-old male participant, the healthcare provider did not clearly explain to him how the disease was caused or how to prevent it,

> *"It is good if the contents include information about the causes of the illness, how to protect oneself from it, and the cautions that we should take after contracting the illness. They (healthcare professionals) said that it is contracted when our body immunity is poor. Yet, I am eager to know how much percent that is precisely."*

7.5.2.2. TB diagnosis categories and their related symptoms

There was also a suggestion to include the symptoms associated with the different TB diagnosis categories. The 29-year-old female participant said the contents of the SMS messages were good, incorporating a variety of information in each day, but she added that it would be good if the diagnosis categories of TB and information about the related symptoms were included in the SMS text messages,

> *"The contents were good. Yet, it is important to include in the messages that TB illness has different types. For example, my sister who is taking TB medication along with me got only a swelling on her neck. She had no cough, no fever, only a swelling on her neck. We did not guess it was TB. We attributed it to Goiter for she had that case and the swelling developed on her neck. She got different examinations at different facilities. It was lastly she was diagnosed with TB. Thus, it is good to indicate that TB can have varying symptoms and to have a checkup if one or another symptom is experienced. A very few people know of different cases of TB illness. Very few! For example, we did not have such knowledge except after the case of my sister. Thus, I think that it is very*

good if such information is included in the text messages so that better awareness will be created."

Some participants also suggested that information about the different TB diagnosis categories should be included in the phone communications. For example, the 38-year-old female participant said that *"The question about my health problem is swimming my mind. Mine is not a lung case. I would be happy if you give me information about my specific case."*

7.5.2.3. TB treatment and its side effects

The SMS text messages should also include more information about the side-effects of TB medication, according to some participants. The 21-year-old female participant reported that information on the side-effects was not well explained by the healthcare professional who worked at her health facility,

> *"It is good if awareness is created regarding the side-effects of taking the medication and the causes of the illness. I have asked the healthcare professional at the health facility multiple times about the side-effects of the medication. They did not like to explain to me clearly. They do not like to explain that and the cautions that we should take. I do not know why. It may be because it disturbs us if it is hazardous. I think that it would be better if that is included."*

Similarly, a 30-year-old male participant shared his experience with drug side effects, noting that he was not aware of them beforehand. He recommended including a message about these side effects,

> *"It would be good if the symptoms and signs that the medication causes were included in the messages. For example, I experienced signs like sight delusion, loss of appetite, and others. Had that information been included in the SMS text messages, I would not have been confused if those signs were common side-*

effects or particular to me. I think it is good if concerns around the medication are included."

According to a 60-year-old male participant, it would be useful to ask the patient about their side-effects and their level of adherence via the SMS text messages,

"Furthermore, it would be good if you add content about the side-effects of the medication upon our health. You better send us text messages about this. Not all people have similar experiences. It is better if you can add questions about the side-effects a patient has faced and the level of his/her adherence. This is a point that may be improved."

In addition, some participants suggested that messages regarding the use of drugs on TB, the consequences of not taking TB medication at the same time, and facts about the disease, should be included. The 53-year-old male participant stated that *"I would be happy if you give deeper information about the problem of taking the medication at any time, maybe in the morning or midday or afternoon."* The 30-year-old male participant said that the SMS text messages provided good highlights of the information provided by the health facility, but additional facts about the disease, such as the chances of curability and other facts related to the disease were needed,

"Furthermore, it is good if some facts about the illness are incorporated in the texts. Research findings about the curing possibility of the sick, for example! It is good if patients are given information of promising realities about their health conditions."

7.5.2.4. Food and Nutrition

There were some participants who stated that they would like to have nutritional information included in the SMS texts. A 60–year old female participant suggested,

"It is good if the content includes information about how to protect oneself from it and the cautions that we should take after contracting the illness. I have the idea that it is good if the information about the food items that are vital for the patients are included in the information. People will apply that according to their ability."

Another 35-year-old male participant suggested that

"It is good to be clearly identified and delivered to the patients if there are food items that are forbidden to eat. For instance, there are food items that are defined traditionally not to take while taking certain medication. On my part, I have asked the healthcare professional on the phone calls. They told me nothing."

7.5.2.5. Substance use

Some participants suggested the inclusion of more information about the adverse effects of smoking on TB medication, as well as the effects of smoking on general health. Some of this information was included in the SMS text messages, but participants suggested that more information about the negative effects of smoking should be added. The 22-year-old male participant said that *"It is good if you give more attention and address about the harmful effects of smoking cigarettes. I would be glad if you do so."* Another 60-year-old male participant added that "*the gradual harm of having substance abuse while taking TB medication can cause drug resistance and health problems as result of medication non-adherence*".

7.5.2.6. Question and answer

Participants suggested that the phone intervention could be designed as a 'question' and answer' format to ensure the patients understand the SMS text messages and comply with the advice in the messages. The 27-year-old male participant said that

"*It is better if questions of how much the patient is learning the benefits of the medication and if his/her adherence is good. Additionally, a patient should be asked if he/she is staying away from forbidden things when they take the medication."*

Another 53-year-old male participant explained the importance of asking a questions in the SMS text messages and phone calls added that

"One thing that I want to say is it will be better if you can assess if a client has really understood and practice your recommendations... For example, you may ask him/her to explain the impacts of quitting the medication unduly after creating awareness for him/her. The patients will be able to have good awareness and even can teach others afterwards… The question-answer will enable the patients not to fear to discuss and get rid of doubts about the medication. … Thus, I advise you to have certain question-answer pieces in both the text and phone call communications."

7.5.2.7. Courage to talk and psychological advice

Some participants reported that the healthcare professionals who made the phone calls should be more courageous and supportive in talking to the patients to avoid the phone conversations ending too abruptly. A 30-year-old male participant reported that the healthcare professional who gave calls had a list of questions for the patients, but if the patient had no questions to ask, the phone call would end. The participant stated that

"Very short duration was allocated for the phone call. They would say goodbye and hang up if we say we do not have a question to ask. Anyway, it was useful. It would be good if more time were allocated, and the healthcare professional gave time to listen to the beneficiaries. To tell you the truth, I would not raise a question though I had something in my mind to be asked. I did not ask because of some reason. So far, it might end in less than a minute if the beneficiary

receiving the phone had no question, right? It was good thing to consider 5 minutes as an average, but it will be better if it is improved to 7 minutes. It will be good if the questions of what the patients experience in association with the medication, how they are taking their medication, and other related questions are incorporated. To get their experiences, by asking them what they face for example."

The 35-year-old male participant added that

"Moreover, it will be better if the dialing health workers provide some pieces of advice. Giving us the opportunity to ask them if we have a question is a good thing. Additionally, it will be better if some pieces of advice are provided along. It is better if the dialers talk friendly and encourage the patients to discuss actively. It may be because of me if I consider my particular case indeed. Yet, the health workers who make the phone call shall motivate and push the patients to talk actively. That is about the phone call. And I do not have recommendation about the text message."

7.5.3. Comprehension

Most participants reported that the SMS text messages were easy to read, and their meaning was easy to understand. The 27-year-old male participant said that ***"****Yes, it has been very clear. The language is very easy to read and understand".* Another 30-year-old male participant added that *"They were clear and brief! They were good. It had nothing difficult. Nothing was puzzling; they set them clearly. Nothing was ambiguous."* The 60-year-old male participant also said that *"For sure, I have not seen any difficult concepts. They were advice to have some proper behaviour. I have not seen anything difficult to understand. It was a simple language."*

In addition, participants reported that the SMS text messages were easy to understand because they were prepared in Amharic (the national official language of Ethiopia). The 29-

year-old female participant stated that *"I have followed them accordingly. They were prepared in Amharic language. There has been no difficulty. They were clear enough to transmit the intended information. They were good."* Another 38-year-old male participant added that

> *"I read and used it properly. All the points are good. Nothing challenged me. I have used the messages accordingly. Yes, doing that in the Amharic language is a very good decision. I could not have read or understood had it been prepared in English language."*

However, one male participant, aged 22 years, said that the SMS text messages were understandable, but some texts had spelling errors that sometimes made the message difficult to comprehend,

> *"Yes, they were understandable for I am a student. Yet, some errors exist in the texts, spelling errors for example. It is sometimes difficult to get the meaning. It needs to cut and merge to have meaningful sentence. It is okay for me indeed. I can understand them correctly. However, it may be difficult for those who are not educated or lower graders. On my part, I have managed to understand the messages of the texts. I am telling as a recommendation for you. I did not face a challenge on my part.*"

Similarly, other participants reported that the phone communication was clear and understandable. The 27-year-old male participant stated that *"There has been no terminology that I could not understand either. It has been going well."* Another 22-year-old male participant added that *"No! The dialogue is so brief indeed. They ask me shortly and I also respond to them shortly."*

7.5.4. Time of delivery

7.5.4.1. Evaluation of the time of delivery

Most participants reported that the delivery times of the SMS text messages were convenient for their TB medication reminders. The SMS text messages were scheduled for 7:30am, and most were delivered between 7:30am and 8:00am in the morning. The 29-year-old female participant said that *"I do not have complaint about the timing of the text messages. It was proper time to remind me to take my medication. It was in the morning and before you begin a daily life journey."* Another 35-year-old male participant added that *"It reminded me when I was about rising from bed. Commonly, it is the time that people get prepared to kick-off to job or else. I think it was a good time."* Another 60-year-old female participant also said that *"It is very suitable time. The clients are reminded right after they wake up. It is good timing. Yet it sometimes arrives late. Generally, it is good. Keep it up."* The 22-year-old male participant also reported that the SMS text messages and phone calls were made to him in the early morning before class time,

> *"The messages and phone calls were given early in the morning, before work or class time. To me for example, he gives me a phone call before 08:00am. You go nowhere before 08:00am, you are at home. It is similar for text messages as well. I could read right away at that moment."*

However, some participants reported that sometimes, the SMS texts and phone calls had reached them late, after 8:00am.

7.5.4.2. Suggested time of delivery

Some participants suggested scheduling the delivery of the SMS text messages according to the patients' actual time of taking their medication. The 28-year-old male participant said that

> *"Generally, it is good for me. The thing I have mentioned for improvement is to make the text message delivery exactly fitting to the time that the patients take*

their medication, delivering the message on 07:00am if patients tend to take their medication at that hour."

Another 38-year-old male participant added that

> *"This depends on the time that the person wants to take the medication. Some may prefer to take it at 08:00am; some others may need to take it at 07:30am. On my part, I take it around 06:00am most often. I take at that time for I need to leave for job earlier. I took it earlier.*"

The 22-year-old male participant also said that

> *"It is good if you send the message in accordance with the time that patients take their medication. I will take it at 06:00am. For example, it is meaningful if the reminding message reaches a patient at 06:30am if he/she takes the medication at 07:00am. It may not be meaningful to receive the message at 07:30am for such a patient."*

Other participants suggested sending the SMS text messages before 7:30am in the morning because people wake up early to get ready for work. The 38-year-old female participant reported that the SMS text messages were delivered while she was getting ready to go to work, so she had not seen the text messages immediately,

> *"As I have told you, it could have benefited me more if it had it been sent to me earlier. I took the medication earlier. And I received the messages somewhat late. It is around 07:30am. However, most often, I see it later. It may be because of the hustle that we have in the morning … I see late, but I use the text for cross-checking that I have taken the medication. I believe that it is better if received earlier in the morning so that it will alert us in advance."*

Similarly, some participants recommended scheduling the timing of the phone calls in the same way as the SMS text messages at 07:00am before the person went to work because people may not pick up their phone when they are busy with their job or routine activities. The 27-year-old male participant said that *"I think that it is better if the phone call takes place at 07:00am instead of 07:30am. I am receiving the call after 07:30am now."* Another 29-year-old female participant suggested that

> *"It is better if given early in the morning for it will support as a reminder as well, if a person has forgotten but has not seen the text message for example. For they are overwhelmed by daily life hustles, some people may not read text messages received. As I have told you, it will be more useful for reminding if the phone call is given early in the morning like that of the text message (07:30am).*"

The 60-year-old male participant added that

> *"I may not pick up my phone when you call me 07:30-08:00am. It is a time to drive to the office for work. I may not respond because I am driving at that time. However, I do not believe that all beneficiaries have similar conditions.*"

7.5.5. Frequency of SMS text messages and phone calls

7.5.5.1. Evaluation of the frequency of SMS text messages and phone calls

Most participants reported that the daily frequency of the SMS text messages was appropriate for reminding the patients about their medication because the medication is taken in the morning on a daily basis. The 27-year-old male participant stated that

> *"Sending text messages everyday has been good because the medication is taken daily. You may forget it sometimes in some conditions, going to work early for example. And texting us every day is very good to be reminded and*

prevent such a gap. The text supports us like that of alarm reminder. One will remember when he/she receives the text."

Another 38-year-old female participant added that

"You may forget to take the medication if the frequency is going to be less. It may be forgettable if the current frequency is reduced. And the current frequency is enough to remind us. I think that the logic of sending us the message every day is that the medication is taken one time in a day."

Another 22-year-old male participant also added that *"Sending text messages every day is very good. It enables the person to be alerted about his/her health if he/she is a patient. To give a reminder every day is a very determinant factor."*

On the other hand, only a few participants said that weekly phone calls to the patients for adherence support would be adequate. A 30-year-old male participant expressed interest in receiving weekly phone calls to prevent monotony,

"I think it is good if the phone call is given 1 or 2 days in a week. Even, I would not remember the day of call. I mean that it has not been dull for it was only one day in a week. It is better if the current frequency is kept on. It may be dull if increased."

Another 27-year-old male participant also stated that *"I think the weekly-based phone call is also good enough to explain one's status and progress. One can explain the feeling that he/she experiences inside. I consider that it has been very good."* Some participants also reported that because the phone calls were made with the support of the daily SMS text message, the weekly phone call was adequate. The 35-year-old male participant said that

"As to me, it is very adequate including the phone call. Calling the patients every week is also good. It is adequate. Giving attention to the patients that

much itself is very good. I am happy about it. It was in addition to the text messages that were sent every day."

Another 60-year-old male participant said that *"I think it is better to have it weekly instead of daily. Along with the text messages, it is enough."*

7.5.5.2. Suggested frequency

There was a consensus among most of the participants to increase the frequency of the phone calls, but some suggested making the phone calls twice, while others suggested three times per week. The participants' reasons were that they could get additional time if they had any health concerns they wished to discuss with the healthcare professional, the weekly phone call may not be adequate for those who were unable to read a text message, the weekly phone calls may not be adequate for patients who do not give due attention to the TB medication, and some mobile phones cannot read Amharic text messages.

Most participants suggested making the phone calls at least twice per week. The 27-year-old male participant said that

"It will be better if the phone call is improved to two days a week. It gives you more opportunity to express all your feelings, including if you face some illness. Notably, the current one-day call is not bad that much, of course. Yet, I think that it will be better if it is given on two days a week. That would be better because a patient may face a challenge and seek explanation from the health workers more frequently."

Another 38-year-old male participant suggested that a weekly phone call may not be adequate because some people who were not very mindful of their TB medication may forget to take it,

"Let me tell you one thing here. It is adequate for me. The current frequency is enough for me. However, it is better if you add one more day and make the phone call two days a week. Some people may forget the medication with the

current frequency. Not all people are similar. Some people may be less attentive to a message that is memorized only one day in a week."

Another 22-year-old male participant added that

"Regarding the phone call, it is enough to me. Indeed, it may be good for others to make the phone calls 2 days a week. You may decide that by hearing the voice others ... It will be better to have more consultation. New symptoms may happen from time to time which may cause fear. It is easier to consult the healthcare professional on the phone instead of going to health facilities. I say it is good. You may add if you think something more is needed."

Other participants suggested making the phone calls three days per week. The 29-year-old female participant said that

"The frequency has been enough for me. However, it may be needed to increase the frequency of phone calls for those clients who may not be able to read and those whose phones may not read the Amharic text letter. As a result, they cannot read and obtain the messages of your texts."

Another 53-year-old male participant said that

"Yes, importantly! For example, there may be beneficiaries who cannot read. Thus, it will be better if the phone call is increased to 3 days in a week, the 1 day shall be improved. Such beneficiaries will be encouraged with the calls they cannot read. There are people who prefer phone calls over text messages. I also think listening is preferrable than reading. On my part, I am okay with the text and phone calls. I benefited from both. However, there are some people who would prefer the phone call. They do not elicit equal messages from text and phone calls. Thus, it is better if we give more phone calls to such patients."

7.5.6. Adherence Intervention period

Most participants agreed that a two-month adherence intervention period was inadequate and needed to be increased to improve medication adherence. However, participants had various suggestions regarding the length of the adherence intervention. Most participants believed that the Ma-MAS intervention would be more effective and desirable if it was implemented for the entire six month of TB treatment period. Participants believed that a 2-month adherence intervention support may not be enough for sustainable medication adherence. The 38-year female participant had doubts about the effectiveness of the intervention because it had been implemented for only 2 months,

> *"I think that the effectiveness of the aim of the effort is questionable. It is good to investigate it from the perspective of its purpose. A person may take the medication rightly for the 2 months. What about in the remaining months? To me, my husband follows up and supports me eagerly and continuously. I would miss some medication if he were not around. I think it is better if the support is provided all the time.*"

The participants recommended the intervention to take place across the entire treatment period, and in particular, to start it at the beginning of the treatment. According to the 22-year-old male participant, the adherence intervention would work best if it was started at the beginning of the TB treatment because it would provide early health advice that would help him to continue taking the TB medication for the entire treatment period. The participant reported that he had the intention to stop taking the TB medication at the beginning of the treatment, but changed his mind after talking to the healthcare professional via the phone calls,

> *"It is better if you can do it starting from the time the patients begin to take their medication. Even, it is in the beginning stage that it is more important. On my part, for example, I was to quit the medication at the beginning. I came to*

continue it after consulting a healthcare professional. It is good thing to have consultation at the beginning time when it is new to follow the medication properly. It is a relief to consult them. And you make a well-informed decision after getting more information. It is better if you begin the service from the beginning."

Another 22-year-old male participant suggested that

"I think, it is better if provided for the whole months/duration. It is most important at the beginning of the medication particularly because the probability of forgetting to take the medication is higher at the beginning. It is challenging in the first 2 months particularly. It will be fine afterwards for it is habituated later. It is better if you work on the first 2 months with great attention."

Some participants also reported that starting the adherence intervention and then quitting was not advisable because some people may act recklessly, have addictive behaviours, may not have family members that would help them to remember their medication, or may not receive adequate advice about the treatment. The 60-year-old male recommended that the intervention should take place throughout the entire treatment period,

"Some people may be reckless. Some people may not have family to remind them. Some may not have adequate advice. Some may have drug addiction behaviour. Your advice is very important for such people. It informs and guides them ... It is good to continue the support. It has no negative effect. It is not good to begin something and quit halfway. It is not bad if clients are provided with advice from the beginning to the end."

Another 49-year-old male participant added that

"It is good if increased. It is better if you stand by the patients and care for them. Providing the reminder service only for 2 months is not enough. Particularly,

patients who have drug addiction have poor adherence. It is difficult for them to have good adherences for all 6 months on their own. You should follow them up and take them forward ... It is just a human engagement. It is good if you continue to give them inspiration."

7.5.7. Privacy and confidentiality

7.5.7.1. Confidence in the intervention

Most participants reported that privacy and confidentiality were not a problem during the adherence intervention support program. Participants were even confident enough to show the text messages to their family and relatives. According to the 35-year-old male participant, good communication with the healthcare professional and having clear information about the disease and the treatment helped him to feel comfortable,

> *"It depends on your personal attitude. I did not have a challenge in that regard. I took cautions to prevent transmission when I experienced cough and other symptoms … I even showed the text messages to others for it helps them to get awareness. Outside the family! (The text shown to outside the family). There is no problem with that. It is me that is the victim. I believe that they would be alerted to protect themselves from infection by getting the awareness from the texts I received. Thus, I did not feel uncomfortable."*

Another 53-year-old male participant added that

> *"No! There was no such problem on my part. I have not faced that so far. Things went on due time. I have even been ready to share information with a person interested to have, because keeping hidden the disease after it has already happened does not have significance. And I did not expect that such a thing would be a risk.*"

Another 35-year-old male participant reported that the messages and calls had no sensitive information that violated his privacy and confidentiality,

> *"No, there was no challenge on my side. There is transparency in my family. And I shared the information with them at the beginning when the first time I visited the health center and knew my diagnosis. I have given them the information that reminding messages are sent to me. I did not have that challenge for my family knows it. Moreover, the messages are not that risky.*"

The 60-year-old male participant reported that people infected with HIV (Human Immunodeficiency Virus) might not disclose their status to avoid stigma, but TB does not present such a problem,

> *"How! I did not have privacy doubt for it is a health issue. I cannot have such privacy at all because it is a common illness that anybody can contract. It is not an illness to be hidden. HIV/AIDs victims may hesitate to expose the illness fearing stigma. In contrast, this illness can be contracted by anybody in different circumstances. I have never thought that there is a problem in exposing one's illness. I have not ever faced a challenge amid exposing it. I have not. I will never face it either."*

Another 28-year-old male participant added that

> *"No, there was no time that I was concerned if somebody may read the text message. No! Nothing is above life. Taking the treatment cannot be a secret. It cannot be beyond saving our life. No! Differently, I think that it is beneficial even for others to get awareness if they see the text I receive.*"

7.5.7.2. Fear of stigma and risks

Although most participants had confidence in the Ma-MAS intervention, some were afraid of stigma and did not want to disclose their health status, so they tried to hide the SMS texts from

others, delete the text messages after they had read them, and/or did not pick up some of the phone calls made in public places. The 22-year-old male participant had an unpleasant feeling when a person next to him looked at the SMS text messages on his mobile while he was travelling on public transport. The participant said that he did not want people to know his health status so that he could avoid unnecessary stigma,

> *"To speak the truth, there is a sort of discomfort. One day, I was on a transportation when a text message was dropped. I took out my phone to look for the message. It was a TB message. I opened it. A person sitting next to me saw it. I felt discomfort when he saw it. I do not feel good when people learn that I am TB patient for they may ostracize me for the illness spreads through breath."*

This participant also mentioned that he felt bad because the passenger reacted after reading the SMS text message and seeing that he was wearing a face mask,

> *"I felt bad when I saw his reaction. I noticed when marginalization happens practically. As a caution, I did wear a face mask. He distanced himself from me. Indeed, I do not blame people because the disease spreads by breath. I am taking cautions to prevent the spread and discomfort of others ... I am a student and I view it critically. I can resist the possible offense. I take caution to prevent its spread to others. I am okay beyond that ... It may be offensive to see when others feel discomfort because of me."*

The participant, however, had no such experience during the phone communications because the phone calls were made while he was at home,

> *"Most often, I receive the call when I am at home. My family knows it and they encourage me to communicate on the phone properly. They take care of me in relation to the phone I receive from the center."*

Similarly, another 30-year-old female participant reported that the daily SMS text message reminded her that she was a patient, and so she read the SMS text messages immediately after receiving them and then deleted them to avoid being seen by other people because she did not disclose her health status to anyone else so as not to cause inconvenience,

> *"Every time I received the text message, my status, "I am a patient" comes to my mind. I say to myself, "they remind me that I am a patient". There was no such challenge regarding the phone call. With the text message however, I have been deleting the messages right away I read them because it is only me that knows my illness. I am not afraid for myself regarding their view of me, but I do not want to create some inconvenience for them. There is nothing harm or favor they do to me but not to cause inconvenience. I have been careful thus. You make interactions with people for man is a social animal. Your companion may request you to call with your phone. And it is the behaviour of our people that they get into their friends' phone and see into their stuff in their phone. That is why I have been deleting the messages."*

The 30-year-old male participant reported that the SMS text messages had no privacy and/or confidentiality issues, but he did not pick up some of the phone calls made while he was on public transport or at the office, which were not considered a convenient place to discuss privacy concerns in public.

> *"I would see the text message when I meant to check time from my phone because I go to work early in the morning. There was no challenge regarding the text messages. Regarding the phone calls, I doubt I might have missed some calls because I might be on transportation when the phone rings, because I have not saved the phone number and I might not know for the number may be new. There was no such challenge. I am married and I live with my wife. She may have seen the message before I saw it and told me to be*

reminded. It was only she that knew about the case. Nobody else knows it. Regarding the phone call, I would not pick some of them. I have been relying on text messages. If I am at the office for example, I may pick it. However, I just listen to the dialer. I do not ask questions for example."

According to the 38-year-old female participant, the SMS text messages created an emotional feeling of illness and discomfort, but these feelings diminished after a short time. The participant also said the risk of discontinuing the TB medication information had made her think about the risk of contracting multi-drug resistant TB, which made her feel quite depressed. Yet, the participant believed that the adherence intervention was beneficial because it alerted her to giving due attention to the TB medication,

"There is a feeling of shock that you face when you receive the message. However, you will manage it by cooling down. It gives some inconvenience when you remember that you are living with the illness. It is overwhelming. It is also frustrating when it is said that dropping the medication may put you to death. The messages thus make you think about the illness now and then. It makes you overwhelmed by the condition. For example, I worry that it may develop to the next stage of TB (multi-drug resistant TB). It gives you certain depression. There was a time that I sat down and cried contemplating that I am in too bad health condition that needs everyday messaging. It may have a good effect of course. You can manage depression and give due attention to the condition. You get back from the uncomfortable mood and pursuing courage."

7.6. Factors associated with adoption intention

In this section, the results of factors associated with the adoption intention of a mobile-assisted medication adherence support (Ma-MAS) intervention are presented. The Unified Theory of Acceptance and Use of Technology model was applied to assess the acceptance of the intervention and its associated factors. Throughout this thesis, the term 'adoption intention' 'behavioural intention' and 'acceptance' are used interchangeably.

7.7. Demographic characteristics of the participants

The adoption intention to use mobile-assisted adherence intervention and the associated factors were assessed by surveying 83 TB patients who received a daily SMS message and weekly phone calls. Among the respondents of the survey, 59% were males and 41% were females. The median age of the participants was 28 years. In each grade, the majority of respondents had completed primary education grade1-8 (43.37%) and followed by above grade 12, which was corresponding to 30.12% (see Table 25). All participants included in this survey had an experience for the mobile–assisted adherence support intervention for two months, and all participants were volunteered to receive a daily SMS text message and weekly phone calls related to TB medication adherence. Additionally, in the regression analysis, the demographic characteristics of the participants (age and gender) had no statistical significance in relation with the constructs of the unified theory of acceptance and use of technology.

Table 25: Demographic characteristics of adult TB patients, Addis Ababa, Ethiopia

Variables	Frequency	Percentage
Sex		
Male	49	59.04%
Female	34	40.96%
Age in years		
Mean (Sd)	31.98 (±11.10)	
Median (IQR)	28 (13)	
Educational status		
No formal Education	1	1.20%
1-8 grade	36	43.37%
9-10 grade	13	15.66%
11-12 grade	8	9.64%
Above 12 grades	25	30.12%

Sd: standard deviation, IQR: interquartile range

7.8. Measurement model

7.8.1. Construct validity and reliability of Unified theory of acceptance and use of technology

For the construct of unified theory of acceptance and use of technology, the measurement items showed convergence validity and reliability within acceptable levels. The AVE value of all constructs in the model was greater than 0.5, and the CR value was higher than the AVE value. There was a greater level of reliability in both the composite and Cronbach alpha which was greater than in the acceptable standard of 0.7 (see Table 26).

Table 26: Construct validity and reliability of unified theory of acceptance and use of technology

Constructs and Items	Factor loading	R^2	AVE	CR	CA
Performance expectancy (PE)					
PE1: Using mobile SMS and calls would help me to remember my daily medication intake	0.832	0.583	0.709	0.906	0.904
PE2: Using mobile SMS and calls would help me to remember my refill medication visits at the scheduled date	0.912	0.722			
PE3: Mobile SMS and calls would be very useful for my follow-up treatment	0.879	0.899			
PE4: Mobile SMS and calls would provide very useful services and information to me	0.734	0.573			
Effort expectancy (EE)					
EE1: Learning to operate mobile SMS and calls would be easy for me	0.793	0.628	0.728	0.888	0.887
EE2: My interaction with health professionals through mobile SMS and calls would be clear and understandable	0.848	0.719			
EE3: It will be easy for me to become skillful at sending, receiving, reading, and interpreting mobile SMS text	0.915	0.836			
Social Influence (SI)					
SI1: People who are important to me think that I should use mobile SMS and calls	0.797	0.523	0.591	0.850	0.850
SI2: People who influence my behaviour think that I should use mobile SMS and calls	0.920	0.817			
SI3: The health professionals of this health facility have been helpful in explaining the use of mobile SMS and calls	0.621	0.363			
SI4: The health facility has indicated that it would support the use of mobile SMS and calls for my treatment follow-up	0.704	0.477			
Facilitating Conditions (FC)					
FC1: I have the resources necessary to use mobile SMS and calls	0.591	0.349	0.590	0.795	0.779
FC2: I have the knowledge necessary to use mobile SMS and calls	0.851	0.724			
FC3: I believe I can get reliable help from health professionals when I have difficulties using mobile SMS and calls	0.794	0.631			
Attitude (AT)					
AT1: Using mobile SMS and calls is a good idea for medication reminders	0.789	0.622	0.606	0.821	0.817
AT2: I believe that mobile SMS and calls can be utilized to improve my medication intake adherence and refill visits.	0.844	0.713			
AT3: Mobile SMS and calls are easy to work with	0.695	0.483			
Behavioural Intention (BI)					
BI1: I predict I will use mobile SMS and calls in the next months for my treatment follow-up	0.866	0.749	0.740	0.895	0.881
BI2: I prefer to use mobile SMS and calls to remember medications intake and refill visits	0.876	0.766			
BI3: I intend to use the mobile SMS and calls for my treatment follow-up when it is available	0.839	0.704			

AVE : Average Variance Extracted, CR is Composite Reliability, CA is Cronbach Alpha

7.8.2. Confirmatory factor analysis

The structural equation modeling analysis found that the construct validity of the sampling measurement items met the acceptable standard. The items relationship with respective construct were statistically significant; performance expectancy (4 items), effort expectancy (3 items), social influence (4 items), facilitating conditions (3 items), attitude (3 items) and behavioural intention (3 items). The model fitness of the construct validity met the acceptable standard criteria; the RMSEA and SRMR were less than or equal to 0.06 and 0.08, respectively and the CFI and TLI were greater than 0.95.

7.8.3. Construct correlation coefficient and discriminant validity

The correlation matrix between the constructs of unified theory of acceptance and use of technology indicated that there was a statistically significant positive correlation among the constructs of performance expectancy, effort expectancy, social influence, facilitation conditions, attitude and behavioural intention (P value < 0.01) (see Table 27). The measurement model of UTAUT fulfils the discriminant validity standard criteria, the square root of AVE is greater than the correlation coefficient value of the construct with another construct.

Table 27: Descriptive statistics, correlation coefficient, and discriminant validity of UTAUT

Construct	No. Items	Mean (SD)	PE	EE	SI	FC	AT	BI
PE	4	18.15 (2.04)	**1**					
EE	3	13.59 (1.63)	0.74	**1**				
SI	4	17.81 (1.78)	0.58	0.65	**1**			
FC	3	13.32 (1.49)	0.67	0.75	0.63	**1**		
AT	3	13.49 (1.31)	0.69	0.65	0.69	0.71	**1**	
BI	3	13.18 (1.80)	0.62	0.62	0.69	0.58	0.72	**1**
Average Variance Extracted (AVE)			0.709	0.728	0.591	0.590	0.606	0.740
The square root of AVE			0.84	0.85	0.77	0.76	0.78	0.86

7.9. Structural model of Unified theory of acceptance and use of technology

7.9.1. Original UTAUT model analysis

In the original unified theory of acceptance and use of technology model, performance expectancy and social influence had a statistically significant positive direct effect on behavioural intention (β=0.22 and β=0.47, respectively, P value <0.05). Therefore, hypothesis 1 and 3 in the originally proposed unified theory of acceptance and use of technology are supported. However, there was no statistically significant relationship between effort expectancy and behavioural intention prediction of mobile-assisted medication adherence support intervention adoption. The original model of UTAUT explained 56% of variance in behavioural intention of mobile-assisted medication adherence support intervention adoption.

7.9.2. Modified UTAUT model analysis

In the modified unified theory of acceptance and use of technology, social influence and attitude had a direct influence on behavioural intention of mobile-assisted adherence intervention (β=0.30 and β=0.54, respectively, P value <0.01). However, performance expectancy and facilitating conditions had only indirect positive effects on behavioural intention mediating through attitude. Performance expectancy, social influence, and facilitating condition had a direct positive effect on attitudes towards mobile-assisted medication adherence support interventions (β=0.21, β=0.25, β=0.29, respectively, p value<0.01). However, the effort expectancy had no statistically significant positive direct effect on attitude and behavioural intention. Therefore, under the modified unified theory of acceptance and use of technology model, hypotheses 2, 5, 6, and 8 are supported (P value<0.01). The modified unified theory of acceptance and use of technology model explained 62% of variance in behavioural intention and 66% of variance in attitude of mobile-assisted medication adherence support intervention. (see Table 28)

Table 28: Construct path relationship in unified theory of acceptance and use of technology

Construct relationship	**Original UTAUT model**	**Modified UTAUT model**
PE → BI	0.22**	0.070
EE → BI	0.15	0.15
SI → BI	0.47***	0.30***
FC → BI		-0.089
AT → BI		0.54***
PE → AT		0.21***
EE → AT		-0.045
SI → AT		0.25***
FC → AT		0.29***
CFI	1	1
TLI	1	1
RMSEA	0	0
R^2 BI	0.56	0.62
R^2 AT		0.66

*P value <0.10, ** P value <0.05, *** P value <0.01,

CHAPTER 8: DISCUSSION OF THE FINDINGS

8.1. Introduction

This research aims to investigate the effectiveness of a mobile-assisted medication adherence support (Ma-MAS) intervention on TB medication adherence. The intervention is developed using the MRC framework for complex intervention with seven non-linear steps and consists of two components: (1) SMS text messages and (2) phone calls. The Ma-MAS intervention is designed based on the Information, Motivation, and Behavioural skills (IMB) model and the behavioural change technique taxonomy. To ensure the quality of the intervention, senior experts and health professionals who worked at the ground level were involved in the validation of the SMS text messages and reviewing the checklist questions for phone calls. Before the effectiveness trial began, the feasibility and acceptability of the Ma-MAS intervention were also assessed.

The effectiveness of the Ma-MAS intervention was evaluated using a randomised control trial, while patients' perceptions, experiences, and adoption intention were further evaluated using empirical and interpretive research approaches. The findings of this study will make a valuable contribution to the promotion of TB medication adherence using mobile technology.

8.2. Key findings

The following major findings were discovered:

1. The Mobile-assisted medication adherence support (Ma-MAS) intervention significantly improved adherence to TB medication by 15.25% after eight weeks of the intervention compared to the standard care alone in the control group. Ma-MAS also significantly improved adherence to TB medication by 15.30% after four weeks of the intervention compared to the control group.
2. Although the Ma-MAS intervention using the information-motivation-behavioural skills model and behavioural change techniques was shown to be useful to improve TB medication adherence as measured by a urine test for isoniazid (INH) metabolites, Ma-

MAS did not have a statistically significant positive effect on self-reported TB medication adherence. However, in the post-intervention interpretive study most patients reported that Ma-MAS intervention had a positive effect on their TB medication adherence.

3. The Ma-MAS intervention was useful for awareness creation related to the consequence of discontinuing TB medication and the precautions while taking TB medication. Some patients changed their intention of quitting TB medication after discussing the potential consequence of discontinuing TB medication with their healthcare provider through phone calls. The daily SMS text message helped to avoid forgetfulness due to being busy with work or other social activities. The Ma-MAS intervention was also found to be useful to motivate patients to properly adhere to their TB medication and to develop the habit of taking TB medication at a consistent time.
4. The Ma-MAS intervention can also enhance professional care by improving the communication between health professionals and patients that motivates the patients to comply with health advice and take their medication. The Ma-MAS intervention was also found to be useful for health consultation through phone calls without needing to visit the health facility.
5. The Ma-MAS intervention was found to be feasible in terms of access to mobile phones and patients' ability to operate their mobile phone. Most patients were willing to receive SMS text messages and phone calls for TB medication and clinic appointment reminder.
6. Most patients who received SMS text messages and phone calls had a positive attitude and willingness to adopt the intervention, not only for TB treatment care but also other healthcare services in the future.
7. Privacy and confidentiality issues were not a major concern in the implementation of the Ma-MAS intervention. Nevertheless, some patients were afraid of stigma and did not want to disclose their health status. This was particularly the case among TB-HIV co-infected patients.

8.3. Factors affecting non-adherence to TB medication

TB medication adherence is a complex and dynamic phenomenon because multiple factors influence it.[6, 197] Non-adherence to TB medication and lost follow-up from TB treatment remain a public health problem in Ethiopia.[11, 12] This research has identified multiple factors that have been found to affect non-adherence to TB medications in Ethiopia through literature review and qualitative interviews. In different geographical settings, these factors might have a different character or level of influence, but they overlap largely in developing countries.[197]

In this study it was found that some of the influencing factors of non-adherence to TB medication reflect the findings of previous systematic reviews in Ethiopia.[11, 12] These influencing factors for non-adherence to TB medication were forgetfulness, lack of awareness about the disease and its treatment, psychological distress, perceived barrier, long waiting time, drug side effects, pills burden, co-morbidity, being in the continuation phase of treatment and travel distance and associated transportation cost.

However, the current study identified several additional factors contributing to non-adherence to TB medication that had not been identified in the previous two systematic reviews. These factors were patient-centred factors such as perceived wellness, perceived risk and denial of the disease, negligence, and fatigue during the long treatment regime. The social factors were lack of social support, busyness with work, being away from home, perceived and experienced stigma and discrimination. The economic factors were inability to afford sufficient food and being homeless, work type such as daily labour and long-distance drivers. The health service factors were the DOT standard not being correctly implemented, health professional's low commitment to follow through patients' treatment, lack of counselling at the time of diagnosis of TB, poor patient-healthcare provider relationships such as communication gaps and disrespecting patients, quality of the healthcare service, patient (dis)-satisfaction, lack of incentives for healthcare providers to work over the weekend. The treatment related, and lifestyle factors were the persistence of symptoms after initiation of treatment, and the use of substances including the use of alcohol, smoking, and khat chewing.

The Mobile-assisted adherence support (Ma-MAS) intervention is designed considering these underlying factors of non-adherence to TB medication in the local setting. The Ma-MAS intervention includes key information about the disease, its treatment, misconceptions, drug side-effects, the link between non-adherence and treatment outcomes, and the link between substance use and treatment outcomes. The Ma-MAS intervention also includes motivational messages related to attitude and beliefs about the outcome of adherence or non-adherence for example the negative and positive effect of non-adherence and adherence on treatment outcomes. Behavioural skill information was also an element of the Ma-MAS intervention; designed to develop the self-efficacy to self-manage and to remember their TB medication, to manage the side-effects, and other problem-solving skills, such as what the patients can do when they away from home or unable to come to a health facility to collect their medications and other non-adherence challenges. Therefore, the mobile-assisted medication adherence support intervention was expected to bring positive improvement in adherence to TB medication because it was designed with locally available evidence to overcome factors of non-adherence to the prescribed TB medication. This intervention is particularly important in low resource settings like Ethiopia because there is no governmental or non-governmental organization sustainably implementing an adherence intervention to promote TB medication adherence. The Ma-MAS intervention may also be useful when the DOT standard program is interrupted or not correctly implemented such as occurred during the COVID-19 pandemic.

8.4. Effectiveness of Ma-MAS intervention

The experimental trial showed that Ma-MAS significantly improved adherence to TB medication after eight weeks of intervention. The Ma-MAS group participants had 15.25% higher TB medication adherence compared to the control group participants who received the standard care alone. After eight weeks of follow-up, the predicted probability of adherence to TB medication in the Ma-MAS group participants was higher (86%) compared to the control group participants (70%). Participants who received the mobile-assisted medication adherence support intervention had 1.2 times higher adherence to TB medication than those

who only received standard care alone. This improvement is a crucial finding, emphasizing the potential of Ma-MAS in enhancing adherence to TB medication. The positive effects of Ma-MAS were not limited to the eight-week, the experimental trial showed that Ma-MAS had similar effect after four weeks of intervention. The Ma-MAS group participants had 15.30% higher adherence to TB medication compared to participants who only received the standard care alone in the control group. After four weeks of follow-up, the predictive probability of adherence was higher in the Ma-MAS group participants (93%) than the control group participants (77%). The Ma-MAS intervention effect remained the same after sensitivity analysis which includes the missing and loss to follow up outcomes in the analysis (see Appendix Seven).

The experimental trial showed a notable decrease in adherence proportion for both the Ma-MAS and control groups participants, with reductions of 5.86% and 5.81%, respectively, from week four to eight. Despite these declines, the Ma-MAS intervention maintained its effectiveness in improving TB medication adherence. The decrease in the proportion of adherence observed in both the Ma-MAS and control groups from week four to eight might be due to the duration of treatment. This needs further study on the factors contributing to the observed decreases and the development of potential strategies to sustain the adherence over time.

Although the Ma-MAS intervention significantly improved TB medication adherence when measured by urine tests for isoniazid (INH) metabolites after four and eight weeks of intervention, Ma-MAS did not show statistically significant improvement on self-reported TB medication adherence; this needs further investigation. However, this might be because self-report adherence can be affected by various types of bias such as recall bias, social desirability bias, the way questions are asked, and the way the questionnaires are constructed, and thus might not be a reliable measurement for adherence to TB medication.[138]

There is a conflict in the evidence regarding the effectiveness of SMS texts on self-reported TB medication adherence. Some SMS text message-based interventions did not show significant improvement on self-reported TB medication adherence. For example, in randomised control trials in Pakistan,[121] Argentina[69], and Cameroon,[122] a daily SMS text message did not show significant improvement in self-reported TB medication adherence.

However, in India a quasi-experimental design found that daily SMS text message and weekly phone calls for 90-days significantly improved self-reported TB medication adherence,[198] and in China a randomised control trial, the combination of an audio reminded medication monitor and SMS text messages, showed a significant improvement in TB medication adherence.[123] Another randomised control trial in China found that a daily SMS text message caused a significant improvement, reducing missed doses of TB medication.[125] In Saudi Arabia a randomised control trial, a daily SMS text message during the first two months of treatment, significantly improved self-reported TB medication adherence.[199] In Indonesia, a quasi-experimental study indicated that SMS text messages can replace DOT supervision by a healthcare provider and be effective and efficient for TB medication adherence.[200]. Another Indonesian a quasi-experimental study found that a daily SMS text message significantly improved adherence to TB medication compared to the control group who only received the standard care.[201] In Ethiopia a randomised control trial, using text messages with a graphic based reminder, was found effective for self-reported TB medication adherence.[85]

The Ma-MAS intervention was found useful to raise awareness for patients about the consequence of discontinuing TB medication and the necessary precautions while taking TB medication. As a result, some patients changed their intention to quit their TB medication after they discussed the possible consequences with a healthcare provider through phone calls. The phone calls allow the patient to ask questions related to TB disease and its treatment. Awareness about the seriousness of TB and discontinuing its treatment is important for adherence to TB medication.[83] In a study in Peru, SMS text messages were found useful for

raising awareness of the disease and its treatment.[67] A Sudan study also found that SMS text messages and phone calls were effective in improving knowledge about TB treatment.[202] A study in India also found that phone calls were useful for patient communication about side-effects, symptoms of the disease and nutrition.[203]

The current study demonstrates that daily SMS text messages can remind patients to take their TB medication. The daily SMS text message helps to avoid forgetfulness due to being busy with work or other social activities. The SMS text messages reminded patients when they did not remember to take their medication. The same findings were reported in studies conducted in Uganda and Pakistan which reported patients believe that SMS text messages improve TB medication adherence because they are a good reminder about their medications.[204, 205] The current study also found that the daily SMS text message was useful to embed the habit of taking TB medication at a consistent time.

The Ma-MAS intervention using SMS text messages and phone calls was also useful to motivate patients to properly adhere to their TB medication. The daily SMS text message was found to be useful to avoid negligence and ensure adherence to TB medication. The same finding was reported from Uganda, Mozambique and in Pakistan studies that reported adherence monitoring through SMS text messages enhance the patients' motivation and commitment to adherence to TB medication, which helps to develop the habit of taking TB medication at a consistent time.[68, 132, 205]

The Ma-MAS trial also discovered that the SMS text message and phone call intervention also enhanced the patients' sense of receiving professional care. Patients were able to ask questions and obtain answers from a health professional through phone calls which enhance the patients' feeling of receiving professional care and satisfaction with care. Patients feeling cared for and having a good relationship with their healthcare provider should enhance the patient's commitment to adherence. This is consistent with a previous trial in Northwest Ethiopia, involving text messages with a graphic based reminder, that significantly improved

healthcare provider-patient relationship.[85] The same finding was also reported in Mozambique, Uganda and Pakistan studies which found SMS text messages enhance the patient-healthcare provider relationship; patients feeling cared for and supported by health professionals.[68, 204, 205] A Canadian study also reported that SMS text messages for TB medication reminder were found to be useful and promoted a feeling of being cared for and having a good relationship with a healthcare provider.[206] A Lesotho study also found that a mobile-based SMS text messages intervention enhanced patient-healthcare provider communication for HIV/TB treatment support. [207]

The Ma-MAS intervention (phone calls) was found to be useful for health consultations beyond adherence improvement. Patients were satisfied because they were able to consult health professionals regarding any health issues without going to a health facility. The central and northwest Ethiopia studies also showed that HIV Patients would like to receive health advice through mobile phone SMS text messages or phone calls. [71, 208]

8.5. Ma-MAS intervention design

The way the adherence intervention is designed and how the outcome (adherence to medication) is measured is important in randomised control trials. Ma-MAS showed promising results that could help to improve adherence to TB medication, but a large-scale test and more evidence are needed. Most previous adherence interventions were not designed based on a theoretical foundation, using local evidence or a behavioural change models and techniques, which might be the reason they are sometimes ineffective. However, notably, a trial Argentina that developed SMS text messages based on the IMB model, [209] and sent reminders twice a week for 8 weeks, did not show a significant improvement in TB medication adherence.[69] In the current study, the Ma-MAS intervention using validated SMS text messages sent daily for 8 weeks and weekly phone calls to reinforce the SMS text messages was found to be effective. The Ma-MAS intervention is designed to be broadly useful, beyond use as a simple reminder of TB medication adherence, building relationships, motivation, and self-efficacy.

Considering the pros and cons of SMS text messages or phone calls, the Ma-MAS intervention was designed to use both SMS text messages and phone calls for promoting TB medication adherence. Health professionals believed that adding a phone call intervention to the SMS text messages can make the adherence intervention more interactive and engaging compared to only using two-way SMS text messages, and it is also a good means of communication to get feedback from patients about their experience, side-effects and health status (see Appendix Two).

Sending SMS text messages or phone calls for TB medication reminders does not cause concern for most patients because they believe that their health professionals' intervention is for their benefit. However, most health professionals did not recommend making a phone call daily, due to the possibility of disturbing patients and the difficulty of reaching a large number of patients every day. Thus, in the Ma-MAS intervention a daily SMS text message and a weekly phone call were designed and implemented in the trial. However, after the trial was implemented, most patients wanted to increase the number of phone calls to at least twice a week because patients would have an opportunity to discuss any health issues encountered during the preceding week. For less educated people or those who struggle to adhere to their TB medication, a weekly phone call might not be adequate. But most participants believe that sending a daily SMS text message was appropriate. Most of the previous trials also used a daily SMS text message (see Table 3).

In this study, patients emphasized their preference for the time of sending SMS text messages and making phone calls to be aligned with their routine TB medication schedule. In pre-intervention assessment, both patients and health professionals believe that morning between 7:30am to 8:00am is appropriate time for sending SMS text messages and making phone calls for TB medication reminders. And, after the trial of Ma-MAS intervention, most patients stated the time of SMS text message delivery was convenient, even if it did not precisely align with their medication intake. Yet, some patients would like to receive SMS text messages and phone calls in the early morning, particularly at 7:00am and earlier. This

difference in preferences indicates the importance of scheduling SMS text messages and phone calls at the time of patient preference.

Most health professionals believe that an adherence intervention using SMS text messages and phone calls should be implemented for the whole TB treatment period. The reason for this was that the daily DOT (Directly Observed Treatment) was generally not implemented in the initial phase of TB treatment after the emergence of the COVID-19 pandemic, and patients became negligent because they feel well (relatively) and at times forget to take their medications or are lost from their treatment regimen during the continuation phase of treatment (see Appendix Two). The Ma-MAS intervention was implemented for eight weeks as an initial trial. After completion of the trial intervention, most patients stated they would like the Ma-MAS intervention implemented for the whole period of treatment. Several claimed this was because some patients may be reckless or have addictive behaviours, or they may not have family members support to remember their medication, and patients might not receive adequate on going advice about their treatment.

Participants in the Ma-MAS intervention believe that the content of the SMS text messages is appropriate and useful to promote TB medication adherence. However, some participants also recommended to avoid repetition of some SMS text messages. Most participants also accepted the information communicated through phone calls because it was designed in the form of open questions that support two-way communication. In the content of SMS text messages and phone calls, participants recommend adding content such as the cause and prevention of TB, TB diagnosis categories and their related symptoms, TB treatment and its side effects, food and nutrition requirements, substance use and mental health advice. Some participants also suggested designing the SMS text messages and phone calls in question-and-answer format. Designing a digital health intervention by considering the feedback of the targeted beneficiaries is highly recommended and should have a beneficial effect on TB medication adherence.[210] Thus, the suggested feedback of the patients' needs to be added in the future scale-up of a Ma-MAS intervention.

The potential privacy and confidentiality issues related to the SMS text messages and phone calls were not considered a major problem by patients. However, some patients were concerned about the stigma of TB treatment and did not want to disclose their health status to other people. As a result, they hid the SMS text messages and some patients did not pick up phone calls when they were in a public place. Privacy and confidentiality issues were especially of concern among TB-HIV co-infected patients.

A similar finding was reported in a Mozambique study which showed that TB and HIV patients had concerns about the privacy and confidentiality issues related with disclosure of their HIV status in SMS text messages.[68] In a Peru study the need for careful handling of patients information to avoid stigma related with the disease was also identified as an issue.[67] The qualitative findings of studies in Uganda and Pakistan also reflected patients concern about disclosure of their health status if other people see the SMS text messages.[132, 205] The concern about privacy and confidentiality was high among TB-HIV co-infected patients.[205] In central and northwest Ethiopia studies, privacy and confidentiality issues were a concern of some patients and related to SMS text messages for promoting antiretroviral therapy (ART) medication.[71, 208]

Therefore, in an Ma-MAS intervention, privacy and confidentiality should be carefully managed, patients should have clear information about the intervention and provide informed-consent before the implementation of the intervention. Further protection mechanisms are also required to protect the privacy and confidentiality of the patient's information.

8.6. Feasibility and acceptability of Ma-MAS intervention

The Ma-MAS intervention was found to be technically feasible to implement because most patients have their own mobile phone or have access to a trusted family member's or caregiver's mobile phone; the proportion of patients with their own mobile phone was 88% and 62.5% of patients without personal mobile phones have access to a family member's or caregiver's mobile phone. On the other hand, a relatively small percentage (4.3%) of patients

did not have personal mobile phones and lacked access to a mobile phone through their family members or caregivers. This was consistent with the demography of Ethiopia and a health survey of 2019 which reports 68% of households in the country have their own mobile phone: 87% in urban and 59% in rural.[28] The current study also found that most patients were confident to operate a mobile phone to receive, read and send SMS text messages. Most patients were also confident to make a phone call (89.7%), please call me back (miss call) (82%) and set a reminder (79%). This indicates the growth in use of mobile phones and high digital literacy are an opportunity to use a mobile-based adherence intervention using SMS text messages and phone calls in Ethiopia.

The mobile adherence intervention was also well accepted by both patients and healthcare providers in this study. The cross-sectional survey indicates that most patients who have their own mobile phone were willing to receive an SMS text message reminder for medication intake (93%) and clinic appointments (92%). In addition, most patients were also willing to receive phone calls for medication intake (91%) and clinic appointment reminders (93%). These results indicate that patients with personal mobile phones were highly willing to receive SMS text messages and phone calls for medication intake and clinic appointment reminders. Most patients were also willing to receive SMS text message and phone call reminders with their caregiver's or family member's mobile phones, even when they did not own a mobile phone. These findings highlight a significant opportunity to promote TB medication adherence and optimize patient and family engagement in TB treatment. The same finding was shown in the interpretive study; most patients believe that SMS texts and phone calls would help them to remember their medications, and some patients also believe that SMS text messages and phone calls can avoid the unwanted consequences of non-adherence to TB medication. These supports the use of mobile based adherence interventions along with treatment administration options such as DOT, VOT, non-daily DOT for promoting medication adherence and treatment outcomes.[5]

The current research findings are consistent with previous studies conducted in Ethiopia among HIV patients, which found high willingness to receive SMS text messages or phone calls for ART medication reminder in central Ethiopia (91%) and northwest Ethiopia among HIV patients (96%).[71, 208] However, the current research shows a higher willingness to receive SMS text messages or phone calls for clinic appointment reminder compared to the central Ethiopia (41%) and northwest Ethiopia (60%) studies. A Uganda study also reported that mobile-based SMS text messages and phone calls were found to be an acceptable intervention.[211] A similar finding was reported in Peru and Indian studies which demonstrate that TB patients were willing to receive phone calls or SMS text messages for TB medication reminder and clinic appointments.[67, 212] Therefore, in most geographical settings a mobile based adherence intervention to promote TB medication has high acceptance by patients and healthcare providers. For example, in an Indian study, 95% of TB patients wished to use mobile phone calls and SMS reminders for TB medication adherence instead of using DOTs.[212]

Participants in the Ma-MAS intervention had a positive attitude towards the SMS text messages and phone calls though some participants preferred SMS text messages over phone calls, while others preferred phone calls over SMS text messages. This study found that participants had high willingness to adopt a mobile-based adherence intervention using SMS text messages or phone calls not only for TB treatment care but also for other healthcare services. Participants in the Ma-MAS intervention believe that the intervention had a positive effect on their TB medication adherence. The same findings were reported from two Pakistan studies which reported SMS text messages were found to be acceptable and useful.[132, 204] In a Uganda study patients supported the usefulness of SMS text messages for TB medication intake and clinic appointment reminder. [213] In the Saudi Arabia randomised trial, after 8 weeks of daily SMS text message, TB patients were satisfied with the SMS text messages, which were perceived to be useful and they were willing to use them in the future.[199]

8.7. Factors affecting adoption intention of Ma-MAS intervention

In the current study, it was found that performance expectancy and social influence can positively predict the acceptance of a mobile-assisted adherence intervention, according with the original theory of acceptance and use of technology model. This indicates that as patients perceive the benefits of the Ma-MAS intervention for adherence, the acceptability of the intervention will increase. And as patient's perceive that their social connections (families, friends, healthcare provider) believe the patient should use the Ma-MAS intervention for their TB medication reminder, the patient's acceptability of the intervention will increase. However, the effort expectancy prediction on behavioural intentions of the Ma-MAS intervention did not have a statistically significant finding. This is not consistent with the original unified theory of acceptance and use of technology.[170] This might be because all participants in the current study had 8 weeks of intervention experience and were digitally literate, which could be the reason the ease of use did not have a significant effect on the intention to use the Ma-MAS intervention.

This study also found that the social influence and attitude can positively predict acceptance of the mobile assisted adherence intervention in the modified unified theory of acceptance and use of technology. This means that when the patient perceived high social influence and a positive attitude towards the Ma-MAS intervention, they were more likely to accept the intervention. This study also found that performance expectancy, social influence and facilitating conditions positively predict the attitude of the participants towards the Ma-MAS intervention. Indeed, performance expectancy and facilitating conditions had a direct effect on attitude and an indirect effect on the acceptance of Ma-MAS intervention. However, the current study contrasts with the modified unified theory of acceptance and use of technology model which indicated performance expectancy and facilitating conditions have a direct effect on the acceptance of technology, and effort expectancy has a direct and indirect effect on attitude and acceptance.[173] This means the ease of engaging with the SMS text messages or phone calls did not significantly affect the acceptance of the Ma-MAS intervention which might be

due to all the participants of this study digitally literate and experienced. This needs further investigation in a larger sample.

8.8. Facilitators and challenges of Ma-MAS intervention

The high coverage of mobile phones, and the high acceptance of a mobile-assisted medication adherence support intervention by patients and health professionals are an opportunity to sustain the Ma-MAS intervention if it is implemented on a larger scale. This is consistent with the literature review which reported the acceptance and positive attitude of mHealth were driving facilitators to mHealth implementation.[214] However, the scale up of a mobile-assisted adherence intervention might be challenged by limited infrastructure such as the availability of telephones in the TB clinic, network interruptions, electricity interruptions, healthcare work load, and some patients may not have their own mobile phone or may not be digitally literate. According to the literature review, these challenges are also experienced in many low-resource settings, and include unreliable network coverage, an insufficient power supply, unstable internet services, a lack of policy to protect data privacy, a lack of funding, an inadequate healthcare workforce, and poor digital illiteracy.[214]

To sustain a mobile-assisted medication adherence support intervention the following conditions are highly recommended: improving the infrastructure including telephone access at each TB clinic, increase network performance and mobile coverage, assure reliable electricity supply, address informed patient consent including privacy and confidentiality concerns, utilizing the patient's preferred time for SMS texts and phone calls, using a relative's mobile phone with mutual agreement when the patient does not have a mobile phone or cannot read and understand SMS text messages, checking the functionality of each patient's mobile phone during registration, an immediate substitution of mobile phones when the patient changes or loses their mobile phone, giving a unique health service name for the sender of SMS text messages and phone calls to increase the chance that the recipients will read and answer calls, and drafting the messages in the patient's preferred language.

In summary, the Ma-MAS intervention, based on the content of information, motivation, and behavioural skills combined with behavioural change techniques, can address major factors of TB medication non-adherence and therefore is capable of improving TB medication adherence. The Ma-MAS intervention was found to be useful for TB medication reminder, habit formation, awareness creation, patient motivation, perceived professional care and health consultation. Thus, the current research supports the use of the information, motivation, and behavioural skill model [160, 215] combined with a behavioural change technique taxonomy [158] based on local evidence and cultural context for promoting TB medication adherence.

8.9. Strengths and limitations of the study

This study has several strengths, including the use of a behavioural change model and a behavioural change technique to develop an adherence intervention using SMS text messages and phone calls, based on local evidence about non-adherence to TB medication and cultural context, including utilizing local language. Unlike previous adherence interventions, this trial combined SMS text messages with phone calls, which resulted promising outcomes. Developing the intervention systematically and measuring the outcome correctly are crucial for the validity of the randomised control trial. As a result, the intervention was systematically developed and validated in the local context through a collaborative effort involving senior experts, health professionals, and patients, responding to the needs of the target audience. The primary desired outcome of medication adherence was assessed using a reliable measurement (IsoScreen kit) to detect NIH metabolites in urine, which is a strength of the study. The Ma-MAS intervention was evaluated using interpretive and empirical studies, which is also a strength of the study.

However, the study also has some limitations. The IsoScreen test kit only showed short-term medication adherence of 72 hours, which is not indicative of long-term adherence. This was the reason that the IsoScreen kit test was conducted at two points; at the fourth and eighth

weeks of intervention. Although self-reporting can imply long-term adherence and is inexpensive, it lacks reliability and can be affected by recall bias and social desirability bias. As result, a discrepancy was observed in the proportion of adherence measured by the IsoScreen test kit and self-reported adherence. This study was conducted only for eight weeks, so the long-term effect of Ma-MAS on adherence and treatment outcomes is unproven and needs further research.

Although the Ma-MAS intervention was expected to improve the attendance at clinic appointments, the assessment of clinic appointment attendance was, in part disrupted by the COVID-19 pandemic, not successful, and needs further research. The Ma-MAS intervention might be affected by repeated use of some SMS text messages during the eight weeks of the intervention. The SMS text messages and phone calls were not scheduled to match with the patient's real-time medication intake or clinic appointment, which could affect the outcome of the Ma-MAS intervention. The Ma-MAS intervention could not address all non-adherence barriers, including economic factors, travel distances, stigma, discrimination, and other moderating factors that require additional interventions. Some participants without personal mobile phones have enrolled in the randomised trial using their family members' or caregivers' mobile phones. The patient may not always have access to their family member's or caregiver's mobile phone during the scheduled daily messages and weekly phone calls, and the family members or caregivers may forget to communicate the messages to the patients. This could potentially affect the outcome of the Ma-MAS intervention.

The English version questionnaires, SMS text messages, and phone call checklist guide were translated into Amharic, the Ethiopian national language, by a professional language translator and were checked by the principal investigator. However, the translated questionnaires, SMS text messages, and phone call checklist guide were not retranslated into English to check for consistency.

The sample size for structural equation modelling might not be adequate to examine the construct path relationship in the unified theory of acceptance and use of technology, which needs further investigation. It is important to note that interpretive studies do not necessarily indicate statistical significance, and further hypothesis testing with empirical studies is needed. Overall, while this study has several strengths, it also has some limitations that need to be addressed in future research.

CHAPTER 9: CONCLUSIONS AND RECOMMENDATIONS

9.1. Introduction

This chapter encompasses the conclusions and practical recommendations derived from the studies. The conclusions and recommendations are based on the results and discussions of previous chapters. The recommendations are provided across various sections, including implications for policymakers and program managers, implications for health education and communication, implications for health science education and implications for future research.

9.2. Conclusions

The mobile-assisted medication adherence support intervention using SMS text messages and phone calls is a feasible and acceptable intervention that can improve TB medication adherence, especially if it is designed in the local context and supported by an appropriate behavioural change model and technique. This research has shown that a mobile health intervention, using SMS text messages and phone calls, has the potential to improve TB medication adherence.

The effectiveness of the Ma-MAS intervention on TB medication adherence can be explained by the various ways it has been shown to be useful. First, the Ma-MAS intervention serves as a reminder for patients to take their TB medication. This is important as forgetting to take medication is a common reason for non-adherence to TB medication. Second, the intervention promotes habit formation by helping patients establish a routine for taking their medication at a consistent time. This can be particularly helpful for patients who are struggling to adhere to their medication regimen. Third, the Ma-MAS intervention raises awareness about TB and its treatment. This can help patients understand the importance of taking their TB medication as prescribed and the consequences of non-adherence. Fourth, the intervention motivates patients to adhere to TB medication by providing support and feedback. This can help patients feel more engaged and committed to their treatment plan. Fifth, the intervention improves perceived professional care, as patients feel more supported and cared for, which

can help patients stay on their medication regimen. Finally, the Ma-MAS intervention facilitates access to health consultation, which can help patients to discuss any health issues without going to a health facility. However, the success of this intervention depends on how well it is designed and implemented. It is important to tailor the intervention to the local context and the needs of the patients. Additionally, an appropriate behavioural change model and technique should be incorporated to maximize the effectiveness of the intervention.

The current study showed that patients who received SMS text messages and phone calls had a positive attitude and willingness to adopt the intervention for their TB treatment care, as well as for other healthcare services in the future. This suggests that the use of SMS text messages and phone calls could be an effective way to engage patients in their healthcare and improve their adherence to medication. Additionally, the current study found that some patients preferred to receive phone calls rather than SMS text messages, while others preferred SMS text messages over phone calls to remind them of their TB medication. It is important for healthcare providers to take into account these individual patient preferences when implementing Ma-MAS intervention for promoting TB medication adherence.

Although Ma-MAS was found to be effective in improving medication adherence as measured by IsoScreen urine test of INH metabolites, it did not show a statistically significant improvement in self-reported TB medication adherence. This suggests that further investigation is needed to better understand the reasons for this discrepancy and to identify strategies for improving self-reported adherence.

Privacy and confidentiality are crucial to the safety and well-being of patients, and protecting their privacy is a key component of creating a supportive and safe environment. Although privacy and confidentiality were not major concerns expressed by patents during the implementation of the Ma-MAS intervention, some patients, particularly those with TB and HIV, may still be hesitant to disclose their health status due to stigma. In addition to obtaining

informed consent from patients, protection mechanisms are required to safeguard the privacy and confidentiality of the patient's information.

The high coverage of mobile phones and the acceptance of the mobile-assisted medication adherence support (Ma-MAS) intervention among patients and healthcare professionals underpin the opportunity to sustain the intervention on a larger scale. However, the scale-up of a mobile-assisted adherence support intervention can be challenging due to limited health infrastructure, such as the availability of telephones in the TB clinics, communications network and interruptions to electricity supply, healthcare workload, and the relative digital literacy of patients. Some patients may not have access to their own mobile phones or a network, this is particularly challenging in rural settings with limited mobile phone coverage. Addressing this issue may require additional support to effectively improve TB medication adherence.

Non-adherence to TB medication is a complex issue influenced by various factors, including forgetfulness, inadequate knowledge, psychological distress, drug side effects, co-morbidity, healthcare inaccessibility and transportation cost. The current study identified additional factors such as economic constraints, living away from home, poor healthcare provider-patient relationships, healthcare quality, lack of social support, perceived and experienced stigma and discrimination, beliefs towards the disease and treatment, and substance use that also play a role in non-adherence to TB medication. Healthcare managers, providers, and researchers need to consider the underlying factors when designing adherence interventions and may need to implement additional interventions such as social support, financial assistance, improving communication and patient-provider relationships, ensuring adequate support and counselling at diagnosis and addressing the implementation of DOT standards. The Ma-MAS intervention, although designed based on underlying factors, did not tackle all non-adherence factors such as economic constraints, stigma, and discrimination, that underpin the need for extra interventions.

In conclusion, this study suggests compelling evidence supporting the effectiveness of mobile-assisted intervention approaches to medication adherence. This rigorous combination of randomised control trial and interpretive study provides robust outcomes. The results demonstrate the potential use of mobile-assisted intervention in improving medication adherence, particularly in settings where adherence to medication is vital for positive health outcomes but challenging to achieve using conventional approaches. Based on these findings, the implementation and testing of mobile-assisted intervention in other settings, diseases, and medication adherence contexts are highly recommended.

9.3. Recommendations

9.3.1. Implications for policy makers and program managers

The mobile-assisted medication adherence support intervention has shown a promising result, improving TB medication adherence, which can be scaled up to a larger population and different local languages, and for the entire period of TB treatment. Policy makers and program managers should prioritize the development and validation of a locally tailored adherence intervention that addresses the specific needs of the target audience and utilizing the MRC framework.

Sending daily SMS text messages was useful for promoting TB medication adherence, but the frequency of phone calls should be increased from once a week to at least twice a week. It is recommended to implement the Ma-MAS intervention throughout the entire treatment period to obtain the maximum beneficial effect on TB medication adherence and treatment outcomes. To maximize the effectiveness of the intervention, it is important to schedule SMS text messages and phone calls at the patient's preferred time. In situations where a patient does not have their own mobile phone it may be necessary to utilize a relative's mobile phone with mutual agreement. This should be taken into consideration in any efforts to scale up a Ma-MAS intervention. Additionally, during patient registration, it is essential to check the functionality of each patient's mobile phone and ensure immediate substitution in case of any

change or loss. The content of the SMS text messages and phone calls was found useful and acceptable, but the contents of SMS text messages and phone calls may be supplemented, based on the feedback of patients. Drafting messages in the patient's preferred language and giving a unique health service name for the sender of SMS text messages and phone calls may increase the likelihood that recipients will read and answer the phone calls.

Healthcare providers must ensure that privacy and confidentiality of their patients are protected by health policy and procedures, especially for those who may be vulnerable and experience stigma and discrimination. Providing training to healthcare providers on how to support and respect patient privacy will further contribute to the development of a trusting relationship with patients.

The mobile-assisted medication adherence support intervention does not require a smartphone or internet connection, making it highly scalable in low resource settings. However, to sustain the intervention, it is essential to strengthen infrastructure, such as telephone access in TB clinics and other resources. In addition, the SMS text message and phone call intervention can be implemented separately or together with other digital technologies, such as electronic pill boxes or smartphone applications, to further improve TB medication adherence. By combining these technologies and strengthening infrastructure, especially in countries with poorly resourced health systems, it may be possible to sustain and improve the effectiveness of the medication adherence support intervention, ultimately leading to better treatment outcomes.

Moreover, when it comes to sending SMS text messages, choosing the right cloud platform is crucial for ensuring uninterrupted delivery. The selected cloud platform must have the capacity to handle large volumes of SMS traffic and provide reliable service. In addition, a monitoring mechanism is essential to detect any issues that may arise during the delivery process. The monitoring mechanism should be able to identify any failed deliveries and provide insights into the reasons behind those failures. This will enable the sender to take

appropriate action and ensure that all messages are delivered successfully. It is also important to consider factors such as security, scalability, and cost-effectiveness when selecting an SMS text message cloud platform. The platform should have robust security measures in place to protect the privacy and confidentiality of the messages being sent. It should also be able to scale up or down depending on the volume of traffic being handled and be cost-effective for the intended usage.

9.3.2. Implications for health education and communication

The research has demonstrated that healthcare providers can easily communicate with patients and provide them with necessary information and guidance regarding their TB treatment through SMS text messages and phone calls. This can lead to improved patient engagement and adherence to their treatment regimen. Additionally, patients feel they received professional care, leading to increased trust and satisfaction with their care. However, effective communication through phone calls or SMS text messages requires healthcare providers to have good communication skills. Therefore, providing training to healthcare providers in communication skills is essential to ensure that they can effectively communicate with patients and address their concerns and questions. This training may include techniques for active listening, empathy, and clear communication. By improving their communication skills, healthcare providers can build stronger relationships with patients, resulting in improved patient satisfaction, adherence to treatment, and ultimately, better treatment outcomes.

Patient education through SMS text messages and phone calls to promote TB medication adherence is highly recommended. This is because the current study demonstrated that a behavioural intervention using SMS text messages and phone calls is effective in increasing patients' awareness of the consequences of discontinuing TB medication and the precautions they need to take while taking the medication. By using SMS text messages and phone calls, healthcare providers can easily reach out to patients and provide them with the necessary

information and support they need to adhere to their TB medication regimen. This approach is particularly important in the context of TB treatment, as the medication regimen is long and complex, and patients may need ongoing encouragement and education.

In addition to providing information about TB medication adherence using SMS text messages and phone calls, this approach can also help to identify and address any barriers or challenges patients may be facing related to TB treatment. For example, if a patient is experiencing side effects, unable to come to a health facility for medication refill, or travel to other places, healthcare providers can work with them to find solutions that work best for their individual needs.

9.3.3. Implications for health science education

The use of the MRC (Medical Research Council) framework for developing and evaluating complex interventions in a randomised controlled trial (RCT) is considered to be a rigorous and systematic approach to research. Therefore, the current research, which follows MRC framework, can be an exemplar and used in educational material for students, researchers, and practitioners.

The current research can serve as a useful reference for those who want to understand the process of developing and evaluating a complex intervention. The MRC framework used in this research provides a clear and structured pathway for researchers to develop and evaluate an intervention and can lead to better outcomes. By understanding the steps involved in this framework, researchers can learn to develop an intervention and are more likely to succeed.

The research can also be used as a reference for future research. By documenting the intervention development process, the evaluation, and the outcome, the research provides valuable insights for future researchers. The findings can be used to inform the development of new interventions, to identify areas for further research, and to guide the design of future RCTs.

Moreover, the research can be used for educational purposes to teach students about the MRC framework, intervention development, and the importance of RCTs. Students in health-related fields can learn about the systematic approach to intervention development and evaluation, and how to apply this knowledge in their own research.

9.3.4. Implications for future research

The Ma-MAS intervention has shown promising results in a small-scale study. However, the long-term efficacy of this intervention on TB medication adherence and treatment outcomes in large geographic settings is not yet fully understood and requires further investigation.

In order to effectively scale up the Ma-MAS intervention and implement it in a large population, it is important to develop and validate additional content for SMS text messages and phone calls based on the behavioural change technique and model. This will allow for more personalized and targeted SMS text messages that consider individual patient characteristics and needs in different sub-populations or language groups.

This study was conducted among TB patients who took their medication for six months. Therefore, the findings of this study may not be generalizable to patients with multi-drug resistant TB (MDR-TB) or TB patients who take their medication for more than six months, and further research is needed to study the effectiveness of the intervention on TB medication adherence for these populations.

Furthermore, while the current research has focused on the acceptability and effectiveness of the Ma-MAS intervention, it is also important to assess the economic value of this intervention. This will help to determine the cost-effectiveness of the intervention and whether it is a feasible and sustainable solution for improving TB medication adherence in resource-limited settings.

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APPENDIX ONE: FACTORS INFLUENCING PATIENT ADHERENCE TO TB MEDICATION IN ETHIOPIA

Table 29 : Summary of reviewed articles showing factors influencing non-adherence or default or loss to follow up from TB treatment

First Author (year)	Region	Study Design	Sample size	Population	Associated factors of non-adherence to TB medication and loss to follow up/default from TB treatment
Tesfaye et al. (2019)[106]	Oromia	Prospective cohort	268	Active TB Patients	Khat and alcohol use were associated with non-adherence with TB medication. Educational and occupational status were also associated with non-adherence to TB medication.
Sahile et al.(2018) [93]	Addis Ababa	A qualitative study	10	Active TB Patients	Forgetfulness was the factor of TB medication non-adherence. The perceived risk and perceived wellness were also associated with TB medication non-adherence.
Mekonnen et al. (2018) [94]	Amhara	Cross-sectional study	314	Active TB patients	Being in the continuation phase of treatment, the presence of more than one co-morbidity, inadequate knowledge of TB and its treatment, poor-patient provider relationships, and alcohol use were statistically associated with non-adherence to TB treatment. Additionally, forgetting to take medication, being busy with work, and being out of home/town were the reasons mentioned by patients for non-adherence.
Gube et al. (2018)[117]	SNNPR	Cross-sectional study	271	Active TB Patients	Drug side effects, a far distance from the health facility, and prolonged waited time to get healthcare service were statistically associated with non-adherence.
Woimo et al. (2017)[101]	SNNPR	Cross-sectional study	261	Active Pulmonary TB patients	Inadequate knowledge of TB and its treatment, health information at each medication refill visits, a far distance from a health facility (more than 10 km), transportation cost, and cost of medications other than anti-TB.

Tola et al. (2017) [107]	Addis Ababa	Cross-sectional study	698	Active TB patients	Perceived barrier over and perceived benefits directly associated with non-adherence TB medication. Cue to action and psychological distress were indirectly influence non-adherence mediated through perceived barriers and benefits.
Tola et al. (2017) [13]	Addis Ababa	Cross-sectional study	698	Active TB patients	ART status, economic status, alcohol use, perceived barrier, and psychological distress were statistically associated with non-adherence to TB medication.
Gugsa et al. (2017)[113]	SNNPR	A qualitative study	22	Active TB patients	Lack of adequate food, poor communication between healthcare providers and patients, beliefs in traditional healing, unavailability of the healthcare service nearby, drug side-effect and pill burden, stigma, and discrimination.
Getahun et al. 2017 [110]	Addis Ababa	Mixed method design	649	Active TB patients & healthcare provider	Among lost to follow-up patients, inadequate information about TB, healthcare provider-patient relationship (respect and value to patients), lack of support such as transport and nutrition support, less commitment of healthcare provider to towards with the patients were reported as reasons for lost to follow-up.
Ayele et al. (2017)[95]	Amhara	Cross-sectional study	154	Latent TB-HIV patients	Lack of information about isoniazid preventive therapy (IPT), drug side effect, forgetfulness, and being away from home was found factors for non-adherence to isoniazid preventive therapy (IPT).
Diriba et al. (2016) [105]	Oromia	Cross-sectional study	67	Active TB patients	Lack of family support, a far distance from the health facility, drug side-effect, extremely ill, feeling better, education level, and being HIV positive were the factors that lead to non-adherence to TB medication.
Ayele et al. (2016)[114]	SNNPR	Prospective cohort	162	Latent TB-HIV patients	Patients experiencing a high level of HIV stigma and having opportunistic infections statistically associated with non-adherence to isoniazid preventive therapy (IPT).

Tesfahuneygn et al. 2015 [96]	Amhara	Cross-sectional study	200	Active TB patients	Forgetfulness, being away from home, drug side effects, being unable to go to the health facilities on the date of appointment and being hospitalized. TB-HIV infected, alcohol use, smoking, khat chewing, dissatisfied with healthcare service, long waiting time to get the health service significantly associated.
Yasin et al. (2015) [97]	Oromia	Cross-sectional study	53	Active TB-HIV co-infected	Forgetfulness, a far distance from the health facility, and low income were the factors for non-adherence to TB medication.
Mindachew et al. (2014) [98]	Addis Ababa	A qualitative study	12	Latent TB-HIV patients	Forgetfulness, lack of patient information, knowledge about the disease and its treatment, mental health status makes them reluctant to attend follow-up and clinic appointment, not disclosing their HIV status to their family members because of fear of stigma and discrimination and lack of support from family lead them to non-adhere to isoniazid preventive therapy (IPT).
Kiros et al. (2014)[102]	Tigray	Cross-sectional study	278	Active TB patients	The drug-side effect, and knowledge associated non-adherence to TB medication.
Eticha et al. (2014)[99]	Tigray	Cross-sectional study	120	Active TB-HIV co-infected	Patients who don't have caregivers and people who don't have to remind them to take their medications more likely non-adhere to TB medications. Forgetfulness, feeling sick, and being far away from health facilities were the mention of the main reason by the TB-HIV co-infected patients for missing medication.
Berhe et al. (2014)[111]	Addis Ababa	Cross-sectional study	381	Latent TB-HIV patients	Patients who took their medication for ≥ 5 or months high likely to be adherent than those who took for 1-2 months. Patient's friend decision to take the medication less likely non-adherent to isoniazid preventive therapy (IPT).

Nezenega et al. (2011) [116]	SNNPR	Cross-sectional study	531	Active TB patients	Employment status, area of residence, perceived time spent with a healthcare provider, perceived accessibility, perceived waiting time, perceived professional care and overall patient satisfaction were associated with non-adherence to TB medication.
Adane et al. (2013)[19]	Amhara	Cross-sectional study	280	Active TB patients	Forgetfulness, being in the continuation phase, HIV co-infection, and persistence symptoms of TB were the factors for non-adherence to TB medication.
Tadesse et al. (2013) [108]	Amhara	A qualitative	26	Active TB	Access to health facilities, financial burdens, quality of health services and social support are the main reasons for failing to fully adhere to TB medication.
Kebede et al. (2012) [100]	SNNPR	Cross-sectional study	24	Active TB-HIV co-infected	The educational status associated with non-adherence to TB medication. Forgetfulness and transportation cost was mentioned as a reason for non-adherence to medication.
Mindachew et al. (2011)[112]	Addis Ababa	Cross-sectional study	319	Latent TB-HIV patients	Patients who did not received information about IPT, patients not comfortable to take IPT in front of other people, who were not attended regular clinic appointments and drug side effects were associated to non-adherence to isoniazid preventive therapy (IPT).
Gebremariam et al. (2010) [109]	Addis Ababa	A qualitative study	38	Active TB-HIV co-infected & Healthcare Providers	Side effects, pill burden, economic constraints, lack of food, stigma with lack of disclosure, and lack of adequate communication with health professionals were barriers for adherence. While beliefs in the curability of TB, beliefs in the severity of TB in the presence of HIV infection and lack of support from families and health professionals were influenced the non-adherence to TB medication.
Mesfin et al. (2009)[115]	Tigray	Cross-sectional	237	Active TB patients	Lack of supervision and incapable of dealing with patients' illness more likely to interrupt and default from treatment.

Sagbakken et al. (2008) [18]	Addis Ababa	A qualitative study	50	Active TB patients Healthcare providers & Relatives	Transportation costs, poor health status due to illness or slow progression, have not got social support and those did not manage to restore their health and social status were factors for non-adherence.
Shargie et al. (2007)[118]	SNNPR	Prospective cohort study	404	Active TB patients	Continuation phase of treatment, a far distance from the treatment center, and necessity to use public transport were the factors for default from TB treatment.
Michael et al. (2004) [104]	Oromia	Cross-sectional study	114	Defaulted TB patients	Far distance from the health institution, transportation cost and unaware about TB were the major reasons contributing to defaulting.
Tekle et al. (2002)[103]	Oromia	Case-control	1367	Active TB patients	Being in the continuation phase of treatment, lack of family support, inadequate knowledge about treatment duration and drug side effects.

SNNPR: South Nations, Nationalities, People Region, ART: Antiretroviral therapy

APPENDIX TWO: QUALITATIVE ASSESSMENT FOR Ma-MAS INTERVENTION DEVELOPMENT

Demographic characteristics

A total of 21 health professionals were included in the in-depth interviews conducted for the purpose of intervention development, consisting of 10 males and 11 females. Out of the 21 health professionals, 15 were TB focal persons who worked at health facility, and 6 were TB prevention and control experts who worked at the health office. The participants' ages were uniformly distributed within a range of 26 to 58 years. The majority of participants held a bachelor's degree (n=16) (see Table 30).

Table 30: Demographic characteristics of health professionals, Addis Ababa, Ethiopia

Characteristics	n	Participants																				
		A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
Gender																						
Male	10	M							M		M		M	M	M	M		M	M			M
Female	11		F	F	F	F	F	F		F		F					F			F	F	
Age group																						
25-29 years	5				29		26						29			28		29				
30-34 years	5									30	32			31	34							32
35-39 years	4		37			35			35												39	
40+ years	7	47		50				42				53					58		45	47		
Education																						
Diploma	2				D													D				
Bachelor's degree	16		B	B			B		B	B	B	B	B	B	B	B	B		B	B	B	B
Master's degree	3	M				M		M														
Job possession																						
TB focal person (TB-FP) at health facility	15			TB-FP	TB-FP		TB-FP			TB-FP	TB-FP		TB-FP	TB-FP	TB-FP	TB-FP	TB-FP	TB-FP	TB-FP	TB-FP	TB-FP	TB-FP
TB prevention and control expert (TB-PCE) at health office	6	TB-PCE	TB-PCE			TB-PCE		TB-PCE	TB-PCE			TB-PCE										

Education: D is Diploma, B is bachelor's degree, M is master's degree

A total of 15 adult TB patients were included in the in-depth interview, consisting of 10 males and 5 females. The majority of the participants were between the ages of 35-39 years (n=5), followed by those between the ages of 25-29 years (n=4). The majority of participants had completed education beyond grade 12 (see Table 31).

Table 31: Demographic characteristics of adult TB patients, Addis Ababa, Ethiopia

Characteristics	n	**Participants**														
		A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
Gender																
Male	10	M	M	M			M	M			M	M	M	M		M
Female	5				F	F			F	F					F	
Age group																
20-24 years	2											22				24
25-29 years	4				26	26	27		25							
30-34 years	1		33													
35-39 years	5			37				38		35				36	38	
40+ years	3	67									48		67			
Education																
Grade 1-8	3			7				7	8							
Grade 9-12	5										12		12	12	10	10
Grade 12+	7	D		B	D	D	D			D		D				

Education: D is Diploma, B is bachelor's degree

Theme, sub-theme and categories

The thematic analysis of the data identified five themes in relation to the intervention development for TB adherence to medication. The first theme, adherence, explored the factors that influence adherence to TB medication. The second theme, history of health system practice, examined participants' experiences with health system practices related to TB management. The third theme, acceptability of Mobile-assisted Medication Adherence Support (Ma-MAS) intervention, focused on participants' perceptions and attitudes towards mobile-assisted medication adherence support intervention. The fourth theme, convenience, investigated the design of mobile-assisted adherence interventions for optimal convenience. Lastly, the fifth theme, Barriers and Facilitators of Mobile-Assisted Adherence Interventions, explored the factors that hinder or facilitate the success of mobile-assisted adherence interventions. Each of the five themes had several sub-themes, and some of these sub-themes were grouped into categories, which are presented in Table 32.

Table 32: Theme, sub-theme and categories

Theme	Sub-theme	Categories
Adherence: Adherence to TB medication and influencing factors	1. Adherence to TB medication	
	2. Factors affecting TB medication adherence	B. Patient centered factors C. Social-related factors D. Economic related factors E. Health system factors F. Therapy related factors G. Lifestyle related factors H. Geographic access factors
History of health system practice in TB management	1. Adherence intervention and monitoring mechanism 2. DOT standard care during COVID-19 emerged	
Acceptability of mobile-assisted medication adherence support intervention	1. Acceptability and benefits of mobile-assisted adherence intervention 2. Acceptability and preference: SMS versus Phone calls	
Convenience: mobile-assisted medication adherence support intervention design	1. Language of the message 2. Content of the message 3. Comprehension 4. Interactivity 5. Frequency of intervention 6. Time of delivery 7. Duration of the intervention 8. Privacy and confidentiality	
Barriers and facilitators of mobile-assisted adherence interventions	1. Facilitators of mobile-assisted adherence intervention	A. Willingness and high acceptance B. High mobile coverage
	2. Barriers of mobile-assisted adherence intervention	A. Digital illiteracy and ignorance of messages or phone calls B. Have no won mobile or telephone C. Patient's registered wrong phone number or change their phone number D. Health professionals work burden E. Sustainability of the adherence intervention
	3. Suggestions	A. Availing telephone at TB clinic B. Briefing the mobile-assisted adherence intervention C. Using family member's or caregiver's mobile phone D. Checking and updating the patient's phone number E. Giving the project a unique name

Page Break

Theme 1: Adherence to TB medication and influencing factors

Adherence to TB Medication

According to health professionals, non-adherence to TB medication or lost follow-up from TB treatment was a problem at public health facilities in Addis Ababa, Ethiopia. Moreover, they noted that non-adherence to TB medication was more aggravated after the emergence of the COVID-19 pandemic in which the standard DOT program was not implemented. The 53-year-old female TB prevention and control expert stated that

> *"Yes, non-adherence to TB medication is a problem in our sub-city. I am saying so based on the evidence that we have in this sub-city. One of the pieces of evidence is that the effort to follow, tracing and returning patients to medication is not always successful..."*

Another 37 years female TB prevention and control expert added that

> *"Yes, non-adherence to TB medication is still a problem in the city. The magnitude of the problem, of course, varies from time to time. But it is still a problem even though we are observing a decline in recent years. The increase of drug resistance TB that we are observing is one of the indicators for the existence of non-adherence to TB medication."*

In addition, most health professionals from health service delivery point also reported non-adherence to TB medication is a problem in their health facilities, especially this is devastating after the emergence of COVID-19. The 30-year female TB focal person stated that

> *"Yes, it is a problem that we experience in our health facility. We observe the problem from time to time. Before the emergence of COVID-19, non-adherence was not a major problem. But since we have stopped the DOT system, we have observed an increase in the magnitude of the problem. The official guideline is that we should give a one-month medication to reduce risks associated with*

exposure to COVID-19. But in the second month, we discovered three patients who tested positive. This was something that we do not often observe. As a result of that, we are giving one-week medication instead. We also observed that two patients tested positive at the end of their fifth month of the medication. In addition, there was also one patient who was difficult to track. Based on these experiences we have now reverted to the DOT system."

The 28-year-old male TB focal person reported that

> *"In our health facility, it was rare to observe patients who stop the medication before COVID-19. There were no lost patients before COVID-19. ... After COVID-19 emerged we had two lost patients."*

Another 32-year-old male TB focal person said that

> *"We have observed patients who fail to forget their medication ranging from a few days up to many weeks."*

Another 47 years female TB focal person also added that

> *"Yes, non-adherence to TB medication is a problem in our health facility. For instance, I have come across three patients who relapsed and tested positive after taking their treatment. But I have not come across patients who interrupt their medication."*

However, one health professional respondent reported that non-adherence to TB medication or lost to follow up was a problem before the emergence of COVID-19 because patients must come to the health facility daily to take their medication during the intensive phase of the treatment. The 29-year-old male TB focal person said that

> *"It was a problem in the past, especially before the emergence of COVID-19. The standard procedure for administration of TB medication was the DOT system before COVID-19. Now I am doing follow-up with patients every two weeks. It was a problem before the emergence of COVID-19. The DOT was the standard practice and patients must come to the health facility daily to take the medication. ...Some patients may not have the money to cover transportation costs. In addition, some patients may have a job that they have to attend to feed their family and at times they may not be able to come to the health facility."*

Some health professionals hold the view that non-adherence to TB medication or loss to follow-up from TB treatment is not a significant public health concern. The 35-year-old male TB focal person said that

> *"The standard for loss to follow-up from treatment must be below 5% of the total TB patients. In our sub-city, the proportion of patients that lost follow-up from TB treatment currently is a little over 1%. But I still believe that we should be able to reduce this number even though it is below the maximum percentage. The number shows that we have a positive performance."*

Another 29-year-old male TB focal added that

> *"We do not experience that problem while working in this health facility. We often do take the necessary precautions to make sure that we do not experience this problem. When a patient starts the medication, we offer the proper counselling about the importance of adherence and taking the medication as prescribed. We also try to get patients to fully understand the consequences of non-adherence to the medication."*

Another 39-year-old female TB focal person also stated that

> *"No, it is not a problem. I have been working in this position for the last five years. When I compare adherence between the time I started to work here and now, there is a significant improvement. Patients now are very much aware of the importance of adherence to the medication and the possible negative consequences of non-adherence. Nowadays if we are late arriving at the health facility to give the medication to patients, they would call us and urge us to be there on time so that the time for the medication will not pass."*

There was also no indication that patients were not adhering to TB medications in any of the responses of qualitative interview. However, it is important to note that qualitative research may not capture the magnitude of non-adherence to TB medication, as it is not empirical study. The 67-year-old male TB patient said that

> *"I want to get better as soon as possible. So, I take the medication on time. Every day in the morning I take the medication at 8:00 am. I always make sure that not one-minute passes before taking the medication at the time. I am so eager about getting cured. I also do not have alcohol addiction or any other similar matter. I always take the medication on time."*

Another 25-year-old female TB patient also stated that

> *"No, I have never forgotten to take the medication. Even at one time in the past when I went to visit a relative in another town, I had taken the medication with me to take at my relative's home. At one time I also got extremely sick, and I had to stay with another relative who lives in this town and my husband had to get up early at 5:00 am and bring the medication to the place I was staying at, and I was able to take the medication on time. I have always been able to make sure that I have taken the medication on time."*

Factors affecting adherence

Patient-centred factors

According to some health professionals, forgetfulness due to patients' busy work schedules was a contributing factor to non-adherence to TB medication and clinic appointments. The 47year-old female TB prevention and control expert said that

> "*I have observed that sometimes patients would forget their refill visit because of their hectic work. Sometimes the reason could just be they are attending private activities. Sometimes, they may exhaust their medication on a Saturday, or Sunday and they may forget to collect their medication a day before Saturday…"*

Another 32-year-old male TB focal person added that *"They just forget to take the medication, or they may have to attend some personal matter and so they may fail to take the medication."*

According to some health professionals, non-adherence to TB medication is attributed to a lack of awareness about the disease and its consequences of discontinuing TB medication. The 39-year-old female TB focal person said that

> *"The main factor is the patients do not have awareness about the seriousness of failing to take medication properly. Many patients tell us that they do not know the seriousness of non-adherence. Some patients assume that they may not need to take the medication for the whole medication period. But when we sit with them and inform them about the consequences of non-adherence, we observe how their perception changes. Other patients did not realize how important it is to take the medication for the whole period. It is often patients that are not aware of the consequences of non-adherence that are likely to fail to take their medication."*

Another 28-year-old male TB focal person added that

> *"The main factor is lack of awareness of the importance of completing the whole six months period of the medication"*.

Health professionals reported that beliefs associated with treatment and disease were one of the factors contributing to non-adherence to TB medication, the perceived wellness after taking some TB medications being the most raised reason. The 28-year-old male TB focal person said that

> *"For most of them, the reason is that they are feeling better or observing improvements as full recovery and then stop taking the medication. But on the other hand, there are also patients who may not show recovery sooner and who then decide to stop the medication and try other options"*

Another 26-year-old female TB focal person added that

> *"They will still stop their medication when symptoms start to disappear despite repeatedly being told that they should continue to use the medication for the whole six-month period."*

Another 37 years female TB prevention and control officer also stated that

> *"…. Some patients have shown substantial progress in their health after taking some medications and feel that they are cured that could lead them to discontinue their medication."*

In addition, a 47-year-old female TB focal person reported that denial of the disease is one of the contributing factors for non-adherence to TB medication and not starting the TB medication,

"*One of the driving factors for non-adherence to TB medication is that patients may be in denial about their situation. Some of them may be unaware of the issue and may assume that their case is not TB. This is a common issue that we observe with patients that have extra pulmonary TB. The physical pain they experience may be on their knee and ask how their case is TB. These patients have a challenging time accepting the diagnosis and the medication."*

Most TB patients reported that they were adhering to the TB medication because they knew the consequences of non-adherence. The 38-year-old female TB patient said that

"I also know the nature of the disease and the importance of taking the medication on time. Just because I saw an improvement in my health does not mean I would take the medication less seriously. I know that the disease can relapse if the patient stops the medication. I have seen a relapsing disease in my neighbor. My neighbor was taking the medication in the past. But she stopped taking the medication at some point when she observed an improvement in her health condition. But at later time, the illness relapsed, and she later died because the medication did not work."

Another 37-year-old male TB patient added that

"There was a one friend that told me he had to take the medication for another six months because he interrupted the medication for the first time. He informed me that the disease relapsed because he did not take the medication properly in the first instance. He shared his story as a warning for me not to make the mistake that he made. My wife is there to check on me and to inform me to take the medication when the time nears. When I am away from home, she also calls me and asks me if I have taken the medication."

The 35-year-old female TB patient reported that she does not forget TB medications because she knows the consequences of nonadherence,

> *"... If I stopped or forget to take the medication, I will be the one who gets the consequence. I know this is a serious matter and I make sure that I always take the medication in the morning."*

Another 26 years female TB patient added that

> *"I have observed an improvement in my health since starting the medication. But that does not mean I will ponder stopping the medication. That is because I have been made aware of the possible consequences of failing to take the medication for the whole six-month period. I know I must take the medication regardless of the health improvements that I observe myself..."*

In addition, some other TB patients reported that perceived wellness after taking some TB medication is a contributing factor to non-adherence. The 26-year female TB patient said that "O*ne of the reasons is that patients fail to continue to strictly take the medication when they see an improvement in their health. Patients may stop taking the medication because they think that they have been cured."* The 37-year male TB patient also said that *"Some patients may not be aware of the seriousness of the illness. As a result, they only take the medication when they experience physical pain."*

Some health professionals suggest that negligence and fatigue could be contributing factors to non-adherence to TB medication. Patients may become overwhelmed by the demands of their treatment regimen, leading to unintentional non-adherence. Additionally, fatigue or other physical or mental health issues could make it challenging for patients to adhere to their medication regimen. The 50-year-old TB focal person reported that fatigues was commonly observed in young men in the last month of treatment,

"*We observe fatigue in some patients at the end month of the treatment, and patients are not being consistent in taking their medications. We observe these problems among young men. Young men who frequently use motorbikes to earn their livelihood are often exposed to the disease and we also observe the problem of non-adherence with them. Adult people are more careful about their treatment.*"

Another 31 years male TB focal person added that

"One of the reasons for non-adherence to medication is that patients may become negligent and fail to take the medication properly."

Social related factors

According to some health professionals, family support can have a positive impact on TB medication adherence. Patients who receive support from their family members may be more likely to adhere to their medication regimen and attend clinic appointments. The 32-year-old male TB focal person said that

"They also may not have a close family that lives with them and that can support and take care of them as they take the medication."

Another 29-year-old male TB focal person added that

"...there are also patients who may have a job that they have to attend to feed their family and at times they may not be able to come to the health facility. Family or friendship support can influence a patient to consistently take the medication."

Additionally, some TB patients indicated that their families could remember and monitor their TB medication usage. The 48-year-old male TB patient said that stated that

> *"I have a family that depends on me, and I make sure that I take the medication on time for my own and my family's sake. My whole family also checks on me every day to see if I have taken the medication. My wife, my mother, and my sisters always check and ask if I have taken the medication. Therefore, I have never failed to take the medication so far."*

Another 25-year-old female TB patient added that

> *"Initially, my husband used to tell me not to forget taking the medication when he wakes up around 6:00 am to head to his place of work. But later, I became accustomed to taking the medication at that time and I normally wake up at 6:30 am and get water and take the medication."*

Economic factors

According to most health professionals, individuals with low economic status face difficulties in adhering to TB medication. Economic constraints, such as the inability to afford sufficient food, can impact the ability to follow up on TB treatment. Health professional respondents also reported that there were some homeless patients who do not have a contact person and a mobile phone to trace and back them to the treatment when they lost. It is impossible for these patients to afford adequate food and, as a result, they are unable to attend TB treatment appointments on a regular basis. The health 30-year-old female TB focal person said that

> *"The second factor is related to economic status and ability to afford the required diet to take the medication. Taking the medication without the recommended diet supplement is a challenge. This is the case that we observe with HIV AIDS patients who are also taking TB medication."*

Another 58 years female TB focal person added that

> *"One of the reasons for patients to fail to continue to take the medication is related to diet. Patients who may be unable to afford the needed diet may be afraid to take the medication. That is why we observe interruptions with patients."*

The 53-year-old male TB prevention and control expert also said that

> *"Another driving factor for non-adherence is related to economic factors. One of the challenges that patients complain about is taking medication without the appropriate diet. Besides, patients who are at risk of unemployment and loss of income while being at home or coming to a health facility to take the medication may also experience non-adherence. I suspect such a challenge that young patients who are normally engaged in daily and casual labor may be exacerbated due to the impact of COVID-19 on overall economic activity."*

According to health professionals, patients who are homeless or live on the streets often face challenges in adhering to medication due to their lack of a fixed address. Bringing such patients back to treatment can be difficult and requires extensive efforts in tracing them. The 47-year-old male TB prevention and control expert added that

> *"…in the city, there is a large number of TB patients who are homeless. This is the poorest population and as a result, they are often most likely to default from the treatment."*

Another 45-year-old male TB focal person stated that

> "*One of the reasons for non-adherence to the medication is that some of our patients are homeless and people who live on the streets. These patients do not have a fixed address and tracing them and bringing them back to treatment*

is a difficult matter. Other patients may come from other towns to start the treatment. But after a certain period, they may not be able to continue the medication because they do not have a place to stay here and because they are unable to afford to live here. Therefore, economic instability is one of the drivers of non-adherence to medication with these patients."

Another 26-year-old female added that

"It (non-adherence) is mainly much more with patients who live on the street. These patients do not own a personal mobile phone number and we are not always able to reach out to them whenever they miss a refill day or when they fail to come to the health facility to take the medication in the first two months."

Furthermore, the nature of patients' work has an impact on their adherence to TB treatment, as they may be unable to attend regular treatment appointments. Patients engaged in daily labor or those who work night shifts and sleep during the day may miss their scheduled health facility appointments for medication refills. Barriers to adherence to TB medication also include long-distance drivers, whose job nature makes it challenging to follow up on treatment. As a result, this job category may not be suitable for the Directly Observed Treatment (DOT) program, which requires daily presence at the health facility. The 47-year-old male TB prevention and control expert said that

"*The other reason may be related to their work to earn income for their family that may not be fit with their treatment schedule and may not be able to frequently follow their treatment. Sometimes they may work the night shift, and they want to sleep during the daytime and as a result they may not appropriately follow their medications. Some long driver patients may move from one place to the other as a result they may discontinue the treatments."*

Another 42-year-old female TB prevention and control expert said that

> *"I have observed that sometimes patients would forget their refill visit because of hectic work. Sometimes the reason could just be that they are attending a private matter."*

A 32-year-old male TB focal person added that

> *"Some of them may need to go to another town for work and they may at times forget to take the medication with them. So, the movement for work is one of the factors that contribute to non-adherence."*

Health system factors

Most health professional respondents reported that changing the Directly Observed Treatment (DOT) standard from daily medication intake to monthly medication refill visits had a negative impact on medication adherence. This change in the DOT standard made it more challenging for healthcare providers to monitor patients' medication adherence and provide support as needed. Additionally, some health professionals reported an increase in loss to follow-up from TB treatment after the DOT program was changed. The 47-year-old male TB prevention and control expert said that

> *"... Giving one-month medications and not having a follow-up system for checking the patients taking the medication may affect medication adherence. Especially for those in the intensive phase of treatment, the follow-up should have been daily and now it is only done once a month and even for those on a continuation phase of treatment, the follow-up has been pushed to once a month from a weekly basis. This is all done due to the measures taken to slow the spread of COVID-19, but it may affect non-adherence..."*

Another 42-year-old female TB prevention and control expert added that

> *"Changing the DOT system where patients used to come to health facility daily to self-administered medication at home for a month can contribute to non-adherence to medication."*

On the other hand, some health professionals reported that the daily Directly Observed Treatment (DOT) standard posed a challenge for some patients who needed to come to the health facility every day. Patients with limited transportation options may find it difficult to attend daily clinic appointments, which can lead to missed doses of TB medication. The 47-year-old female TB focal person stated that *"On top of that, having to come to the health facility daily frustrates the patients and leads them to interrupt the medication."* Another 29-year-old male TB focal person said that *"The DOT was the standard in which patients were expected to come to the health facility daily to take the medication."*

Some health professionals reported that a lack of commitment from healthcare providers to monitor patients' treatment can have a negative impact on adherence to TB medication. Patients who do not receive adequate support and monitoring from healthcare providers may be more likely to miss doses or discontinue their medication regimen. The 37-year female TB prevention and control expert said that

> *"In intensive phase, I observed two factors that may contribute to non-adherence. The first one is that healthcare professionals do not strictly monitor and observe the patients' medication intake. There is also not a custom for health professionals to contact the patients by phone to check whether they are properly taking their medication once the patients start the continuation phase of treatment. Thus, a lack of commitment by a healthcare professional to monitor patients' medication intake may contribute to non-adherence."*

Additionally, a lack of communication between healthcare providers and patients can lead to misunderstandings or misinformation about TB treatment, which can further impact TB medication adherence. Unable to provide appropriate counselling to the patient at the diagnosis of TB and poor health professional patient relationship also negatively affect adherence to TB medication. The 29-year male TB focal person stated that

> *"There are also gaps in health professionals' commitments in providing counselling and essential information regarding the risks and problems associated with non-adherence. The medication is taken over an extended period and there is always a risk of non-adherence, especially if there is a gap on the side of experts in providing proper counselling. Therefore, counselling can affect medication adherence."*

Another 47-year-old female TB focal person added that

> *"The gap here usually is with the physicians that prescribed the TB medication without properly explaining to the patient about their diagnosis. Such patients are likely to stop the medication. Patients are often more likely to trust their physicians than us (health professionals working primary health care) who give them medication. But if the physician did not explain their case fully, we will have a challenging time convincing the patient... The physician may not tell the patient about the length of medication that he/she prescribed to them. When patients start the medication and inform them of the length of the treatment, they interrupt the medication for a certain period to reach their physician to confirm the length of the medication time. They will interrupt the medication for two or three days and come back to continue the medication."*

Another 39-year-old female TB focal person shared her experience on how poor health professional patient relationship affect adherence to TB medication,

> *"There was, for instance, one patient who lives in the streets around… and he came to our health facility to take the medication. He started the medication in another health facility. Because he did not like how they treated him in that health facility. He was not informed that he will take the medication for six months. But fortunately, he came to our health facility, and he was given all the information that he needed, and he was finally cured... Physicians do not stress why the patient will take the medication for six months. Providing proper information on the consequences of non-adherence will always contribute to addressing the problem..."*

Some patients reported that the health information they received from the health facility about the consequences of non-adherence encouraged them to take their TB medications properly. Patients who are well-informed about the risks associated with non-adherence may be more motivated to adhere to their medication regimen and attend clinic appointments. The 26-year-old female TB patient said that

> *"They (the health professionals) have told me that I will not be cured if I do not take the medication correctly on time. They told me that if I did not take the medication properly, then I would not be cured and that I might be forced to take the medications for up to two years. To avoid that I am taking the medication properly and at the right time.*

Another 36-year-old male TB patient *added that*

> *"When I started to take the medication, the health care experts at the health facility informed me about the consequences of failing to take the medications correctly. They informed me that if I missed the medication for a day or two the*

illness would relapse. After realizing the possible consequences of failing to take the medication as recommended, I have been taking extra care to ensure that I am taking the medication on time."

Some health professionals reported that TB focal persons' lack of incentive to work over the weekend poses a problem with adhering to TB medication. Therefore, some health facilities did not work on weekends. The 47-year-old male TB prevention and control said that *"One of the gaps from the healthcare system is that professionals assigned to work on weekends to administer the medication do not always adhere to the working schedule. Health professionals are not incentivized to work on the weekends that is one of the gaps from the healthcare structure side."*

Therapy-related factors

Some health professionals reported that drug side effects as one of the factors that negatively influence TB medication adherence. The 32-year-old male TB focal person said that

"… the adverse effects of the medication contribute to non-adherence to the medication. Patients experience adverse reactions such as vomiting and nausea until their body becomes familiar with the medication and there may be patients who skip the medication due to these adverse reactions. Patients complain about the adverse reactions until they enter the continuous phase of the treatment."

Another 58-year-old female TB focal person added *that*

"In addition to these, some patients may interrupt their medication due to some of the adverse effects of the medication. The adverse effects may be strong on some patients and patients may choose to stop taking the medication for a few days to get relief."

According to some health professionals, the pill burden associated with other co-morbidities can have a negative impact on adherence to TB medication. The 53-year-old female TB prevention and control expert stated that *"One of the reasons for adherence that we observe with HIV AIDS patients who are also taking TB medication is the Pill Burden."* Another 32-year male TB focal person added that *"sometimes patients experience another disease in addition to TB and they may not take the TB medication for some time."*

Some health professionals have reported that a long treatment regimen can also have a negative impact on adherence to TB medication. The 34-year-old male TB focal person stated that *"One of the reasons for non-adherence has to do with the fact that the medication is taken for a longer period. This means that there is a risk for patients to become forgetful."* Another 50-year-old female TB focal person added that *"The main reason for non-adhering concerning TB patients is the length of the TB treatment period. The medication is expected to be taken for six months, and people who are unstable due to either their working condition or other personal factors are likely to be non-adhere."*

Lifestyle factors

According to some health professionals and TB patient respondents, having an addiction to alcohol was a contributing factor to non-adherence to TB medication. Alcohol addiction can lead to forgetfulness, decreased motivation, and an increased risk of adverse drug reactions. The 30-year-old male TB focal person said that

> *"There are patients who have alcohol and other types of addictions. At the bus station there are a lot of young people working there. Most of them have addiction issues. Those who take TB medication tend to stop taking the medication to revert their addictive behaviour. With some patients, we also observe that they forget to take their time. For instance, one of the patients skips the medication when he takes alcohol. He said he is afraid that taking the medication after having alcohol will damage his liver."*

Another 37-year male TB patient also said that *"...Some other patients may take alcohol and may stop taking the medication."*

Geographical access factors

Most health professionals reported travel distance and transportation cost as factors affecting TB medication non-adherence. It was reported that some patients live far from the health facility, which results in high transportation costs. It is especially difficult during the intensive phase of treatment when medication must be taken daily at the health facility. The 47-year-old male TB prevention and control expert said that

> *"One of the main reasons for non-adherence to medication is that most TB patients are economically low. For some of them, transportation is a challenge because they may not even be able to pay for the taxi, as a result they may default from the treatment."*

Another 37-year-old female TB prevention and control expert added that

> *"…patients may not have sufficient income to pay for transportation to come daily to health facilities to take their medication. Thus, their economic status may have an impact on non-adherence to TB medication."*

Another 29-year-old male TB focal person said that

> *"One of the factors that can lead to non-adherence to TB medication is the distance from patients' residential area to the health facility. The greater the distance between patients' homes and the health facility, the patient is more likely to interrupt medication. To prevent this, when a patient starts the medication, we also check if the distance between the two locations is far..."*

Another *32-year-old male TB focal person added that*

> *"The other factor is distance. Some patients may not be able to afford to pay for a transportation cost for a 'Bajaj.' Most of the TB patients in the first stage as they take the medication are very weak and they cannot walk to the health facility daily. Such patients who cannot afford the transportation cost are more likely to skip taking the medication."*

Theme 2: History of health system practice

Adherence Intervention and mentoring mechanism

According to health professionals surveyed, there is currently no sustainable governmental or non-governmental organization implementing interventions to improve TB medication adherence. However, there were plans for interventional research aimed at improving TB medication adherence. Most health professionals mentioned the ASCENT project, a large cluster randomised trial that was in the pilot phase before the emergence of the COVID-19 pandemic. At the time of the assessment, the project had not yet started. The ASCENT project was planned to be implemented in Addis Ababa and nearby cities in the Oromia region, using digital equipment to send text messages to remind patients to take their medication and sound an alarm if they missed their medication time. The project was planned for implementation in 36 health facilities in Addis Ababa, Ethiopia. Detailed information of the trial is available at the link below.

https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=12241.

The 47-year-old male TB prevention and control expert said that

> "*There was one project called ASCENT. We did the baseline assessment for the pilot program with them. But the project never progressed to the implementation phase. It uses a digital system that sends a text message to a central server when patients open the medication strip. It is aimed at promoting the effective use of technology to monitor medication adherence."*

Another 53-year-old female TB prevention and control expert added

> *"I know there was a plan by one non-governmental organization that came up with the idea of using a digital system to remind patients about taking their medication. It was initially planned to be implemented in a selected few health facility. They planned to utilize a digital box. It provides a reminder service for the patient. When the patient takes the medication, the TB focal person will get a message indicating the patient has taken the medication."*

Most health professionals have reported that they occasionally make phone calls to patients or treatment supporters when patients miss their medication refill appointments, fail to show up for clinic appointments, or are lost from treatment. They may also make phone calls when patients need to undergo sputum tests. Additionally, some health professionals make phone calls to patients who have not taken their medication correctly. The 32-year-old male TB focal person said that

> *"We do not call all the patients. We identified three patient groups to make follow-up calls. The first patient group is those who may struggle economically. The second patient group is those who live in a relatively distant place and far away from the health facility. The third patient group is those who have a low educational qualification. These are people who we think are more likely to be non-adherent to taking the medication. On the other hand, we do have patients*

who are homeless and who live on the streets. These patients are likely to experience non-adherence because of their living conditions and we call them to check if they are taking the medication properly. We also call them to remind them to come and collect the medication. There are of course patients who may not have a phone. For these patients who may not have their own phone, we get a contact person's phone. The contact person is a person who is close to the patient and that we can call if we cannot reach the patient."

Another 32-year-old male TB focal person stated that

"W*e call patients when they fail to come to the health facility for a number of days. But we use our phones to call patients. There is no phone available for us to call. The rule is that if a patient does not come to the health facility for a week, we should start the tracing process and one of the ways is to try to call them."*

Another 58-year-old female TB focal person added that

"We use phone calls to reach patients in the intensive phase of treatment who forget to come to take the medication. The same goes for patients who forget to come on a refill appointment date in the continuation phase of treatment. We also make phone calls to remind patients to come for a sputum test. But we do not make calls to remind patients to take the medication."

Another 45-year-old male TB focal person added that

"Yes, we call patients when they fail to come on their appointment dates. Back when the DOT system was employed patients used to come to the health facility daily. But now since patients come every other week and some of them once a month, we do not have the opportunity to closely monitor their progress as we used to. A phone call is one way for us to reach patients who fail to come

on the appointment date. ...For example, if a patient who takes home a one-week medication fails to come after seven days, we will call him and remind him to come and take the medication as soon as possible. In this manner, we have been using phone calls to follow up with patients to come and get the medication."

Another 50 years female TB focal person said that *"when we see patients default from the treatment, we make phone calls and tell them to continue their TB medications. We often make a phone call to back them to the health facility and give them counselling and guidance services to let them know the importance of taking the TB medications properly and as prescribed by medical experts and if it is discontinued it has a risk."* Another 35 years old female TB prevention and control expert added that "W*hen we identify these patients that are defaulted to their TB treatment, we try to trace their contact information. We also keep the contact information of another person that is close to them, and we make calls and try to get them to continue taking the medication."*

Some health professionals would make a phone call to remind some patients to refill their medications and schedule sputum tests. The 29-year-old female TB focal person said that

"We make calls to monitor how properly they are using their medications. We make at least one phone call per week for all patients. We do not have many patients and we make the phone call once or sometimes twice a week to monitor if they are taking the medication. I am the one who is responsible for making the phone calls. In the past, we would always make phone calls to patients who forgot to come to the health facility for the medication refill visit. We would also make phone calls to patients who have a sputum sample examination. We always keep the contact information of the patient and a family member or some other person who is close to the patient. So, we make phone calls as needed. But the phone calls in the past were not made as part

of monitoring and follow up mechanism to check if patients are taking the medication."

Another 29 years male TB focal person added that

"We give priority to patients on the DOT stage (the first two months of treatment). In addition, we also prioritize patients who were weaker physical status when they start the medication. We make sure that we make phone calls to these patients more frequently. We make a phone call for patients on the continuation phase of treatment every two or three weeks."

Another 47-year-old female TB focal person reported that she would make a phone call for the medication refill visit and sputum test examination before one or two days of the scheduled date,

"When I give a patient a one-month medication, I will record the date for the refill date after exactly one month. When that date nears, I will call the patient to come to collect additional medication. I usually call patients the day before the refill and remind them to come to collect the medication. Most of the patients will call me themselves right before the refill date and check if I will be available in the health facility. In addition, I also call patients and remind them about the sputum tests that they take at the end of the second, fifth and sixth months of medication. Most of the patients call me themselves. I also tell them to call me two days before the appointment date and check if I am available and take the medication. I also told them that I will not be available over the weekends. If the patient will have a sputum test tomorrow, I will make the call today."

Health professionals reported that the health extension workers have the responsibility to provide health education during home-to-home visits. A 58-year-old female TB focal person from the health facility said that

> *"Health extension workers are mainly tasked with this responsibility. They conduct a home-to-home visitation and counsel TB patients about the importance of adherence and the consequences of failing to properly take the medication. In addition, we also counsel them about the importance of adherence whenever we get the opportunity to speak to patients as they come to take the medication or on a refill date."*

Another 37 years female TB prevention and control expert from the health office added that

> *"Several activities and efforts have been carried out to address non-adherence to TB medication. The first one that I can mention and still is being carried out is the work done by the health extension workers at the community level. They are conducting an awareness creation campaign to make patients visit health facilities and adhere to their medications. Despite the efforts made, there is still a varying level of non-adherence once after the patients starting their medications."*

The health extension workers will also trace patients when they are lost from the treatment through home-to-home visit. The 30-year-old TB focal person said *"Another opportunity may be that health extension workers can support the program. Health extension workers working with me are particularly good at tracing and returning patients to treatment. We can give them the patient's phone number and they can even trace patients home to home."* Another 42-year-old female TB prevention and control expert also said that *"We try to deal with default to TB treatment through the engagement of Family Health Groups and Health Extension workers who would go home to home. We provide the list of TB patients to health extension workers who are responsible to trace the defaulters and bring them back to treatment. This list, which contains the name and phone numbers of each defaulter in the village that given to the health extension worker assigned to cover that village. They will also trace defaulters and bring them back to treatment."*

At the beginning of the TB treatment, health professionals usually educate the patient on the consequences of non-adherence to TB medication. The 29-year-old TB focal person said that

> *"We only make sure that we give patients the proper counselling to ensure that they are taking the medication. We explain in detail to patients in the intensive phase why we are giving a one-week medication. We will tell them that we are giving them a one-week medication because we are trying to reduce their exposure to COVID-19. We also inform them about the importance of strictly adhering to taking the medication. The same counselling is also given to patients' treatment supporters. We inform them that they should support the patient and make sure that they are taking the medication daily. We also explain to them the risk of developing MDR if the patient fails to take the medication properly. We take these counselling and discussions with patients and treatment supporters as potential non-adherence prevention mechanisms. But we do not have any guarantee that the patient will take the medication after taking it home."*

Another 58-year-old female TB focal person said that

> *"We counsel the patients and inform them about the consequences of failing to properly take the medication. We also tell them about MDR TB and the consequences that come with it. Before COVID-19, health extension workers will carry out a home to the home visit of patients who fail to come to take the medication or for a refill visit clinic appointment."*

Another 47-year-old TB focal person stated that

> *"There is no way we can truly confirm if a patient is taking the medication at home. The only means available to encourage patients to consistently take the medication on time and without interruptions is to counsel them about the*

importance of adherence to medication and the negative consequences of non-adherence and medication interruptions. I inform patients that we are giving them the medication to bring to their homes because we wanted to reduce their exposure to COVID-19. We try to stress as much as possible about the importance of strictly taking the medication and that if they are experiencing any form of adverse reaction to the medication, we tell them to reach out to us instead of just stopping the medication."

Monitoring patients' medication adherence through treatment supporters is a control mechanism that has been reported by health professionals. Treatment supporters can be close family members or caregivers who use a paper card to monitor the patient's correct intake of medication. Patients are expected to bring paper cards when they visit the health facility for medication refills each week. Additionally, if a patient is lost from treatment, the treatment supporters will be contacted. The 47-year-old male TB prevention and control expert said that

"Previously patients in the continuation phase were contacted by treatment supporters every week. The treatment supporter is checking if the patient is taking their medication and recording on the card. The treatment supporters try to see if patients had failed to use the medication at any time of the week. A treatment supporter is a person close to the patient and they are also supported by the health extension workers during the home-to-home visit. The patients will bring that card when they come to the medication refill visit. The health professional checks whether the patient had missed any medication."

Another 53-year-old female TB prevention and control expert added that

"*We use the treatment supporters of the patients to check if patients are taking the medication properly. The treatment supporters are usually members of the*

patients' families. We try to check how well patients are properly taking the medication when they come to the health facility by accompanying patients."

However, according to a report by health professionals, paper-based monitoring cards were not properly implemented in most health facilities. In some health facilities that do implement it, patients may not bring the monitoring card to the health facility during refill visits. For example, the 32-year-old male TB focal person said that *"They are expected to bring the card. Most of them bring the cards with them when they come here. But some of them forget to bring it. But check their overall status at the end of the intensive phase."*

Another method of monitoring patients' adherence is through healthcare professionals who typically check whether patients come and refill their medications on time. The 32-year-old male TB focal person said that

"We put the date the patient comes to the health facility and then we put the date that he will be coming back after a week. We also keep the scheduled date on the card and track the dates. We make sure that the patient comes to collect the medication for sixteen weeks. For instance, if the next appointment is on the 24th and if the patient comes on the 26th, then that is an indication that the patient has skipped the medication for two days. It helps us in following up and monitoring patients."

Another 50-year-old female TB focal person added that

"There is no mechanism to monitor the patients to confirm they are taking the medication. Our observation mechanism is whether the patient is coming on the scheduled date of the appointment. There is no way we could effectively monitor non-adherence. We just try to inform patients about the importance of taking the medication as prescribed by experts and about the consequences of failing to adhere to TB medications and their side effects. When they come

back to refill their medications for the next week, we try to have a conversation with them to check how well they are properly taking the medications. Then we will give them two weeks' medication. We try to ask them at what time they are taking the medication."

According to some health professionals, they use various methods to monitor patient adherence, such as counting the number of medication stripes left, checking the refill appointment date, or asking the patients if they are taking their medication. The 28-year-old male TB focal person said that

"One of the ways we use to check if the patients are taking the medication is to see if they have any medications on their hand that they have not taken yet. If they have a pill on their hand, it means they have not taken the medication properly. If I give the patient seven days of medication to take home and if they do not have any on the eighth day when they come, that is an indication that they have taken the medication. The second way we check is to ask the patient if they have taken the medication. Another indication can also be whether the patient comes on the refill date or not."

Another 39-year-old female TB focal person said that

"We also request patients to bring the empty strips with them when they come for a refill appointment and even though it is not conclusive evidence that they have taken the medication, we consider that as evidence too. An additional thing is that we often inform patients to come for an appointment date on the day they take the last medication that they took from their last refill. When they come, they will also bring the strips and if there is any medication left on the strip, it is an indication that they have not taken the medication properly. If there is no medication on the strip, then it is an indication that they have taken the

medication properly. But the main factor is that we inform the patient about the consequences of failing to take the medication properly."

Another 31-year-old male TB focal person said that

"In the period before COVID-19, we use the DOT system and patients come to the health facility daily. We tally patients' attendance. If a patient is absent or if a patient is late, we call them and check why or if they experience anything. In the intensive phase, the medication is taken here (health facility), and patients come daily. We know if a patient did not come. In the continuous phase of the treatment, we check the medication stripes. We give them a two-week medication to take at home."

Another 26-year-old female TB focal person added that

"We try to tell the patients to bring the empty stripes when they come back for a refill. We take that as one of the indications that they have taken the medication. They would tell us they know taking the medication is for their own sake. The sputum test is also taken as an indicator. The symptoms would reappear if they were not taking the medications. We use these indicators to evaluate if patients call them and check things. We also remind them to continue to properly take the medication."

Furthermore, some health professionals have also stated that a patient's sputum test can indicate whether the medication is being taken correctly. The 30-year-old female TB focal person said that "*The first indication is the tests that they take. I have worked with TB for two years now. It was rare to find a patient who tested positive in the second month of the treatment. Now, we have found three patients that have tested positive. This is an indication that they are not taking the medication properly."*

The DOT standard care during COVID-19 emerged

The Directly Observed Treatment (DOT) program for drug-susceptible TB treatment initially required patients to take their TB medication at the health facility for the first two months of treatment, followed by non-daily DOT where patients take their TB medication at home and visit the health facility weekly to refill their medications from two to six months of treatment. However, health professionals have reported that the standard DOT program has been interrupted since the emergence of the COVID-19 pandemic. The 47-year-old male TB prevention and control said that

> *"The DOT program has been disrupted and is not being applied due to COVID-19 pandemic. Patients at both the intensive and continuous phase of treatment now are taking their medications in their own homes. This has been made to reduce the movement of people and not to contribute to the spread of COVID-19. A one-month medication is given to all patients, and they will come and collect after exhausting the medication."*

Another 53-year-old female TB prevention and control expert added that

> *"Since the COVID-19 pandemic happened, we have changed the medication procedure. Patients in both the intensive and in the continuation, phases are taking a one-month medication home. If the patient is not able to come to a health facility to collect the medication, a decision has been made for a family member to collect the medications on behalf of the patient. This is how currently the medication is being given to patients."*

Another 35 years male TB prevention and control expert said that

> *"In the first two months, patients go to health facility daily and take the medication at home. This is the DOT phase. But since the emergence of COVID-19, there has not been a uniform standard that is used by all health*

facilities within the sub-city. The official standard passed down from the ministry of health is that patients should come once a month and take a one-month medication to their home. But in some health facilities, a two-week medication is given to patients."

However, the medication refill visit schedule program was not consistently implemented by health facilities. Some health facilities used weekly or biweekly refill visits during the intensive phase of treatment and then switched to monthly refill visits during the continuation phase, while others used one-month refill visits throughout the treatment. The 32-year male TB focal person stated that

"Since the emergence of COVID-19, the standard DOT has been changed. Now we are giving a week's medication to patients at the intensive phase of the treatment. For those in the continuous phase of medication, we are giving them a one-month medication."

Another 29-year-old male TB focal person stated that

"...But in our health facility, we have been giving patients in the intensive phase a one-week medication while giving patients in the continuation phase a two-week medication. We adopted this system because it is more convenient for us to follow patients' adherence."

Another 29-year-old male TB focal person said that

"Yes, the directive that we received from the Sub-city health bureau states that we should provide medication for one month for patients to take home since the emergence of cases of COVID-19 in Ethiopia. But in our health facility, we first provide medication for two weeks at the start of TB medication. That is because there are adverse reactions that patients may experience, and we

want to have the opportunity to closely monitor those reactions… But after the first two weeks, patients will be given medication for a month."

Another 34-year-old male TB focal person said that "*…But after COVID-19, changes have been made to the standard and since then patients are taking a one-month medication to their home. The change was officially introduced by the Ministry of Health."*

According to some health professionals, the schedule period for medication refills depends on the patients' behaviour as well as other factors, such as side effects and distance from the facility. The 58-year-old female TB focal person said that

"Currently, we are giving the medication depending on the status and behaviour of patients. For patients that we believe will take the medication properly without interruptions, we will give them a two-week medication to take to their home. There are even patients that we give a one-month medication because we do have confidence that they will take the medication properly. For weak patients and for patients whose contact person may not be able to come weekly to get the medication, we will always give them more medication that can last them for more days. For patients that can come weekly, we will give them one-week medication. But for patients who are newly starting the medication and entering the intensive phase, we would want to have the opportunity to make sure that they are taking the medication properly. We would also want to observe and check their adverse reactions to the medication. We will want to see if they have vomiting and other reactions."

Another 32-year-old male TB focal person said that

"...But we do not necessarily employ the new standard for all patients. We apply it to patients who may likely have challenges with work and who may have to work away from Addis Ababa and who may have to stay there for a longer time.

For instance, one of our patients is a long-distance truck driver who would go to Djibouti and back and for him, we are giving him a one-month medication. But for patients who are just starting the medication, we would not give them a one-month medication. We first give them five days of medication to monitor their progress."

Since the emergence of the COVID-19 pandemic, only one 30-year-old female TB focal person from the health facility reported that the standard DOT program had continued in their health facility. According to the health professional, they are implementing daily DOT for the first two months and weekly refills from two to six months of treatment, even though they were instructed to give one month's worth of medication at each refill visit.,

"The official direction given is that we should give a one-month medication to reduce risks associated with exposure to COVID-19. I have scheduled for all patients to come to the health facility in the morning at around 7 am. It is for patients in the first two months of their medication. For patients in the continuation phase, I am still giving them a one-week medication."

Theme 3: Acceptability of mobile-assisted adherence intervention

Acceptability and benefits of mobile-assisted adherence intervention

According to most health professionals, mobile-assisted medication adherence support intervention can promote TB medication adherence. The healthcare professionals believe that SMS text message and phone calls can avoid forgetfulness of medication intake. The 32-year male TB focal person said that

"I think it can improve adherence. Phone calls and text messages can be an important reminder for patients because patients may forget to take their medication. Patients may be busy with work or personal matters and sometimes they may be away from town and may forget to be back for a refill

date. As a result, patients may not properly be taking the medication. They may experience interruptions. Phone calls and text messages can help to remind the patients."

Another 53-year-old female TB prevention and control expert also reported that SMS text messages and phone calls could be a solution for non-adherence to TB medication,

"Y*es, it will be a solution to the problem of non-adherence especially with those patients who tend to forget to take their medication in time. Some patients may be busily engaged in work and, as a result, may forget to take the medication. We often see patients who forget the medication time. Implementing such an intervention can contribute a lot in reminding patients to take their medication at the right time which in turn can promote adherence to TB medication."*

Another 39-year-old female TB focal person reported that mobile-assisted medication adherence intervention especially very important for those who do not have close family support,

"There are patients that do not have a contact person and a treatment supporter. These patients usually live alone, and their family and relatives may be living in another town. I believe this intervention would be extremely useful for these patients. It can also be helpful for patients who may be living with their families."

In addition to simple reminders, health professional respondents believed that SMS text messages and phone calls could help improve patient awareness of TB medication adherence. The 53 female TB focal person said that *"Yes, it can be a solution. We can use phone calls and text messages to promote patients' awareness about the importance of medication adherence."* Another 35-year-old male TB prevention and control expert added that *"I think it will have a positive role in creating awareness about the importance of*

medication adherence… In addition, it can be used to remind patients to take the medication at the right time. Patients always tend to focus on either work or other personal matters as time goes on and they may forget to take the medication. Such a program can be used to address this gap."

Health professionals believed that adherence interventions using phone calls and SMS texts could improve the quality of professional care. By improving communication between health professionals and patients, it can motivate patients to follow health advice and properly take their medication. Additionally, health professionals reported that SMS text messages and phone calls could reduce the spread of TB and workload. The 32-year-old male TB focal person stated that

> "*Patients will also be satisfied when they observe that we are calling them. One of the main benefits will be that we will be able to reduce interruptions related to medication. In addition, it can also reduce workload by inducing behavioural change in the patients. I believe patients will be motivated to take the medications properly when health care professionals consistently call them and send them reminder text messages to take the medication properly. It can foster a sense of professional care which can also promote behavioural change. In addition, it can also contribute to TB prevention. The behavioural change as well as the fact that patients take the medication properly means that we can also reduce its transmission."*

Another 29-year-old male TB focal person added that

> *"They (patients) could view it as professional care. There are also patients who ask us for our phone numbers and call us every time they have a question to ask or when they experience some adverse effects of the medication. In addition, we also interact with them freely and we try to make them comfortable."*

Another 53-year-old female TB prevention and control expert added that

> *"Yes, it can reduce the workload. In addition, it can also foster interaction and communication between the patient and the health care professional. If we can successfully ensure that our patients are taking the medications properly, then that will contribute to the reduction in the transmission of the disease. The intervention not only benefits patients but also the wider community."*

Additionally, some health professionals believed that SMS texts and phone calls have a role in reducing multi-drug resistant TB (MDR-TB) through proper medication adherence. The intervention is particularly important during COVID-19 pandemic in which the standard DOT program was not properly implemented. The 31-year-old male TB focal person said that

> "*Yes, I believe it will be a useful solution. Firstly, it will play a crucial role in reducing MDR-TB. The prevalence of MDR-TB was high in the past when we were using the DOT system. Now patients are taking a one-month medication at home, and we can expect an increase in MDR-TB because there is no way for us to verify the patient is taking the medication. If a mobile SMS text or a phone call-based intervention is to be implemented, I believe it can promote adherence especially in such a time DOT is not used."*

Another 28-year-old male TB focal person added that

> *"The intervention can promote adherence. It can reduce MDR-TB. It can ensure that we will not lose patients. In addition, it can ensure that we will have information about patients. It can also help the professional in easily following up patients."*

Some health professionals also reported that SMS text messages and phone calls could be useful reminders for medication refill visits and clinic appointments. The 47-year-old male TB prevention and control expert said that

> *"I think it would be helpful if the SMS text and or phone call reminder is done a week before for the monthly clinic attendance schedule to collect their medication for the next month. We ready medication kits for all patients and such reminder text messages or phone calls could be made a week or two to three days before their scheduled date so that patients could schedule early and have time to do the refill medication visit. Patients at times may be in a distant place for work or any other reasons and such reminders could help to avoid non-adherence."*

Another male TB focal person 34-year-old added that *"...we can also add a short message to remind the patient about their upcoming medication refill date. If we are sending the text daily and if the phone call is also made more frequently, patients can also be reminded about their refill date of medication without having to implement it as a separate intervention."*

In addition, most patients believed that SMS texts and phone calls would help them to remember to take their medication. The 67-year-old patient said that

> *"I believe it can help patients who forget to take the medication on time. I also personally welcome such an intervention. It can be a useful intervention. I normally make sure that I never forget to take the medication on time. My family is also on my side, they are supporting me and making sure that I take the medication on time. But such an intervention can also be helpful for other patients that are especially likely to forget to take the medication on time."*

Another patient of the same age and gender as above reported that patients may not give the same attention when they have medication in their hands to take at home and thus SMS text messages and phone calls can be useful reminder,

> *"...I think people are more careful to take the medication. But I also understand that people may not always pay attention to take their medication at the same*

time as they have the medication in their own hands at home and when they do not have to go to the health facility daily to take the medication. I think it can be a useful reminder for patients. We may be busy, and we may at times forget the medication even though it is the most important aspect of our day-to-day life as TB patients. Having such a reminder intervention available to us is an important thing."

Another 22-year-old male patient said that *"I believe the intervention will be useful. I have been taking my medication properly so far. But as time goes on, the attention and focus that I give to the medication may not be as similar as it has been so far. Having such a reminder would help a lot"*

Some patients also reported that SMS text messages and phone calls can avoid the unwanted consequences of non-adherence to TB medication. The 25-year-old female patient said that

"I think it is a particularly good thing that you have come up with this idea. I have been informed about the consequences of non-adherence. I have been told that it can cause serious problems where patients can be forced to take the medication for more than two years. Therefore, trying to address this challenge and supporting patients so that they will take the medication on time is an incredibly positive thing. Patients forget to take the medication, and this is an extremely useful intervention that can address the problem."

Another 33-year-old male patient reported that patients are highly likely to forget the medication when they are taking medication for a long time at home and feel well,

"I believe that it will be useful for patients. Patients at a time may forget to take their medication on time. Patients are likely to forget to take their medication on time because the medication period is extended, and they must take the medication at home. The attention they give to the medication time may be less

and less as the time goes on, and as they see improvement in their health status. If the phone calls and the SMS messages are going to reach the patient regularly, then the patient will always be reminded to take his medication on time. In doing so you will prevent the patient from developing MDR."

However, one 25-year-old female patient reported that SMS text messages and phone calls are only good and acceptable only for medication refill visit clinic appointment reminders but not for remembering medication intake, *"I do not think it will be a good idea to call or message patients daily to remind them or to ask them if they have taken their medication. What I think would be a good idea is to remind patients about their refill appointment dates."*

Acceptability and preference: SMS text versus phone calls

Most health professionals preferred phone calls over SMS text messages to promote TB medication adherence. The main reasons for the respondents were that SMS text messages are easily ignored as many texts are currently being sent from multiple organizations, patients may not check their phones for SMS text messages, some patients cannot read and understand SMS text messages, and phone calls are more engaging than SMS text messages for promoting TB medication adherence. The 29-year-old male TB focal person said that

"*The phone call would be more impactful and more appropriate to achieve the needed results. This is because text messages are more likely to be ignored by patients. Literate patients may be able to read and understand the texts. But text messages could still be ignored."*

Another 45-year-old male TB focal person added that

"*In my opinion, the phone call would be the most impactful mechanism to ensure that patients are receiving the message we want to convey. A potential problem with the SMS text messages is that they could be missed because*

patients may receive several text messages from different people and organizations."

Another 35-year-old female TB prevention and control expert reported that phone calls communication is more engaging and useful for those who cannot read and understand, *"The phone call is more engaging which is one advantage compared to the text message. For people who may not read, we could not send the texts and we cannot also expect a reply for the text message. So, the text message may not be engaging. But the phone call could be more engaging."*

There were some health professionals who preferred SMS text messages over phone calls for adherence intervention. The major reasons for choosing SMS texts were that giving a phone call in the morning may be disruptive, it may not be feasible to reach all TB patients through phone calls, repeated phone calls may bore them, patients may not pick their phone when they are busy at work or engaged in other activities, a text message can be seen at any time when patients are free and sending SMS text message is easy. The 26-year-old female TB focal person said that

"*I think sending text messages is better than phone calls. This is because making repeated phone calls to people can be boring for them and at times patients may be at work and busy or handling personal issues. Sending the text message is easier for them and they can see it whenever they have the time."*

Another 42-year-old female TB prevention and control expert added that

"Overall, SMS text messages can be a useful reminder. It may not be possible to make phone calls to all TB patients. Some people may miss the phone calls and the text messages can be an important reminder."

Some health care professionals suggested both phone calls and SMS text messages are useful to promote TB medication adherence. The 32-year-old male TB focal person said that

> *"If that is possible, I think it would be more impactful. Having both (SMS and Phone calls) would be the best choice. The text message may be missed. Therefore, having the phone call can be an important guarantee to ensure that we are delivering our text messages to the patients."*

Another female TB focal person with the same age as above added that

> "*I would say both are more appropriate. The phone calls can be used to check if patients are reading SMS messages. You can even decide if it is going to be useful to continue to send the SMS messages especially if patients are not seeing and reading the SMS messages."*

According to some other health professionals, the choice between SMS text messages or phone calls will depend on the target audience. For educated patients, SMS text messages are the most appropriate means of communication, and for uneducated patients, phone calls are appropriate to promote TB medication adherence. In this regard, the 47-year-old female TB focal person said that "T*he SMS would be appropriate to patients that are literate that can read and write. To remind patients, the SMS text message would be more successful in reminding patients. For those unable to read and write, the phone call is more useful."* Another 34-year-old male TB focal person said that *"The text message will be more impactful with patients who are literate and/or able to read. For illiterate patients, the phone call will have more impact."*

Similarly, some patients preferred to get phone calls over SMS text messages while some other patients preferred SMS text messages over phone calls to remind them of the TB medication. Patients who prefer phone calls for medication reminders mainly cited the following reasons: multiple SMS texts sent from various organization that bore the patient,

patients are less likely to read the SMS, SMS text message notifications may not be heard, and patients can ask a question and get answer from health professional through phone call. The 67-year-old male patient said that

> *"A potential problem that I see with the SMS message is that, as you might have been aware of it, we receive a lot of SMS messages from different organizations. People are already fed up with these SMS messages and we always do not care to read the message that they sent us. I am afraid patients may consider the reminder messages as one of those other messages that we usually ignore. So, the phone call may be more appropriate and more likely to succeed. I also do not think patients will be disturbed because they will realize that the phone call is made for their own benefit."*

Another 24-year-old female patient said that *"Patients will start to think about the medication once they see the text message sent from you. But they may not necessarily read the SMS text message when they realize that the text message is sent from you or some known phone number. The phone call may be more acceptable for them."* Another 26-year-old female patient believed that both SMS text messages and phone calls are useful, but the phone call is advantageous to ask questions and get an answer and stated that *"I think both are applicable and I think most patients own a phone. But the phone call has more advantages because it allows for patients to ask questions and get clarification on issues they do not understand."*

There were three major reasons why patients preferred SMS text messages for medication reminders over the phone calls; they do not want to be interrupted by phone calls in the morning, they do not want to discuss their medication in public, and they do not want to pick up unknown phone calls. The 22-year-old male TB patient had preferred an SMS text message, but he also told phone call is important for people may not see the text message,

> "*If the aim is to remind patients to take their medication by a phone call or a text in the morning, then my preference will be the SMS text message. Some people may not like to be disturbed by a phone call in the early morning. But, for people who may miss looking at a text message, then the phone call would be useful."*

Another 35-year-old female TB patient said that

> *"I think the SMS message is preferable. That is because people may not like to receive a phone call early in the morning. In our culture, when someone calls them in the morning people assume to announce sad news, and phone ringing in the morning may be disturbing them. As a result, it may not be right to call them in the morning. But a text will not be that much of a source of discomfort for them."*

Another 33-year-old male patient had concerned the acceptance of phone calls intervention by some patients because of the privacy issues, *"The phone calls may not be acceptable to some patients due to privacy issues. This is because some patients may be with people whom they did not disclose their health status. When you call them, they may not be comfortable to pick up the phone call and discuss their health status. But that still will not be a problem with all patients. There might just be some patients that may not feel comfortable to speak over the phone about their health condition."*

Some patients believed that the choice of SMS text messages or phone calls for medication reminders depends on the patients' literacy level. For example, the 36-year-old male patient suggested *"For people who are literate and can read and understand the content of the text message, I believe the SMS text message will be sufficient. The problem may be for patients who may not be able to read. For these patients, the phone call will be the appropriate choice."*

Theme 4: Convenience: mobile-assisted adherence intervention design

Content of the message

Some health professionals suggested to include information regarding how long the medication must be taken, the necessity of following the prescribed medication, and the consequences of not following the prescribed medication, the disease transmission, prevention, signs and symptoms, the diagnosis category of TB, how the medication should be taken, and nutritional-related information in the SMS text messages. The 28-year-old male TB focal person stated that

> *"Instead of only sending a reminder text message that tells the patient to take the medication, we can also add a message about the importance of adherence to medication and the consequences of non-adherence."*

Another 32-years-old male TB focal person also suggested,

> *"Concerning the contents of the SMS (Short Messages Service) message, one of the components should be about the methods through which the disease is transmitted. Additionally, preventive methods such as ventilation and the use of a face mask should also be included. Information about the signs and symptoms of TB as well as the existence of types of TB could also be shared with patients through SMS messages. Advice about how the medication should be taken and about the types of nutrition the patient should take could also be included."*

Some patients also suggested including information about TB and the consequences of non-adherence to TB medication. The 38-year-old female patient reported that the SMS text messages would be more useful if the SMS text messages include information about the disease and the consequence of non-adherence to TB medication and stated that

"*If the intervention is going to be employed to inform patients about the disease, I believe that will be a useful solution too. That is because the attention that you give to taking the medication on time is dependent upon your awareness of its significance and the negative consequences of interrupting the medication or failing to take the medication on time. If people know the seriousness of the issue, they will pay attention to the medication. This is also dependent upon whether the physician has informed the patient about the disease and the medication. If patients are informed about the importance of taking the medication for the whole six months period and the danger of not taking the medication when they see a health improvement, then they will take it more seriously."*

Language

Most health professionals suggested using the Amharic language (the national official language) for SMS text messages and phone calls adherence interventions. The health professionals reported that most of the patients can speak and understand the Amharic language in Addis Ababa, Ethiopia. The 31-year-old male TB focal person said that

"*The vast majority of TB patients that I have come across in this health facility can speak Amharic. I have not come across a patient that does not speak Amharic. But some may not be able to read."*

Another 39-year-old female TB focal person added that

"When it comes to language, it is better to use Amharic to compose the SMS message. That is the language that most people in the city can speak and understand. As far as language is considered, we have always been using Amharic. There is a small portion of patients that are not able to speak and understand Amharic always come with a relative who lives here and who speaks and understands Amharic."

However, most health care professionals also agreed that some patients cannot speak and read the official Amharic language, and thus suggested to include other major languages of the country to make the intervention more inclusive and successful. In this regard, the 47-year-old male TB prevention and control expert said that

> ***"****It should consider the language variations and the languages that are comfortable in communicating and best able to comprehend messages. It is possible to use a common language in the country, which is the Amharic language, but all people may not know that. If it is possible, it would be best to find the language preferences of the patients in the city. That is because people from various parts of the country with diverse cultural backgrounds come to the city, and thus they may not be fluent speakers of the Amharic language, even though it is the official working language. Adding Afan Oromo and other languages could be extremely useful."*

Another 26-year-old female TB focal person from the health facility added that

> *"We need to prepare the contents of the SMS text messages or the phone calls in different languages. It may also be important to have callers who speak some of the major languages in the country. That is because even though most people in the city speak Amharic, they come from various parts of the country to get the treatment. These patients may not be fluent speakers of Amharic"*

Most patients also agree that the Amharic language can be used to design SMS text messages and phone calls information. The 36-year-old male TB patient said that

> *"I believe the Amharic language should be used to compose the messages. That is the language that most patients in the city can understand."* However, a few other patients suggested to include other major languages in addition to the Amharic language for the SMS text messages and phone calls.

Another 38-year-old female TB patient said that

> *"I think that depends on the language that the patient can speak and understand. In the area that I am currently living, …, there are people who are more comfortable speaking Afan Oromo than Amharic. For people who live in the city, Amharic would of course be the right choice."*

Another 33-year-old male patient added that

> *"I think using Amharic and Afan Oromo would be useful. I do not think English will be relevant. If it is possible, other languages can also be included depending on the number of patients that is comfortable speaking that particular language."*

Comprehension

Most health professionals agree that SMS text messages and phone calls designed to encourage TB medication adherence should be short and easy to understand in the way patient's educational level. The 45-year-old male TB focal person said that

> *"When designing text messages, we need to make sure that we use a language that is easy to understand for an average person. People receiving the text message must have an easier time understanding the content of the text message. The SMS text messages that we send them must be as short and as easy to understand as possible."*

Another 35-year-old female TB prevention and control expert added that

> *"One of the things with SMS text messages and phone calls content is that we should perhaps refrain from using medical and technical terms. To make sure patients understand everything that we want to convey in the messages, we should use language and words that they understand."*

Some patients also indicated that the message of the SMS text and the phone calls should be simple and understandable. The 36-year-old male patient said that *"In addition, the message must be crafted using simple language and terminologies that the average patient can understand."*

Interactivity

Some health professionals believe that a phone calls intervention added to SMS text messages can make the intervention more interactive and engaging than using two-way SMS text messages. The reasons for this, according to health professionals, were that phone calls are more trusted and more inclusive for those who are uneducated, it is a good means of communication to get feedback from patients about their experiences like drug side-effects and ask their health status. The 34-year-old male TB focal person said that

> *"I think, it (adding phone calls) is important to make it more engaging for participants. It would be more helpful if there was also a way to have patients' feedback and experience as they take the medication. It will be more acceptable for patients to make it more engaging so that they can share their experiences including the adverse reactions to the medication."*

Another 26-year-old female TB focal person reported that adding phone calls in the SMS text messages could makes the communication more engaging and interactive, *"Keeping the phone calls in addition to the text message can make it more engaging. The phone calls allow for more discussion to happen. So, phone calls are more engaging than text messages. Designing the text messages to be more of a reminder for the patient to collect his medication would be impactful. Having both the phone call and the SMS text message could be useful and make it more engaging."*

Some health professionals suggested a two-way SMS text messages to make the intervention more successful and engaging. The 45-year-old male TB focal person said that *"If a resource is available, I believe that it (two-way SMS text messages) would make the intervention most*

successful. I think it has an advantage." Another 29-year-old female TB focal person suggested to design the SMS text messages in question-and-answer format that could increase the replay messages from the patients and it engage the patients in the communication, *"I think to do that, it may be important to consider including a question in the SMS text message that patients could respond to so that we would have more information on how they are taking the medication."*

However, some other health professionals had doubted the success of two ways SMS text messages because it requires the patients' ability operate their mobile phone, and the patient may be tired to reply to the SMS text message. The 32-year-old male TB focal person was guessed that 50% of the patients may replay to the text message if two SMS text message is implemented,

> *"I would say that there is only a 50% chance that it would be successful. That is because there are patients that are not literate and able to write a message. Even for literate people, they may be busy and unable to respond to the message."*

Another 31-year-old male TB focal person said that

> "*It is possible to make it interactive by allowing patients to respond when they receive the reminder text message. But that will depend on whether the patients can type a text message and send it. For digitally literate patients, that is very much possible. For those that are not able to operate their mobile phone, then the reminder text message will be the only choice. Designing the intervention so that patients can reply can be weary for patients and we need to consider that."*

Frequency

In order to promote adherence to TB medication, most health professionals recommended sending an SMS text message daily. Most health professionals also believed that phone calls should not be frequent because a daily phone call might disturb patients and might not be possible for many patients in health facility. Indeed, most of the health professionals suggest once a week or twice a week phone calls are adequate. The 32-year-old male TB focal person stated that

> *"Making a daily phone call may not be good. Patients will get tired of it if the phone calls are going to be made regularly and if it is going to be repetitive. You would need to prepare a schedule and decide the number of calls that you need to make per week. It may depend on the number of the patient. The SMS text messages could be sent as a daily reminder and the phone call could be less frequent in a week."*

Another 47-year-old female TB focal person added that

> *"A daily phone call to the patient may not be appropriate. That is because it can disturb the patients. This is because patients may be on their job, and it can disturb them. Such a patient may not pick their phone at all. But the SMS text messages can be sent once a day."*

However, some other health professionals believed that daily SMS text messages and phone calls could make the intervention more successful to promote TB medication adherence. For example, the 32-year-old male TB focal person believed that the daily SMS text messages and phone calls could make a more positive impact on TB medication adherence,

> *"I believe the higher the frequency of the phone calls and the text messages, then the higher their impact. People would be more alert, and they tend to expect to receive phone calls or text messages when we frequently send it to*

them. If sending the texts or making the phone calls daily is not possible, then we can either do it every week or every three days."

Some other health professionals also suggested twice a week for both text messages and phone calls to remind the patients to take their medication. The 50-year-old female TB focal person stated that

"I think it would be better not to send a message every day. We do not want to annoy the patients. We can send an SMS text message once every three days. Sending over the weekend could be useful too. People tend to relax at the weekend because they may be off work and sometimes away from home to visit a relative or a friend and they may forget to take the medication."

Another 42-year-old female TB prevention and control expert added that

"I am afraid it may be too frequent to send texts or make the daily phone calls. Twice a week would be good enough. Sending SMS text messages, or phone calls every two or three days will not be too much."

Some other health professionals reported that the frequency of the phone calls could be decided based on the patients' situation that can support them to remember their medication. The 29-year-old male TB focal person suggested,

"The phone calls can be made once a week. Additionally, we can also review the extent of family support for patients and make a varying number of phone calls for patients depending on it. For patients where there is strong family support that ensures patients are taken care of at home, we may need to call only once a week to assess adherence. For patients who do not have a family support system, we can make phone calls twice a week."

Another 39-year-old female TB focal person added that

> "*Making a phone call daily may not be necessary. Some patients also have their family members who remind them to take the medication. Also, calling patients daily in the morning may be inconvenient for them. In this regard, I do not see a problem with the SMS message."*

Some other health professionals believed that the frequency of SMS text messages or phone calls could be determined based on the patient's treatment phases. The 30-year-old female TB focal person suggested, *"for patients on the DOT phase, making daily phone calls and text messages are good. For patients in the continuation phase, I think once a week will be enough."* Whereas some other health professionals believed that twice a week SMS text messages or phone calls is enough in the intensive phase of treatment, and three times a week is enough in the continuation phases of treatment. The 47-year-old male TB prevention and control expert suggested *"If the DOT system is going to continue to be implemented, then phone calls or SMS texts could be sent twice a week for patients in the intensive phase of treatment and three times a week in the continuation phase of treatment. Otherwise, if there is a desire to discontinue the DOT and replace it with the current practice it should be done daily for patients in both phases of medication."*

Most patients also believed that the daily SMS text messages or phone calls made for TB medication reminder would not be problematic. Most patients believed that the intervention comes from health professionals is for the benefit of the patients. The 48-year-old male patient reported that if patients are convinced about the aim of the intervention frequency would not be a problem,

> "*I do not see the problem with both (SMS and phone calls) being done daily. That would be a proper thing if the aim is to remind patients to take their medication. As long as patients are convinced about the aim of the intervention, I do not see any inconvenience that it will create."*

Another 27-year-old male patient added that

> *"I do not think people will complain about the frequency. The intervention is designed to support patients and I do not think they will complain about receiving too many texts or phone calls that remind them to take their medication."*

Some patients, however, suggested making SMS text messages daily, but less frequently for the phone calls. The 25-year-old female patient suggested *"I think the daily SMS message is a more appropriate reminder. The phone call would be more useful to remind patients about their refill medication dates."* Another 33-year-old male patient added that *"The reminder messages only need to be sent frequently because the medication should be taken daily."* Some patients yet believed that weekly or monthly SMS text messages or phone calls frequency is enough. For example, a 22-year-old female patient stated that *"I think sending SMS messages or phone calls once a week is an optimum frequency and I do not think patients will have a problem with this frequency."* Another 26-year-old patient suggested *"I would say once a month would be enough. That is because I think people will remember to take their medication on time once they are made aware of the serious consequence of failing to take the medication on time."*

Time of delivery

All health professionals believe that the morning is the appropriate time for SMS text messages and phone calls for TB medication reminders because most patients take their medication in the morning. The health professionals reported that during the late morning, patients may go out for work or may be busy with other activities, which could make it difficult to reach them. The 32-year-old male TB focal person said that

> *"I prefer to send text messages every morning. TB patients take medication and other treatments early in the morning. Therefore, the right time will be either at 7:30 am or at 8:00 am. Some patients had to go to work after taking the*

medication at that time. The morning time will therefore be the most appropriate time to make the phone calls and to send the text messages."

Another 34-year-old male TB focal person added that

"I think it will be better if the phone calls are made in the morning. They take the medication in the morning. Therefore, the right time is to send the text or make the phone calls in the morning. Making it in the afternoon after they took the medication or after they forgot to take the medication is not going to be helpful."

Most of the TB patients also believed that the early morning time is appropriate for SMS text message or phone calls at the time of medication intake and before the patients go out for work or other personal activities. For example, the 37-year-old male patient said that *"I think the best time to send the SMS text messages and phone calls is in the morning or in a time that we know the patient will take the medication. If you send text messages at the time the patient should take the medication, it can increase the likelihood of the patient taking that medication. If a patient is taking the medication at 7:00 am, then we should send the medication right before 7:00 am to ensure the patient will take the medication."*

Duration of the Intervention

Most health professionals believed that the adherence intervention using SMS text messages and phone calls should be implemented for the whole six-month period of TB treatment. The reason for this was that the daily DOT (Directly Observed Treatment) was not implemented in the initial phase of treatment after the emergence of the COVID-19 pandemic, and patients become negligent when they feel well and may forget to take their medication or become lost from their treatment during the continuation phase. The 29-year-old male TB focal person said that

"*I think it will be beneficial if we focus on both phases of the treatment because forgetfulness can happen in both phases. Despite health professionals providing all the counselling, negligence can always happen. Patients may become familiar with the routine of taking the medication daily in the beginning stages. But after the first two months, they may start to be negligent because they are taking the medication at home, and they may fail to take the medication in case they move to another town. But in general, I think 70% of the focus must be on the intensive phase and 30% of our effort should focus on the continuation phase. Or we can opt for a 65% focus on the intensive phase and 35% on the continuation phase makes more sense.*"

Another 31-year-old male TB focal person also suggested that adherence intervention should be implemented for the whole period of treatment because patients were taking medication at home for one month due to the COVID-19 pandemic. The participant also reported that the intervention could focus on the continuation phase if the standard DOT was reintroduced in the initial phase of treatment,

"*I believe it would be most impactful if we implement the intervention throughout the whole period of medication. Now, we are giving a one-month medication for patients in all phases of medication as part of a measure to reduce patients' exposure to COVID-19. Therefore, the intervention must be implemented throughout the whole medication period. If a decision is made to go back to using the DOT in which patients in the intensive phase come and take the medication at the health facility daily, then the focus of the intervention could be the continuous phase...*"

Another 37-year-old female TB focal person suggested,

"The medication is taken for six months, and I believe sending reminder SMS text messages is important for the whole period. Especially the continuation

phase is where healthcare professionals will not be able to contact patients and it is also a period where patients feel a sense of recovery. Therefore, the continuation phase of treatment is the time where there is likely to be non-adherence and it is important to pay more attention to this phase."

However, some health professionals disagreed about where the focus of the adherence intervention should be the intensive phase or the continuation phase of treatment. Some professionals believed that the intervention is most effective during the intensive phase, while others suggested that it would be more effective during the continuation phase. Health professionals who recommended the intervention in the intensive phase provided three main reasons: the patients' health status is crucial at this stage, patients may experience drug side-effects, and the standard daily DOT has not been implemented after COVID-19. The 50-year-old female TB focal person said that

"*I think implementing it in the intensive phase of the treatment would be useful. That is because especially now patients are taking their medication at home due to COVID-19. In the future, it may be important to return towards focusing on the continuation phase."*

Another 32-year-old male TB focal person added that

"I believe it would be better to focus on patients who are in the intensive phase of the treatment. More attention should be paid to this phase. But lesser attention should also be focused on the continuation phase. It is important to follow up with patients in this phase and make sure that they are strictly taking the medication. It is a phase of medication where patients experience adverse reactions and there is a need to closely monitor that as well."

The main reasons health professionals believe that the continuation phase of treatment should be emphasized were the patients become more diligent at the beginning of treatment and take their TB medication correctly, but when they feel well, they would start forgetting to take the medication. The 28-year-old male TB focal person said that

"*The focus of the intervention should be the last four months of the medication period. In the first two months, patients are more likely to be careful about taking the medication. During the intensive phase, patients will come to the health facility, and we observe them as they take the medication. It is in the four months after the intensive phase that patients tend to experience disruptions. Therefore, the focus must be four months after the intensive phase ends."*

Privacy and confidentiality

Most health professionals do not believe that privacy issues would be a problem for SMS text messages and phone calls intervention done for TB medication adherence promotion. The 31-year-old male TB focal person shared his experience,

"My experience with TB patients' privacy is not a major problem. We can inform patients that text messages and phone calls are made to remind them to take their medication on time. If there is a patient who is concerned about not allowing their health status to be revealed to other people, they can easily delete the text message once they receive and read it."

Some health professionals reported that there has been some concern about the privacy issues associated with SMS text and phone calls when the goal of the intervention is to ensure ART adherence rather than TB medication. The 34-year-old male TB focal person said that

"Yes, that is true. But the focus of this intervention is TB. As long as we do not raise issues related to the patient's status concerning HIV/AIDS, I do not think it will be an issue. For example, I know about one patient who is taking TB medication and ART. When he wants to take the TB medication, he sends it to his family members. But to collect the ART medication, he will come. We do

have similar experiences. So, I do not think we will have issues concerning privacy while the focus is on TB."

Another 32-year-old male TB focal person added that

> *"I would not say that will be a challenge. It would have been a challenge if the focus was HIV/AIDS. But with TB, other people such as the family members of the patient must be notified of the patient's health status because they must take the necessary preventive measures. So, I do not think privacy is going to be an issue. I have not come across a TB patient who said he is concerned about his privacy. We often inform the patient to inform their family members to take preventive measures. There is a small percentage of patients who come alone. They often come with a friend or a family member."*

Another 39 years female TB focal person added that

> *"I do not think it is going to be a challenge. That is a challenge we experience with ART medication. But we have never had a problem with TB patients. But until patients become familiar with the intervention, they may not pick up their phones. But after they understand the aim of the intervention, I believe they would accept it and be grateful about it."*

Some health professionals, however, believed that implementing SMS text messages and phone calls intervention would pose a privacy risk. This would be particularly more problematic for TB/HIV co-infected patients who do not want to receive SMS text messages or phone calls. The 29-year-old male TB focal person said that

> *"Yes, we may face those challenges. HIV AIDS patients may have a privacy issue with it. In addition, we have also come across patients who do not want their medical status to be revealed to their employer organization."*

Another 37 years female TB prevention and control expert added that

> *"TB patients in our country may not wish to disclose their status to their communities for different reasons. This may be one of the things that should be taken into consideration when designing such interventions. It would be important to make sure that their identities and privacy are always kept confidential."*

Another 50 years female TB focal person added that

> *"One of the challenges can be the issue of confidentiality. Some people do not want to disclose their status or to be at risk of exposure. People, depending on their specific circumstances, may not feel comfortable receiving a phone call or a text. That needs to be explored with the patients by having a conversation with them."*

There was also a concern that sending SMS text messages or phone calls through the contact person could compromise the patient's privacy. The 35-year-old male TB prevention and control expert said that "*Privacy will be an issue if the text is sent to the patient through another person's phone. Otherwise, I do not think it will be an issue.*" Another 45-year-old male TB focal person added that *"one of these scenarios is for example if the patient does not own a mobile phone and if we opt to reach that patient through a treatment supporter that means we are disclosing the patient's issues with another person."*

Most patients did not perceive privacy as a problem when it came to SMS text messages or phone calls because the intervention is aimed at benefiting the patients. The 27-year-old male patient said that

"I do not have issues related to privacy. All my family members and friends are aware of my health status and the medication that I am taking. They have been supportive to me. I do not see any issue related to privacy for getting a message or a phone call that reminds me to take the medication."

Another 25-year female patient added that

"I do not think there will be any challenge that you could face. Currently taking TB medication is not something that people want to hide. So, I do not think there will be problems related to confidentiality."

Another 36-year-old male patient also said that

"I do not think it will be a problem. Patients can decline the calls and can be allowed to decline to receive the SMS messages as well if that is their desire. But I do think that will happen."

However, some patients reported that privacy issues could be a problem to some extent when it comes to sending SMS text messages or making phone calls. The patient respondents reported that some patients may want to keep their health status confidential from friends or family members, and therefore they may not want to receive phone calls or SMS text messages from the health facility. The 33-year-old male patient said that

"Some patients may be worried about their privacy and about not revealing their health status to other people. Besides that, I do not think there will be other challenges."

Another 35-year female TB patient added that

"I do not see that as a challenge at least as far as I am concerned. But there may be some people who may not want their status to be revealed to anyone."

Theme 5: Barriers and facilitators of mobile-assisted adherence intervention

Facilitators of mobile-assisted adherence intervention

The health professionals mentioned that the willingness of TB focal persons to send SMS text messages and make phone calls, the high acceptance of mobile-assisted adherence intervention by patients, and the high coverage of mobile phones were opportunities to implement and sustain the adherence intervention.

Willingness and high acceptance

Health professional respondents from health office reported that the TB focal persons' willingness to adopt mobile-assisted medication adherence intervention was the opportunity to sustain the intervention. The 47-year-old male TB prevention and control expert said that

> *"We do have TB focal persons and communicable disease control case teams established at health facilities. Decisions could be made to use the focal persons or members of the case team to make the phone calls or to send and monitor the SMS text messages. Thus, it is possible to use the existing health system structure."*

As long as the intervention is integrated into the health system, most TB focal persons working at health facilities had willingness to make phone calls, and to send and monitor SMS text messages. A mobile phone or landline telephone should be available in the TB clinic of the health facility, according to most health professional respondents. The 32-year-old male TB focal person stated that

> *"We have been cooperative in making the phone calls. Sometimes they (patients) even leave a text for us to call them back and we would always volunteer and call them back and discuss whatever issue they are*

experiencing. In addition, placing a landline phone or purchasing mobile phones to be used by the clinic can make things easier."

Another 31-year-old male TB focal person added that

"The first opportunity may be that health care professionals will be cooperative in the process of implementing this intervention. Since it is a program that can reduce workload, they will be willing to make phone calls."

Some health professionals also mentioned the high acceptance of SMS text messages and phone calls by patients as an opportunity for intervention success and sustainability. The health professional respondents reported that mobile-based SMS text message and phone call intervention can enhance a sense of professional care, which is highly acceptable to patients. The 47-year-old female TB focal person from the health facility stated that *"patients have a positive outlook overall. They are cooperative and respond when we ask them any question. I believe this is a positive thing that can facilitate this intervention (SMS and phone calls)."*

High mobile coverage

Some TB focal person respondents reported that a large number of patients have their own mobile phone which was seen as a good opportunity for mobile-based SMS text messages and phone calls. The 29-year-old male TB focal person reported that we can get at least one mobile phone in the household that we can use for the intervention even when the patient does not have their own mobile phone,

"We can find at least one phone owned by either the patient or a family member. Almost all patients own a phone. But some patients do not have their own mobile or do not operate their mobile phone because of their age or any other factor. But we can find one person within the family."

Challenges of mobile-assisted adherence intervention

Most health professionals reported the challenges for mobile-assisted adherence intervention were; limited infrastructure of the network interruptions may challenge the delivery of SMS text messages or phone calls, unable to charge mobile phones battery due to electricity interruptions, some patients may not own a mobile phone, healthcare professional workload, some patients may not pick up their phone, some patients may not read or understand SMS text messages, and several private companies send SMS text messages so that patients may ignore them.

Digital illiteracy and ignorance of messages or phone calls

Some health professionals reported that digital illiteracy and ignorance of SMS text messages may be the challenges for mobile-assisted adherence intervention. The 32-year male TB focal person said that

> *"Some patients may not read a text message sent to them in Amharic language. Another challenge that we may face with SMS text messages is the existence of several private organizations that send many SMS text messages... Most people ignore these text messages because they are not very useful. Here the challenge will be to make sure patients who receive the text messages will not be ignored these messages."*

Another TB focal person with the same age and gender as above added that

> *"Concerning the SMS messages, a possible challenge is that everyone receives several messages from different organizations, and we do not always care to check the content of these messages. Patients may be busy with their work sometimes and they may not get the time to check their message at the time that you want them to do. In addition, not all patients can read the messages."*

The 53-year-old female TB prevention and control expert reported that some patients may not like to receive too many SMS text messages and phone calls, "*One of the challenges may be that patients may be tired of receiving these calls and text messages. Patients may not like having too many phone calls and text messages."*

There were some common challenges reported by patients, such as uneducated patients being unable to understand and read text messages or operate their mobile phones. Patients also reported receiving multiple SMS messages sent from a private company that posed a problem, and some patients did not know the SMS messages are from the health facilities. The 33-year-old male patient said that

> *"One thing is that people are extremely irritated by the various SMS messages that they receive from various sources that typically use four-digit numbers. I am afraid some patients may consider the SMS text that you send them as part of this intervention as one of those other messages."*

Another 35-year-old female TB patient added that

> *"Patients may assume that the message is sent from the telecom company and tend to ignore it. People do not tend to check these messages when they are received from the telecom company or from other firms that are not useful to them. I am afraid there could be a chance that patients may consider the message that you are going to send them as one of those SMS text messages. But it depends on the habit and behaviour of the person that actively checks the messages."*

The 22-year-old male patient said that

> *"I think it can be useful. But my concern about that would be how many people would be able to properly operate a mobile phone. I see there are a lot of elderly patients when I go to the health facility to get the medication. These elderly patients do not seem to be able to fully operate a mobile phone and respond to SMS text messages. But for other patients such as myself who can effectively use a mobile phone for communication..."*

In some cases, patients with busy schedules or other activities may not read the text messages. The 26-year-old female patient said that *"That (reading the SMS text) depends on the patient and their way of life. For instance, I am always busy working in my office. As a result, I am not always able to read the text messages that I receive. I may see the notification and I may forget to read the text until I get home at night. But overall, it is important to send patients a text message to remind them to take the medication."* Another 27-year male patient added that "*One of the challenges may be that patients may not always pick their phone. Sometimes patients may be at their work or handling a private matter and they may not see their phones ringing. This is the only challenge that you may experience. If patients are made aware of the phone calls and the SMS text messages when they start taking the medication, the extent of the problem will be lesser."*

Have no own mobile or telephone

Some health professionals reported that some patients may not have mobile phones and their contact person or family member may be busy with their work to get the patient with them which may challenge the intervention. The 58-year-old female TB focal person said that

> "*One of the challenges may be there are some patients who do not own a mobile phone. We are only able to reach them through their contact person. The contact persons may be busy because they may be engaged in job. They may also not be happy when you repeatedly call them (contact person)."*

Another 32-year-old male TB focal person added that

> *"One of the challenges may be that there are some patients who do not own a mobile phone. In addition, we may also face network interruptions. This is a rare problem that we experience. It does not happen often. We are always able to contact the patient or the contact person. Such a problem is likely to happen if the patient does not have their own mobile phone. Patients who are homeless do not own mobile phones nor do their contact person have their own mobile phone. Even this is a rare case. For instance, in the past year, I have come across only two patients who said they do not have their own mobile phone. Many patients that we are treating have their own mobile phone."*

Another 42-year-old female TB prevention and control expert added that

> *"I believe it will be useful. But my question is how many patients own phones and how many of them can read a text message. Overall, a text message can be a useful reminder."*

Most TB clinics in a health facility did not have their own telephones, nor did health professional have airtime cards to make phone calls or send SMS text messages, which could make it difficult to sustain adherence intervention using SMS text messages and phone calls. Most TB focal persons, however, reported that there was a telephone in another room of the health facility which was not convenient for them because they needed to go to other rooms to call patients. The 32-year-old male TB focal person said that

> *"I use my own mobile phone to make the phone call. I also spend my own money to make the phone call. No finance is set aside for us to purchase airtime and make the phone calls. But since they are our patients, we have been cooperative in making the phone calls."*

Another 50-year-old female TB focal person added that

> *"We do not even have a landline telephone in the TB clinic room. I must go to another office to make the phone call. Sometimes I am using my own mobile phone to make the calls."*

Patient's registered wrong phone number or change their phone number

Some health professionals also reported that some patients provided the wrong phone number, which was recorded in the medical chart abstraction, making it difficult to trace the patients when they were lost from treatment. The 58-year-old female TB focal person said that

> *"Yes, that has happened to me before on a limited instance. I have only come across one patient. The patient was a female homeless person…Her phone number never worked when I try to reach her. After multiple trials, the contact person was reached over the phone, and we were able to get the patient to return the patient to treatment. But it is true that patients will give you the wrong phone number."*

Another 45-year-old male TB focal person added that

> "T*he first challenge is that you may find out that patients' phone numbers may not work at all. We have experienced this challenge as well when trying to reach patients. Patients may give you a phone number that may not be functional. The option, in this case, may be to record the treatment supporter's phone number and try to reach the patient through the treatment supporter. We do not call them right when we receive their number to see if it works. We only ask the patient if the phone works or not. They will always tell you that their phone number is active and that it works. But when you try to reach them at a later stage during treatment, you find that some patients' numbers do not work."*

Some health professionals also reported that patients may change their phone number without informing them which challenge to trace the patients when they lost from the treatment. The 32-year-old male TB focal person said that

> *"Sometimes patients change their phone numbers, and it could be a challenge to be able to reach them. We also take the phone numbers of patient supporters. But at times the patient supporter may be away, and they may not be immediately available for the patient as well. This could be a challenge for such intervention."*

Another 30-year-old female TB focal person reported that TB/HIV co-infected patients were change their phone number more frequently and said that

> *"The challenge that we experienced is that they frequently change their phone numbers. Even after telling them to notify us if they change their phone number, they still change their phone number without telling us. We checked if it works, but they still changed the number. At times, the number may be disabled later. This is a challenge that we experience concerning patients taking TB medication and ART."*

Another 39-year-old female TB focal person also said that

> *"Some of them do not always give you their correct phone number. They may also change their number at a later stage of medication. Since we know that problem, we always take the time to inform the patient to give us a phone number that they will use constantly and not another phone number."*

Health professionals work burden

Some health professionals mentioned that the health professionals may also be burdened with phone calls and SMS text messages if they have the responsibility to operate it. The 53-year-old female TB prevention and control expert said that

> "*Concerning health care professionals, if the plan is to use them to make phone calls, a challenge is that many of them may be overburdened with other responsibilities.*

Another 31-year male TB focal person added that

> "T*he first challenge may be that it could be an additional burden of responsibility for health care professionals working at TB clinics if the plan is to deploy them to make the phone calls."*

Another 29-year-old male TB focal person also said that

> *"That (the phone calls) may be a difficult thing for us. Currently, we have about 55 patients. It may be challenging to make phone calls to all patients daily."*

Sustainability of the intervention

Some health professionals had a concern on the sustainability of the adherence intervention. The 34-year-old male TB focal person said that *"One of the challenges is the sustainability of such program or intervention. The problem with such programs has to do with their short-term existence which can exacerbate the problem instead of addressing the issue they want to tackle."* Another 37-year-old TB prevention and control female expert added that *"Sustainability of the intervention is another issue to be considered. If the intervention is carried out by a non-governmental organization that implements the program only for a certain period, or if the organization decides to stop the program, it could have an adverse effect. Therefore, there must be a system where it could be implemented sustainably. To ensure its sustainability we would need to think about having a proper budgeting system. Budgeting and finance should be seen as one of the potential challenges that we may experience in the process of*

implementing this program and we can also view it as one of the basic features of its management."

Suggested solutions

Availing telephone at TB clinic

To sustain the adherence intervention, health professionals advised purchasing a telephone or provide airtime cards to health professionals. The 29-year-old male TB focal person said that

> *"We need to ensure necessary conditions are met to implement such a program (SMS text message and phone calls). For instance, one of the things has to do with the telephone. As I have mentioned we have to go to another office to make phone calls to patients."*

Another 32-year-old male TB focal person added that

> *"Yes, that is one of the challenges that we are experiencing, and I believe covering the airtime cost would solve the problem. We can use mobile phones if the airtime cost is covered. But so far, we have been forced to go to the ART room to make calls to TB patients."*

Briefing the mobile-assisted adherence intervention

Health professionals suggested having clear communication with the patient about the mobile-assisted adherence intervention. The patient needs to be clearly informed about the SMS text messages and phone calls aim which is necessary to avoid problems related to patients' privacy and confidentiality. The 47-year-old female TB focal person said that

> *"What I would like to add here is the patients should first be aware of the plan for phone calls and sending a text message to them. This is because some patients may want to keep their medication status private, and they may not*

want another person or even a family member to be made aware of their situation."

Patient's consent is also crucial to avoid privacy problems and respect their self-determination, according to health professionals. The 28-year-old male TB focal person stated that *"...We should start the implementation by first getting patients' consent. If we get their consent, then we will be clear to implement the intervention..."* Another 53 years female TB prevention and control expert said that *"Firstly, we should get patients' consent and willingness to receive a phone call or a text message that reminds them to take their medication. We should notify them before starting the intervention and we should secure their consent. Some patients may be keeping their status of TB patient as a secret, and we should make necessary preparations to ensure the confidentiality is always respected."* Another 37-year-old female TB prevention and control expert added that *"Yes, confidentiality is an issue of consideration when designing the intervention. When designing the content of the text message, the expert is responsible for designing the text message, and the patient must discuss and agree on the proper way they preferred to be reminded of their medication."*

Health professionals also suggested communicating the patient's preferred time for phone calls and SMS text messages will reduce unanswered calls and increase the readability of the SMS text message. The 29-year male TB focal person said that

"*They answer the phone calls because we call them on their private phones. We will need to consider the time of the phone call. We may need to refrain from calling them during working hours. We can speak to them and ask for the proper time they feel comfortable to receive a phone call. We will also need to ask them if the phone will be with them at the time of texting. I have only experienced such issues with two patients (not answering the phone calls) so far*."

For the intervention to be effective, some patients also report that clear communication and consent are important. For example, the 33-year male patient said that *"I believe getting their consent is important. What I have not mentioned so far is that when you start the implementation, the target patient needs to be made aware of the intervention and all necessary information about the intervention."*

Using a family member's or caregiver's mobile phone

Some health professionals from the health facility suggested using the phone number of a caregiver or family member when the patient has no mobile phone or cannot read and understand messages. The 45-year-old male TB focal person said that

> *"Yes, I think it can be one of the solutions that we can employ. We keep patients' contact information including their phone number. For patients who do not own a mobile phone, we also keep the treatment supporter's contact information. Sending a reminder text message for the patient himself or treatment supporter can be an extremely useful solution to patients who may forget to take their medication on time and who forget the health facility appointment dates."*

Another 50-year-old female TB focal person added that

> *"Yes, it is one of the solutions that, I think, can have a positive impact. But a major challenge may be that patients may not always own a mobile phone. To track patients when they missed the refill visit appointment, we often take two or three phone numbers owned by the patient and another person who is close to the patient that we can reach out to if the patient's phone is not working."*

Additionally, some patients suggested that family members can be involved when a patient cannot read or understand a text message. The 37-year-old male patient said that

"There are some patients who may not be able to read and understand a text message. For these patients, you can inform them to get another person such as their family member to read the text to them. But if the text message is going to be written in Amharic, I believe the majority of patients can read."

Another 27-year male patient added that

"I do not think there are people today who do not read texts. Even if there are people who are unable to read, there are treatment supporters available that can help the patient on the SMS text messages. There may be elderly patients that may not be able to read a text message and it may be better to contact their treatment supporters. But overall, we have made improvements regarding basic literacy, and I think most of the people are literate."

Making a voice message or phone calls to an illiterate

In addition, some health professionals suggested using phone calls, voice messages, and treatment supporters for those who cannot read and understand SMS text messages. For example, the 53-year female TB prevention and control expert stated that

"A possible solution for illiterate patients is to send a voice message ... In addition, we can also use treatment supporters who are literate and able to read a text message. You can provide orientation to treatment supporters and use them to deliver the contents of the SMS text messages to patients."

Additionally, some patients also reported that phone calls are appropriate for those patients who are unable to read and understand SMS text messages. The 25-year-old patient suggested using a phone call when unable to read text messages, *"There are patients who may not be able to read a text message. So instead of a text message, a phone call may be more appropriate. Yes, not all patients may be able to read a message. In addition, some people will also ignore a text message sent to them from a phone number that they do not*

know even if they see a notification. For these reasons, I think the phone call may be a better option."

Confirming and updating the patient's phone number

Some health professional respondents suggested immediately checking whether the patient's mobile phone number is working when the patient provides it to the health professionals. Patients should be made aware of the reason why their phone number is required. The 47-year-old female TB focal person shared her experience,

> *"When I take patient's phone number, I will call back them immediately while they are in front of me, and I confirm if the number they gave me is working. When taking their phone number, we provide them with all the information as to why we need their phone number and why we give them our phone number too. We inform them that they can call us at any time if they experience any problems. Some of them ask for my phone number on their own."*

Another 29 female TB focal person said that

> *"When we take their contact information, we first check the mobile phone is working. In addition, we also take additional phone number for the contact person who is most time a family member or a friend of the patient."*

The 53-year-old female TB focal person also said that

> "*Sometimes, I call back the phone numbers right after registering to check the phone number is working. So, making sure that the phone number is functional is an important thing."*

The 30-year female TB focal person said that

> *"We check if it (the phone number) works. But they still change the number. At times, the phone number may be disabled later. This is a challenge that we experience with patients taking TB medication and ART. You must*

continuously update their contact information as they change their phone number."

Giving the project a unique name

Some health professionals suggested using a unique code or project name for the short number that sends SMS text messages and makes phone calls, in order to distinguish the messages sent from the health facility from other messages. This could help patients to easily identify and read the text messages. The 35-year-old male TB prevention and control expert said that

> *"The text message that we want to send to the patients must be distinct from the rest of text message services. There are many text messages services that the public receives without requesting to receive them. As a result, many people tend to ignore these text messages. We must make sure that we should make the text message for this program is distinct so that patients will not ignore it."*

Some patients also suggested a way to differentiate the SMS text messages and phone calls made from the health facility from those made by other organizations. In this regard, the 33-year-old female patients said that

> *"I do not know how but there needs to be a way for you to differentiate the SMS messages that you plan to send to patients from the other messages sent from different organizations…People do not even bother to check these messages. When we see a mobile SMS message sent from a four-digit number, we usually do not even check the content of the message. So, it will be better to ensure that patients will see a unique identifier instead of four-digit numbers."*

APPENDIX THREE: PROTOTYPE SMS TEXT MESSAGES FOR MA-MAS INTERVENTION USING BEHAVIOUR CHANGE TECHNIQUES TAXONOMY AND IMB MODEL

Table 33: Prototype SMS text for Ma-MAS Intervention using Behaviour Change Techniques (BCT) taxonomy (Michie et al. 2013) [158] and IMB model [160]

Code	BCT	Definition	SMS Text content	IMB
1	**Goals and Planning**			
1.1	Goal setting (Behaviour)	"Set or agree a goal defined in terms of the behaviour to be achieved."	A person infected with TB must take their medications every day at a regular time for at least six months to be cured. Please plan to take all your medications with no interruptions	AM
1.2	Problem-solving	"Analyse, or prompt the person to analyse, factors influencing the behaviour and generate or select strategies that include overcoming barriers and/or increasing facilitators"	Why do some patients forget to refill their medication? You can come to refill any time before you run out of medications. Keep your calendar card in a place where you can see it	ABS
1.2.1			Does feeling well from TB symptoms cause forgetfulness about medications and lead people to discontinue medications TB medications must be taken for at least six months to be cured	ABS
1.2.3			Some patients miss their regular medical check-up. If the appointment scheduled is not comfortable to you, please let know to the healthcare provider to reschedule	ABS
1.2.4			Please ask your family member to pick up your medications for you if you are not able to come to the clinic to refill your medications	ABS

1.3	Goal setting (outcomes)	“Set or agree a goal defined in terms of a positive outcome of wanted behaviour”	If you want to be fully cured from TB, you must take all your medications for at least six months. Please do not forget to come to refill your medication supply	AM
1.4	Action planning	“Prompt detailed planning of performance of the behaviour (must include at least one of context, frequency, duration and intensity). Context may be environmental (physical or social) or internal (physical, emotion or cognitive) (includes ‘implementation intentions’)”	Do you experience difficulties to remember to take your medications every day at the same time as directed? Ask a family member or friend to help you remember	ABS
1.6	Discrepancy between current behaviour and goal	“Draw attention to discrepancies between a person’s current behaviour (in terms of the form, frequency, duration, or intensity of that behaviour) and the person’ previously set outcome goals, behavioural goals or action plans (goes beyond self-monitoring of behaviour).”	Consider some form of self-tracking such as a medication calendar to mark the number of consecutive days that you are adhering. How many days in a row have you taken your medication as prescribed?	ABS
1.7	Review of outcome goal(s)	“Review outcome goal(s) jointly with the person and consider modifying goal(s) in light of achievement. This may lead to resetting the same goal, a small change in that goal or setting a new goal instead of, or in addition to the first.”	Consider discussing how your health is improved while you are appropriately adhering your medication. Tell them if you missed any dose of medications	AM
1.8	Behavioural contract	“Create a written specification of the behaviour to be performed, agreed by the person, and witnessed by another”	Every day when you wake up in the morning, remember to take your medication before your breakfast. Consider asking a family member to remind you	AM

1.9	Commitment	“Ask the person to affirm or reaffirm statements indicating commitment to change the behaviour.”	For how many days have you correctly taken your medication as prescribed? To be cured from TB, you must take all your medications for at least six months	AI
2	**Feedback and monitoring**			
2.2	Feedback and monitoring	“Monitor and provide informative or evaluative feedback on performance of the behaviour”.	Thank you for picking up your medication as per your scheduled date. Keep it up, and take your daily medication as directed	AM
2.3	Self-monitoring of behaviour	“Establish a method for the person to monitor and record their behaviour(s) as part of a behaviour change strategy.”	Plan ahead to visit the health facility to refill your medication supply. Use a calendar card to check off the days when you have taken your medicine	ABS
2.4	Self-monitoring outcome of behaviour	“Establish a method for the person to monitor and record the outcome(s) of their behaviour a part of a behaviour change strategy.”	You can monitor your body weight and health improvement with appropriate medication adherence. Keep taking your medication as prescribed	ABS
2.5	Monitoring of outcome(s) of behaviour without feedback	“Observe or record outcomes of behaviour with the person’s knowledge as part of a behaviour change strategy.”	Plan with healthcare provider to get sputum test and to regular health check-up during treatment while you are adhering your medication	ABS
2.6	Biofeedback	“Provide feedback about the body (e.g physiological or biochemical state) using an external monitoring device as part of a behaviour”	Your healthcare provider monitors your health progress to check the medication is working. Keep up taking your daily medications as directed unless you are told to stop by a healthcare provider	AI
2.7	Feedback on outcome(s) of behaviour	“Monitor and provide feedback on the outcome of performance of the behaviour”	Do you know that those who adhere will have a better chance to be cured? If you missed any dose of TB medications, please tell the healthcare provider	AM

3	**Social support**			
3.1	General	“Advise on, arrange or provide social support (e.g. from friends, relatives, colleagues, or staffs) or non-contingent praise or reward for encouragement and counselling, but only when it is directed at the behaviour.”	We are here to better serve you. Please tell your health care provider whether you correctly adhere or not	AM
3.2	Practical	“Advise on, arrange, or provide practical help (e.g from friends, relatives, colleagues, or staffs) for performance of behaviour”	Please tell the healthcare provider if you are traveling somewhere away from home. They can give you extra medications or link you with another healthcare worker, so you will not run out of medications	ABS
3.2.1			Please tell us if you are feeling ill while you are on your medications. Ask the healthcare provider about the common side effects	ABS
3.3	Emotional	“Advise on, arrange, or provide practical help (e.g from friends, relatives, colleagues, or staffs) for performance of behaviour”	Your health status is our priority. Please Keep in touch with your healthcare provider and family support team for help when needed	AM
4	**Shaping knowledge**			
4.1	Instruction on how to perform a behaviour	“Advise or agree on how to perform the behaviour (include ‘skill training’)”	It is common to experience some side effects while you are taking TB medication. Please tell to your healthcare provider if you experience mild side effects	ABS
4.2	Information about Antecedents	“Provide information about antecedents (e.g. social and environmental situations and events, emotions, cognitions) that	People tend to forget to take their medications when they are away from home. Please remember to have an adequate amount of medications with you when you are away from home	AI

4.2..1`		reliably predict performance of the behaviour”	TB can be cured in almost all cases by taking the medications as prescribed without interruption	AI
4.2.2			Some patients will stop taking TB medications when they experience side effects. Please tell the health care provider if you have any side effects	AI
4.2.3			TB is not caused by exposure to cold air, insect bite, by opening the door/window at home or public transport. It is caused by a type of bacteria, Mycobacterium Tuberculosis	AI
4.2.4			TB is caused by Mycobacterium Tuberculosis that is not seen by eye. It is only cured by taking at least six months of medications	AI
4.2.5			TB is transmitted from one person to the other through inhaling air when infected person cough or sneezing or talking	AI
4.2.6			A cough that lasts 2 weeks or more, chest pain, coughing up blood or sputum, weakness or fatigue, and weight loss are the most typical signs of Tuberculosis	AI
4.2.7			Please bring your household members to a health facility if you see any TB symptoms on them. Early diagnosed TB will be effectively cured	AI
4.3	Reattribution	“Elicit perceived causes of behaviour and suggest alternative explanations (e.g external or internal and stable or unstable)”	Please remember that TB bacteria die very slowly. Simply because you are feeling well does not mean you have been	AI

			cured. You must maintain regular treatment for at least 6 months to be cured	
5	**Natural consequences**			
5.1	Information about Health consequences	"Provide information (e.g written, verbal, visual) about health consequence of performing the behaviour"	Be aware that if you are unable to adhere to TB medication regularly as directed, this can lead to failed treatment, relapse, and multidrug resistance	AM
5.2	Salience of consequences	"Use methods specifically designed to emphasise the consequence of performing the behaviour with the aim of performing them more memorable (goes beyond informing about consequences)"	A person with TB who takes all the medications as directed will be cured and will not be a risk of TB transmission to his/her family and other communities	AM
5.3	Information about social and environmental consequences	"Provide information (e.g written, verbal, visual) about social and environmental consequences of performing the behaviour"	Untreated TB can be transmitted to close family members, friends and other people. Please take your medications until the end of the treatment period as per prescription	AM
5.4	Monitoring of Emotional consequences	"Prompt assessment of feeling after attempts at performing the behaviour."	Did you take your medications at the same time every day? If you did, congratulations! If you didn't adhere, try again, but tell your healthcare provider the doses that you missed	AM
5.5	Anticipated regret	"Induce or raise awareness of expectations of future regret about performance of the unwanted behaviour"	Do you know that if TB treatment fails, you will become sick again, and you may transmit TB to loved family members and friends? Treatment fails if a patient is not adhering to medications	AM
5.6	Self-assessment of affective consequences	"Provide information (e.g written, verbal, visual) about emotional consequence of performing the behaviour"	Imagine what you would feel if you had a multi-drug resistant TB because of non-adherence to medications. It would need long-term treatment and may not ever be cured	AM

6	**Comparison of behaviour**			
6.1	Demonstration of the behaviour	"Provide an observable sample of the performance of the behaviour, directly in person or indirectly."	Consider using a strategy like setting an alarm in your mobile phone, or tell a family member to remember your daily TB medication and refill visit schedule	AM
6.2	Social comparison	"Draw attention to others' performance to allow comparison with the person's own performance."	I know some patients with TB who adhere to their medications. Adhered Patients have a higher chance of cure than non-adhered patients	AM
6.3	Information about other approval	"Provide information about what other people think about the behaviour. The information clarifies whether others will like, approve or disapprove of what the person is doing or will do."	Your healthcare professional, families and friends support you to take your everyday TB medications as per directed. Together you will succeed!	AM
7	**Associations**			
7.1	Prompts/Cues	"Introduce or define environmental or social stimulus with the purpose of prompting or cueing the behaviour. The prompt or cue would normally occur at the time or place of performance"	You must decide the first task in the morning is always to take your daily medication. Keep taking your daily medications at the same time every day as directed	AI
7.2	Cue signalling reward	"Identify an environmental stimulus that reliably predicts that reward will follow the behaviour"	Good morning! Before you eat your breakfast, please take your daily medication	AI
7.4	Remove access to the reward	"Advise or arrange for the person to be separated from situations in which unwanted behaviour can be rewarded in order to reduce the behaviour"	Cigarette smoking during TB treatment can lower your treatment success. Avoid people or places that make you want to smoke as much as possible	AI

7.6	Satiation	“Advise or arrange repeated exposure to a stimulus that reduces or extinguishes a drive for unwanted behaviour”	When patients drink alcohol while taking TB medications they would increase the side effect of the drug so that most people want to avoid alcohol during treatment	AM
7.8	Associative learning	“Present a neutral stimulus jointly with a stimulus that already elicits the behaviour reputedly until the natural stimulus elicits that behaviour”	Some patients take their medication in the morning immediately after they wash their faces. Keep taking your daily medication	AI
8	**Repetition and substitution**			
8.1	Behavioural practice/rehearsal	“Prompt practice or rehearsal of the performance of the behaviour one or more times in a context or at a time when the performance may not be necessary, in order to increase habit and skill”	Please remember to take your medication regularly every day at the same time. Please keep your medications in a safe place where you can see it	ABS
8.3	Habit formation	“Prompt rehearsal and repetition of the behaviour in the same context repeatedly so that the context elicits the behaviour”	Please take your medications every day at the same time in the morning. This helps you to remember to take your medications regularly	ABS
8.6	Generalization of target behaviour	“Advise to perform the wanted behaviour, which is already performed in a particular situation, in another situation.”	Please keep taking your daily medications regularly until the end of your treatment. TB is a curable disease if you are fully adhering to treatment	AM
9	**Comparison of outcomes**			
9.2	Pros and cons	“Advise the person to identify and compare reasons for wanting (pros) and not wanting to (cons) change the behaviour.”	Adhering to TB medications for a long period is not easy. Sometimes it has side effects. But not bad compared to getting a resistance TB and become a risk of transmission to families	AI

9.3	Comparative imagining of future outcomes	"Prompt or advise the imagining and comparing of future outcomes of changed versus unchanged behaviour."	Do you know that patients who fully adhere to their TB medications are more likely to get cured than those who don't adhere to their TB medications?	AI/AM
10	**Reward and threat**			
10.4	Social reward	"Arrange verbal or non-verbal reward if and only if there has been effort and/or progress in performing the behaviour (includes 'positive reinforcement')"	Thank you for picking up your medications. Please remember to take your daily medications at the same time every day	AM
10.7	Self-incentive	"Plan to reward self in future if and only if there has been effort and/or progress in performing the behaviour"	Plan to celebrate your completion of TB treatment with your families and friends together. Keep taking your daily medication	AM
10.9	Self-reward	"Prompt self-praise or self-reward if and only if there has been effort and/or progress in performing the behaviour."	Plan celebrate your medication adherence commitment at every 2 months of TB treatment progress until the end of treatment	AM
10.10	Reward (outcome)	"Arrange for the delivery of a reward if and only if there has been effort and/or progress in achieving the behavioural outcome (includes 'positive reinforcement')"	You are a hero. We appreciate your courage and commitment to adhere and pick-up your medications regularly schedule dates from clinics	AM
10.11	Future punishment	"Inform that future punishment or removal of reward will be a consequence of performance of an unwanted behaviour (may include fear arousal), includes 'threat'."	Do you know that non-adherence to medications may cause multi-drug resistant TB that may need complex treatment for a long time, has more side effects, and may not work or allow you to be cured	AM
11	**Regulation**			

11.1	Pharmacological support	“Provide, or encourage the use of or adherence to, drug to facilitate behaviour change”	Please ask us about your medications and common side effect. Your health is always our first concern.	AM
11.2	Reduce negative emotions	“Advise on ways of reducing negative emotions to facilitate performance of the behaviour (include ‘stress management’)”	If you have experienced any difficulties during treatment, please do not afraid (fear) to ask for help.	AM
12	**Antecedents**			
12.3	Avoidance/reducing exposure to cues for the behaviour	“Advise on how to avoid exposure to specific social and contextual/physical cues for the behaviour, including changing daily or weekly routines.”	Please remember to keep your medications with you anytime when you are away from home	AI
12.3.1			Please remember to avoid alcohol and smoking that will affect your TB treatment success	AI
12.6	Body changes	“Alter body structure, functioning or support directly to facilitate behaviour change”	You will gain body weight and become healthy if you appropriately adhere to your TB medications and lead a healthy lifestyle	AM
13	**Identity**			
13.1	Identification of self as role model	“Inform that one’s own behaviour may be an example to other”	Be a role model and save others from TB transmission by fully adhering to your TB medications regularly to the end of treatment	AM
13.3	Incompatible beliefs	“Draw attention to discrepancies between current or past behaviour and self-image, in order to create discomfort (includes ‘cognitive dissonance’).”	Do you want to be free from TB disease and be healthy? If so, are you taking your everyday medication as per directed?	AM

13.5	Identity associated with changed behaviour	“Advise the person to construct a new self-identity as some who ‘used to engage with the unwanted behaviour”	Do you remember those days when you had a hard time sticking with treatment—that wasn’t really you? Now, remember all the times you stayed on track—that’s who you are!	AM
14	**Scheduled consequences**			
14.4	Reward approximation	“Arrange for reward following any approximation to the target behaviour, gradually rewarding only performance closer to the wanted behaviour (includes ‘shaping’)”	You are almost near to finish your TB treatment. Please contact us for more information about your treatment status.	AM
14.5	Rewarding completion	“Build up behaviour by arranging reward following final component of the behaviour; gradually add the components of the behaviour that occur earlier in the behavioural sequence (includes ‘Backward chaining’)”	Congratulations! You are completed your TB medications. Please contact us for further health examinations.	AM
15	**Self-belief**			
15.1	Verbal persuasion about capability	“Tell the person that they can successfully perform the wanted behaviour, arguing against self-doubts and asserting that they can and will succeed.”	You have the capacity to fully adhere to all your TB medications every day to be cured. Yes, you can do it!	AM
15.2	Mental rehearsal of successful performance	“Advise to practice imagining performing the behaviour successfully in relevant contexts.”	Imagine that you can remember to take your daily TB medications to the end of treatment. Your imagination will become true!	AM
16	**Covert learning**			

16.1	Imaginary punishment	“Advise to imagine performing the unwanted behaviour in a real-life situation followed by imagining an unpleasant consequence (includes ‘covert sensitisation’).”	My worst enemy will laugh at me if I fail to adhere my medication and sick again. My dearest family will cry if I fail to adhere my medication	AM
16.2	Imaginary reward	“Advise to imagine performing the wanted behaviour in a real-life situation followed by imagining a pleasant consequence (includes ‘covert conditioning)”	Imagine that you can remember to take your daily TB medications to end of treatment and get cured. Your imagination has the power to become true!	AM
16.3	Vicarious consequences	“Prompt observation of the consequences (including rewards and punishments) for others when they perform the behaviour”	I know that there is someone just like you who has stuck with their TB treatment successfully.	AM

Am: Adherence Information , AM: Adherence Motivation , ABS: Adherence Behavioural skills

APPENDIX FOUR: VALIDATED SMS TEXT MESSAGES USING BEHAVIOUR CHANGE TECHNIQUES AND IMB MODEL

Table 34: Validated SMS text for Ma-MAS Intervention using Behaviour Change Techniques (BCT) taxonomy (Michie et al. 2013)[158] and IMB model (Fisher et al. 2006) [160]

S.NO	BCT	IMB	SMS text messages English Version
1	Commitment	Information	For how many days have you correctly taken your medication as prescribed? To be cured from TB, you must take all your medications for at least six months
2	Information about Antecedents	Information	People tend to forget to take their medications when they are away from home. Please remember to have an adequate amount of medications with you when you are away from home
3	Information about Antecedents	Information	TB can be cured in almost all cases by taking the medications as prescribed without interruption
4	Information about Antecedents	Information	Some patients will stop taking TB medications when they experience side effects. Please tell the health care provider if you have any side effects
5	Reattribution	Information	Please remember that TB bacteria die very slowly. Simply because you are feeling well does not mean you have been cured. You must maintain regular treatment for at least 6 months to be cured
6	Prompts/Cues	Information	You must decide the first task in the morning is always to take your daily medication. Keep taking your daily medications at the same time every day as directed
7	Cue signalling reward	Information	Good morning! Before you eat your breakfast, please take your daily medication
8	Associative learning	Information	Some patients take their medication in the morning immediately after they wash their faces. Keep taking your daily medication
9	Avoidance/reducing exposure to cues for the behaviour	Information	Please remember to keep your medications with you anytime when you are away from home

10	Avoidance/reducing exposure to cues for the behaviour	Information	Please remember to avoid alcohol and smoking that will affect your TB treatment success
11	Remove access to the reward	Information	Cigarette smoking during TB treatment can lower your treatment success. Avoid people or places that make you want to smoke as much as possible
12	Goal setting (Behaviour)	Motivation	A person infected with TB must take their medications every day at a regular time for at least six months to be cured. Please plan to take all your medications with no interruptions
13	Goal setting (outcomes)	Motivation	If you want to be fully cured from TB, you must take all your medications for at least six months. Please do not forget to come to refill your medication supply
14	Behavioural contract	Motivation	Every day when you wake up in the morning, remember to take your medication before your breakfast. Consider asking a family member to remind you
15	Feedback and monitoring	Motivation	Thank you for picking up your medication as per your scheduled date. Keep it up, and take your daily medication as directed
16	Feedback on outcome(s) of behaviour	Motivation	Do you know that those who adhere will have a better chance to be cured? If you missed any dose of TB medications, please tell the healthcare provider
17	Emotional	Motivation	Your health status is our priority. Please Keep in touch with your healthcare provider and family support team for help when needed
18	Information about Health consequences	Motivation	Be aware that if you are unable to adhere to TB medication regularly as directed, this can lead to failed treatment, relapse, and multidrug resistance
19	Salience of consequences	Motivation	A person with TB who takes all the medications as directed will be cured and will not be a risk of TB transmission to his/her family and other communities
20	Information about social and environmental consequences	Motivation	Untreated TB can be transmitted to close family members, friends and other people. Please take your medications until the end of the treatment period as per prescription
21	Monitoring of Emotional consequences	Motivation	Did you take your medications at the same time every day? If you did, congratulations! If you didn't

			adhere, try again, but tell your healthcare provider the doses that you missed
22	Anticipated regret	Motivation	Do you know that if TB treatment fails, you will become sick again, and you may transmit TB to loved family members and friends? Treatment fails if a patient is not adhering to medications
23	Self-assessment of affective consequences	Motivation	Imagine what you would feel if you had a multi-drug resistant TB because of non-adherence to medications. It would need long-term treatment and may not ever be cured
24	Demonstration of the behaviour	Motivation	Consider using a strategy like setting an alarm in your mobile phone, or tell a family member to remember your daily TB medication and refill visit schedule
25	Generalization of target behaviour	Motivation	Please keep taking your daily medications regularly until the end of your treatment. TB is a curable disease if you are fully adhering to treatment
26	Social reward	Motivation	Thank you for picking up your medications. Please remember to take your daily medications at the same time every day
27	Future punishment	Motivation	Do you know that non-adherence to medications may cause multi-drug resistant TB that may need complex treatment for a long time, has more side effects, and may not work or allow you to be cured
28	Body changes	Motivation	You will gain body weight and become healthy if you appropriately adhere to your TB medications and lead a healthy lifestyle
29	Identification of self as role model	Motivation	Be a role model and save others from TB transmission by fully adhering to your TB medications regularly to the end of treatment
30	Verbal persuasion about capability	Motivation	You have the capacity to fully adhere to all your TB medications every day to be cured. Yes, you can do it!
31	Mental rehearsal of successful performance	Motivation	Imagine that you can remember to take your daily TB medications to the end of treatment. Your imagination will become true!
32	Problem-solving	Behavioural Skills	Why do some patients forget to refill their medication? You can come to refill any time before you run out of medications. Keep your calendar card in a place where you can see it

33	Problem-solving	Behavioural Skills	Please ask your family member to pick up your medications for you if you are not able to come to the clinic to refill your medications
34	Discrepancy between current behaviour and goal	Behavioural Skills	Consider some form of self-tracking such as a medication calendar to mark the number of consecutive days that you are adhering. How many days in a row have you taken your medication as prescribed?
35	Behavioural practice/rehearsal	Behavioural skill	Please remember to take your medication regularly every day at the same time. Please keep your medications in a safe place where you can see it
36	Habit formation	Behavioural skill	Please take your medications every day at the same time in the morning. This helps you to remember to take your medications regularly.
37	Self-monitoring of behaviour	Behavioural Skills	Plan ahead to visit the health facility to refill your medication supply. Use a calendar card to check off the days when you have taken your medicine
38	Practical	Behavioural Skills	Please tell the healthcare provider if you are traveling somewhere away from home. They can give you extra medications or link you with another healthcare worker, so you will not run out of medications
39	Practical	Behavioural Skills	Please tell us if you are feeling ill while you are on your medications. Ask the healthcare provider about the common side effects
40	Instruction on how to perform a behaviour	Behavioural Skills	It is common to experience some side effects while you are taking TB medication. Please tell to your healthcare provider if you experience mild side effects

BCT: Behaviour Change technique, IMB: Information, Motivation, Behavioural skills

APPENDIX FIVE: PHONE CALLS CHECKLIST GUIDE

Checklist for phone calls intervention

(To be completed by a health professional at sub-city clinic when participant get a phone call)

Identification
Sub-city Name: _____
Health facility Name: _____
Participant registration code: _____
Participant mobile phone number: _____

Weekly phone calls intervention checklist form

Questions to be asked of the participant by a health professional:

Please answer the following questions by saying ‘Yes’ or ‘No” based on the intervention you are currently receiving.

			Ask the patient the following questions when you call			
Weeks	**Date (DD/MM/YY)**	Are the patient answered for the phone calls (minimum of 3 repetitive calls)	Good morning, do you take your daily medication?	Are you reading and following the SMS text message instructions?	Do you have any health problems or side-effects you want to discuss?	Do you have a question regarding your treatment?
Week 1						
Week 2						
Week 3						
Week 4						
Week 5						
Week 6						
Week 7						
Week 8						

APPENDIX SIX: DEMPGRAPHIC CHARACTEROSTICS OF ADULT TB PATIENTS WITHOUT PERSONAL MOBILE PHONES

Demographic characteristics

Among the 48 participants without personal mobile phones, 29 (60.4%) were female. More than half of the participants (54.2%) were married, while 17 (35.4%) had never been married. Regarding educational background, 23 (47.9%) participants had no formal education, and 13 (27.1%) had completed primary education grade 1-8. Occupationally, 15 (31.3%) participants identified as housewife, while 11 (22.9%) were unemployed. Family size distribution revealed that 22 (45.8%) participants had a family size of 4-5 people in the household, followed by 15 (31.3%) with a family size of 2-3 people. Concerning income, 31 (64.6%) participants had a monthly income less than 2373 ETB (57 USD). Additionally, 32 (66.7%) participants relied on walking as their primary mode of transportation to reach health facilities (see Table 35).

Table 35: Socio-demographic characteristics of adult TB patients without personal mobile phones, Addis Ababa, Ethiopia

Variables	**Frequency (percent)**
Gender	**n=48**
Male	19 (39.6%)
Female	29 (60.4%)
Marital status	**n=48**
Never married	17 (35.4%)
Married	26 (54.2%)
Divorced	0
Widowed	5 (10.4%)
Educational level	**n=48**
No formal education	23 (47.9%)
Primary education (1-8 grade)	13 (27.1%)
Secondary education (9-10 grade)	6 (12.5%)
Technical/Vocational education (11-12 grade)	4 (8.3%)
Higher education (above 12 grade)	2 (4.2%)
Occupational status	**n=48**
Daily laborer	7 (14.6%)
Governmental employee	0
Unemployment	11 (22.9%)
Merchant	3 (6.3%)
Housewife	15 (31.3%)
Student	2 (4.2%)
Driver	1 (2.1%)
Private employee	2 (4.2%)
Pensioner	3 (6.3%)
Guard	1 (2.1%)
Other*	3 (6.3%)
Family size	**n=48**
Living alone	3 (6.3%)
2-3 people	15 (31.3%)
4-5 people	22 (45.8%)
6 and above people	8 (16.7%)
Monthly income in ETB (USD)	**n=48**
Less than 2373 (57$)	31 (64.6%)
2373 (57$) and above	17 (35.4%)
Transportation used to reach the health facility	**n=48**
Walk	32 (66.7%)
Taxi	16 (33.3%)
Bajaj	0
Bus/Public transport	0

*Farmer, House Servant, ETB: Ethiopia Birr, USD: United States Dollar, Ethiopian Birr (ETB) to USD exchange was made based on the data collection time conversion rate

APPENDIX SEVEN: CHARACTERSTICS OF LOSS TO FOLLOW-UP PARTICIPANTS AND SENSITIVITY ANALYSIS

Demographic characteristics of loss to follow-up participants

Four of five lost to follow-up participants in the Ma-MAS group were males, while one of three lost to follow-up participants in the control group was male. In the Ma-MAS and control groups, the median age of lost to follow-up participants was 38 and 28 years, respectively. Three lost to follow-up participants in both Ma-MAS and control groups had never been married. Three lost to follow-up participants in the Ma-MAS group and one lost to follow-up participant in the control group had monthly income less than 2738 ETB (57 USD), putting them in poverty. Two lost to follow-up participants in the Ma-MAS group and one lost to follow-up participant in the control group did not have adequate food, while these lost to follow-up participants in both groups received food support. Two out of five lost to follow-up participants in the Ma-MAS group had TB/HIV co-infection, whereas all three lost to follow-up participants in the control group had only infected with TB (see table 36).

Table 36: Demographic characteristics of lost to follow-up adult TB patients enrolled in Ma-MAS trial, Addis Ababa, Ethiopia

Variables	Ma-MAS group n=5	Control group n=3
Sex		
Male	4	1
Female	1	2
Age in years		
Mean (Sd)	40.2 (16.39)	31 (12.76)
Median (IQR)	38 (25)	28 (19)
Marital status		
Never Married	3	3
Married	2	0
Educational status		
1-8 grade	1	2
9-10 grade	1	0
11-12 grade	1	0
Above 12^{th} grade	1	1
Occupation		
Governmental	1	0
Daily laborer	3	0
Housewife	1	1
Student	0	1
Unemployment	0	1
Monthly family Income (ETB)		
Less than 2738	3	1
2738 and above	2	2
Access to adequate food		
Yes	3	2
No	2	1
Food support (any source)		
Yes	2	1
No	3	2
TB-HIV co-infection		
Yes	2	0
No	3	3

Sd: standard deviation, IQR: Interquartile range

Sensitivity analysis

Effectiveness of Ma-Mas intervention on primary outcome

The effect of the mobile-assisted medication adherence support intervention on TB medication adherence measured by the IsoScreen urine test was unchanged after the inclusion of the loss to follow-up patients in the sensitivity analysis after 4 and 8 weeks of follow-up (see table 37 and 38).

Assumptions

Assumption one: The worst scenario**;** the lost to follow up patients considered as non-adherent to TB medication.

After 8 weeks follow-up, the Ma-MAS intervention had improved adherence by 12.90% (95%CI: 2.70, 23.16), and after 4 weeks of follow-up, Ma-MAS had improved adherence by 13.97% (95%CI: 4.91, 23.03) compared to the control group who only received the standared care (see table 37).

Table 37: Sensetivity analysis of Ma-MAS effect on TB medication adherence meausred IsoScreen urine test in the worst scenario

Primary outcomes	Adherence measured by IsoScreen test	95% CI	P value, 1-tailed
After 8 weeks of follow-up			
Ma-MAS group	81.72%	[73.86, 89.59]	
Control group	68.81%	[59.40, 78.23]	
Absolute Difference (AD)	12.90%	[2.61, 23.19]	0.020
After 4 weeks of follow-up			
Ma-MAS group	89.24%	[82.95, 95.54]	
Control group	75.26%	[66.50, 84.03]	
Absolute Difference (AD)	13.97%	[4.91, 23.03]	0.0063

Absolute Difference (AD) calculated Ma-MAS group – control group with 95% confidence interval (CI) of 1-tailed, n1=n2=93

Assumption two: The best scenario**;** the loss to follow-up and missing outcomes considered as adherent to TB medication.

The Ma-MAS intervention had a higher adherence by 15.05% after 4th and 8th weeks of follow-up time compared to the standard care in the control group (see table 38).

Table 38: Sensetivity analysis of Ma-MAS intervention effect on TB medication adherence meausred IsoScreen urine test in best scenario

Primary outcomes	Adherence measured by IsoScreen test	95% CI	P value, 1-tailed
After 8 weeks of follow-up			
Ma-MAS group	87.09%	[80.28, 93.91]	
Control group	72.04%	[62.92, 81.16]	
Absolute Difference (AD)	15.05%	[5.49, 24.60]	0.0054
After 4 weeks of follow-up			
Ma-MAS group	92.47%	[87.11, 97.83]	
Control group	77.41%		
Absolute Difference (AD)	15.05	[6.62, 23.48]	0.0020

Absolute Difference (AD) is calculated Ma-MAS group – Control group with 95% confidence interval (CI) of 1-tailed, n1=n2=93

Effectiveness of Ma-Mas intervention on secondary outcomes

The Ma-MAS intervention effect on self-reported TB medication adherence did not statistically differnent after including missing outcomes in the sensetivity analysis. Ma-MAS had no effect after the inclusion of the lost to follow-up (see Table 39 and 40).

Assumptions

Assumption one: The worst scenario**,** the lost to follow up and missing outcomes were considered as non-adherent to TB medication.

After accounting for lost to follow-up as non-adherence, the effect of the Ma-MAS intervention had no statistically significant differnce on self-reported TB medication adherence (see Table 39).

Table 39: Sensetivity analysis of Ma-MAS intervention effect on self report TB medication adherence in worst senario

Secondary outcomes	**Adherence measured by ACTG [95%CI]**	**P value**	**Adherence measured by VAS [95%CI]**	**P value**
Before intervention				
Ma-MAS group	70.97% [61.74, 80.19]		91.40% [85.69, 97.09]	
Control group	79.57% [71.37, 87.76]		92.47% [87.11, 97.83]	
Absolute Difference (AD)	-8.6% [- 20.9, 3.7]	0.174	-1.0% [-8.8, 6.7]	0.787
After intervention		**P value, 1-tailed**		**P value, 1-tailed**
Ma-MAS group	77.41% [68.92, 85.91]		89.24% [82.95, 95.54]	
Control group	78.49% [70.14, 86.84]		87.09% [80.28, 93.91]	
Absolute Difference (AD)	-1.0% [-10.9, 8.9]	0.430	2.15% [-5.6, 9.8]	0.325
DIFF	-7.5% [-21.9, 6.9]	0.193	-3.2% [-13.3, 6.9]	0.302

Absolute Difference (AD) is calculated Ma-MAS group – control group with 95% confidence interval (CI) of 1-tailed, DIFF-Difference in difference, n1=n2=93, ACTG: AIDS Clinical Trial Group adherence questionnaire, VAS: Visual Analogue Scale

Assumption two: The best scenario**;** the missing outcomes were considered as adherent to TB medication.

Ma-MAS had no statistically significant positive effect on self-reported TB medication adherence after accounting for lost to follow-up patients as adhered to TB medication (seeTabel 40).

Table 40: Sensetivity analysis of Ma-MAS intervention effect on self report TB medication adherence in best scenario

Secondary outcomes	**Adherence measured by ACTG [95%CI]**	**P value 2-tailed**	**Adherence measured by VAS [95%CI]**	**P value 2-tailed**
Before intervention				
Ma-MAS group	70.97% [61.74, 80.2]		91.40% [85.7, 97.09]	
Control group	79.57% [71.37, 87.7]		92.47% [87.11, 97.83]	
Absolute Difference (AD)	-8.6% [- 20.9, 3.7]	0.174	-1.0% [-8.8, 6.70]	0.787
After intervention		**P value, 1-tailed**		**P value, 1-tailed**
Ma-MAS group	84.94% [77.6, 92.2]		96.77% [93.18, 100]	
Control group	83.87% [76.3, 91.34]		92.47% [87.1, 97.8]	
Absolute Difference (AD)	1.1% [-7.6, 9.8]	0.4199	4.3% [-1.1, 9.7]	0.0967
DIFF	-9.7% [-23.3, 3.9]	0.122	-5.4% [-13.9, 3.1]	0.151

Absolute Difference (AD) is calculated Ma-MAS group - Control group with 95% confidence interval (CI) of 1-tailed, DIFF-Difference in difference, n1=n2=93, AIDS Clinical Trial Group adherence questionnaire, VAS: Visual Analogue Scale

APPENDIX EIGHT: PUBLICATIONS FROM THE THESIS

Article 1: Factors influencing patient adherence to Tuberculosis treatment in Ethiopia: a literature review

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Review

Factors Influencing Patient Adherence to Tuberculosis Treatment in Ethiopia: A Literature Review

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Abstract: Background: Tuberculosis (TB) is a major global public health problem and one of the leading causes of death among infectious diseases. Although TB can be cured with first-line antibiotics treatment of 6 months regimen, non-adherence to the treatment remains the main challenge for TB prevention and control. Interventions to promote adherence need to address multiple underlying factors linked to non-adherence, which requires a synthesis of studies to understand these factors in the local context. Our review accordingly examines these factors for TB treatment in Ethiopia. Methods: Articles were searched from PubMed and ScienceDirect databases, as well as manual searches through Google and Google Scholar search engines. Both quantitative and qualitative studies that showed factors associated with or reasons for non-adherence, default or loss to follow up from TB treatment were included. A total of 276 articles were screened, and 29 articles were ultimately included in the review. Findings: The extracted factors were synthesized thematically into seven dimensions of patient-centred, social, economic, health system, therapy, lifestyle, and geographic access factors. More than 20 distinct factors were identified under these headings. Some of these factors may also apply quite widely in other settings, with greater or lesser influence, but some are particularly applicable to the Ethiopian setting. Conclusion: Helping patients to achieve full adherence to TB medication is a complex problem as it is influenced by interplay between many factors. Healthcare managers, providers, and researchers need to consider and address multiple underlying factors when designing adherence interventions. This work provides a reference set of such factors for Ethiopian interventions.

Keywords: tuberculosis treatment; medication adherence; Ethiopia

1. Introduction

Tuberculosis (TB) is an infectious disease that is one of the major causes of death, being in the top ten causes of death worldwide and the leading cause of death from infectious disease, ranking above HIV/AIDS in 2018. Globally, one-fourth of the population is either infected with TB or at risk of developing the disease, with an estimated 10 million people infected with TB worldwide in 2018 [1]. Ethiopia has achieved a 50% reduction of TB through the Millennium Development Goals (MDGs) [2]. However, Ethiopia remains one of 14 high-burden TB countries for TB, TB-HIV, and Multi-drug-resistant tuberculosis (MDR-TB). An estimated 165,000 cases of TB incidence were reported for Ethiopia in 2018 [1].

Although TB can be cured with first-line antibiotics treatment of 6 months regimen, non-adherence is the main challenge for TB control and prevention programs. The patient needs to take >90% of TB

medication to facilitate TB cure, and a patient who takes at least 95% is said to be 'high adherence'. Treatment default is defined by the World Health Organization as a patient who interrupts treatment for 2 or more months [3]. The default rate is thus a crude method to monitor adherence [4]. Non-adherence to TB treatment increases the risk of morbidity, mortality, and drug resistance at both the individual and community level [5].

The World Health Organization has recommended Direct Observation of Treatment (DOT) by a trained supervisor, in which a healthcare worker watches the patient take the medication every day, to ensure adherence to treatment [6]. However, implementing DOT in Ethiopia is challenging for both the patient and healthcare provider. For example, one study conducted in Addis Ababa found patients reported that a daily visit to a health facility for the first two months was very difficult for a range of reasons, including severe illness at the initiation of treatment, distance too far for walking, and high transportation cost. Because of these challenges, DOT has not been implemented on a daily basis in Ethiopian standard care after the first two months of treatment [7].

A systematic review found that the pooled prevalence of non-adherence to TB treatment in Ethiopia was 21.3%. Forgetfulness, fear of drug side-effect, waiting time for 1 h or more during the service, and feeling a long distance to health facility were identified as factors associated with this non-adherence [8]. Another systematic review in the same setting found that the pooled prevalence of non-adherence to TB treatment and loss to follow-up were 20% and 5%, respectively. Being TB-HIV-co-infected, transport costs, lack of knowledge, drug side-effect, educational status, forgetfulness, being in continuation phase, perceived physical and psychological barriers, and psychological distress were identified as associated factors [9].

Interventions to promote adherence require addressing multiple components to overcome the barriers to adherence [10,11]. This requires a synthesis of studies to understand the causal factors for non-adherence to TB treatment in the local context. The above-mentioned systematic reviews and meta-analysis conducted in Ethiopia by Zegeye et al. (2019) [8] and Tolla et al. (2019) [9] had their main objective to estimate the pooled prevalence of non-adherence to TB treatment. The associated factors for non-adherence to TB treatment were not comprehensively identified by them, and their reviews included only quantitative studies.

This literature review synthesises both qualitative and quantitative studies to thematically present multiple factors that have been identified as influencing non-adherence to TB treatment in Ethiopia. This includes all types of TB such as active TB, latent TB, and TB-HIV co-infected patients. Therefore, this review could help healthcare managers, providers, and researchers to design and implement adherence interventions based on established contextual factors rather than ad hoc generalisations.

2. Methods

Research articles were searched for from PubMed and ScienceDirect databases, as well as manual search through Google and Google Scholar search engines. Search expressions were developed for TB medication adherence or loss to follow up or default from TB treatment that were published in the English language with no publication date restriction (see Table 1). The same expression of search strategy was used for all databases and search engines. Article searching was undertaken from 15 April to 5 May 2020.

Table 1. Searching strategy.

AND	(TB) OR (Tuberculosis)
AND	("medication adherence") OR (adherence) OR ("treatment adherence") OR ("medication compliance") OR (compliance) OR (default) OR ("loss to follow up")
AND	Ethiopia

Both qualitative and quantitative research articles were included, and articles that did not report original research were excluded. Articles that did not assess factors or reasons associated with TB medication non-adherence or default or loss to follow up from TB treatment were excluded, following the protocol of Figure 1. Data were extracted using an Excel template comprising the author, year, region, sample size, study design, population, and major findings. The article selection and data extraction were performed by the first author of this paper, and consistency was checked by the two other authors. Factors associated with TB treatment non-adherence were extracted from the quantitative type of studies, and reasons for non-adherence or default or loss to follow up were extracted from the qualitative type of studies. The extracted data were synthesized into groups based on the seven thematic dimensions of TB medication adherence factors proposed by Ogundele et al. (2015) [12]. These seven thematic dimensions are patient-centred, social, economic, health system, therapy, lifestyle, and geographic access factors.

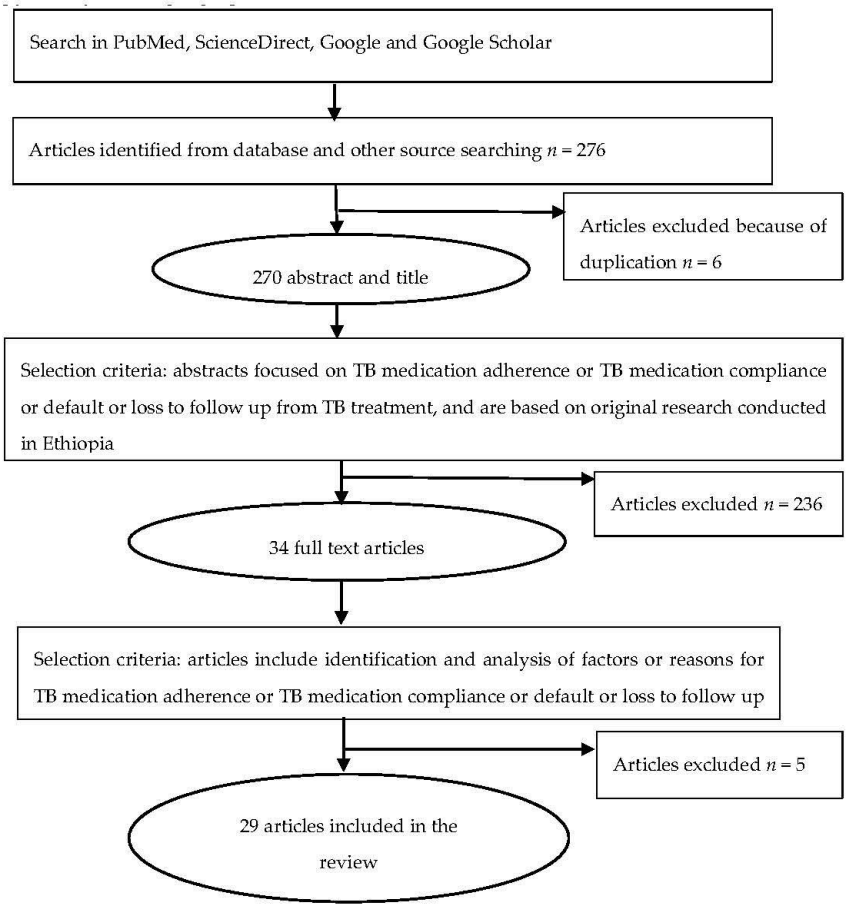

Figure 1. Flow chart for selection of reviewed articles.

3. Findings

A total of 276 research articles were screened, and 29 studies were ultimately included in this literature review. Of these, 6 articles were qualitative studies, 22 articles were quantitative studies (18 cross-sectional, 3 prospective cohort, and 1 case-control), and 1 article used a mixed-method design.

These studies were conducted in Addis Ababa (9); Southern Nations, Nationalities, and Peoples' Region (SNNPR) (7); Amhara (5), Oromia (5); and Tigray (3) regions of Ethiopia. Five studies were conducted among latent TB-HIV co-infected patients, and the remaining 24 studies were conducted among active TB infected patients. Approximately 7382 participants in total were involved in the studies reported in these 29 articles.

The synthesised findings from both quantitative and qualitative studies are presented below, grouped in seven dimensions of adherence influencing factors. The individual studies that showed factors or reasons linked with TB medication non-adherence are presented in Appendix A Table A1.

3.1. Patient-Centred Factors

Forgetfulness [13–21] and inadequate knowledge about tuberculosis and its treatment regimen [14,18,22–25] were the two major patient-centred factors. Three studies conducted in Oromia [26,27] and SNNPR [21] regions showed that the patient's educational status was associated with non-adherence to TB medications: the more the patient was educated, the less likely was non-adherence to TB medication. Psychological distress was another factor: two studies conducted in Addis Ababa reported that this indirectly positively influences non-adherence to TB medication [28,29]. Another qualitative study conducted in Addis Ababa also stated that poor mental health status of a patient would make them reluctant to regularly attend follow up and clinic appointments [18].

3.2. Social Factors

Several studies reported that patients not getting social support from families and neighbours in remembering to take their medication, food, and financial assistance were the major social factors that influenced non-adherence to TB medication [18,19,24,26,30–33]. Additionally, one study in Addis Ababa conducted among latent TB-HIV co-infected patients reported that the patients' friends' decision to take the medication would make them less likely to be non-adherent to isoniazid preventive therapy (IPT) [34]. Another study among the same subjects and setting found that patients who were comfortable to take IPT in front of other people were less likely to be non-adherent [35]. Being busy with work [14] and away from home for work or other social-related activities were also found to influence non-adherence to TB medication [14–16]. Perceived and experienced stigma and discrimination also led the patient to non-adherence [18,36–38]. These particular factors were highly noted in studies conducted among TB-HIV co-infected patients [18,31,37,38]. As one study indicated, because of fear of stigma and discrimination, the patients were not disclosing their HIV status to their family, which in turn influenced their non-adherence to TB medication [18].

Beliefs about the disease and treatment, such as perceived wellness or cure, perceived risk, and perceived barriers over the benefits, were influencing factors for non-adherence to TB medication [13,26,28,29]. One study conducted in Addis Ababa reported that a patient's belief in curability and severity of TB in the presence of HIV infection would make them less likely to be non-adherent [31]. Another study in Addis Ababa found that the perceived risk of discontinuing TB medication was the reason for adherence, while perceived wellness was the reason for patients have intention to discontinue TB treatment [13]. One study conducted in SNNPR also reported that belief in traditional healing influenced non-adherence to TB medication [36].

3.3. Economic Factors

The patient's economic constraints (which impact the financial burden) was the main economic factor that influences non-adherence to TB medication [17,29–31]. Economic constraints limit the patient's ability to have adequate food which influences non-adherence [31,36]. The cost of medication other than TB medications is also a factor for non-adherence in one study conducted in SNNPR. Another study conducted in SNNPR reported that the patient being not employed was associated with non-adherence [39].

3.4. Health System Factors

Poor healthcare provider–patient relationship with communication gaps was a major factor that influenced non-adherence to TB medication [14,31,32,36,39]. For example, one study conducted in Addis Ababa among loss-to-follow-up patients reported that the healthcare providers were seen as disrespectful of their patients and less committed to their profession [32]. The quality of healthcare service and a patient's satisfaction with healthcare service affect non-adherence to TB medication [16,30,39]. When patients perceived that they received less professional care and less time spent with the healthcare providers, and waited a long time to get healthcare service, they were more likely to be non-adherent [16,32,39,40]. Health information/education is also crucial for adherence: a few studies showed that the patients who did not receive health information/education from health facilities were more likely to be non-adherent [15,18,22]. Additionally, one study done in Addis Ababa found that cues to action were reported as a factor for non-adherence [28]. Lack of supervision and healthcare providers incapable of managing the patient's illness were also reported as influencing factors for interruption and default from TB treatment [38].

3.5. Therapy Factors

Many studies reported that drug side-effects were the major therapy-related reason for non-adherence to TB medication [15,16,23,24,26]. Pill burden was also reported as a factor for non-adherence to TB medication among active TB and TB-HIV co-infected patients [31,36]. The presence of more than one co-morbidity including TB-HIV co-infection was also reported as a factor for non-adherence to TB medication [14,16,20,26,37]. One study conducted in Addis Ababa also found that being on Antiretroviral Therapy (ART) was a factor for non-adherence to TB medication [29]. Symptom presence after initiation of anti-TB treatment and slow progression of the health status were also found as non-adherence factors [19,20,26,33]. Being in the continuation phase of the treatment (after the initial 2-month clinic-based treatment period) was a factor for non-adherence and default [14,20,24,34,41]. This might be due to the patient's perceived wellness or cure because a daily DOT was not implemented after the first two months of treatment in Ethiopia.

3.6. Lifestyle Factors

Alcohol consumption was reported as a factor that influenced non-adherence to TB medication in several studies [14,16,27,29]. Cigarette smoking and khat (herbal stimulant) chewing were also found as factors associated with non-adherence [16,27].

3.7. Geographical Access Factors

Healthcare inaccessibility from residence location was a major geographical access factor for non-adherence and default from TB treatment [17,19,22,26,30,36,40]. Due to inaccessibility, patients were unable to keep regular clinic appointments and follow up treatment in two studies, conducted in Addis Ababa and Amhara regions [16,35]. Distance of the health facility was related to transportation cost, which was also a factor for non-adherence [21,22,25,33].

4. Discussion

Adherence to TB medication is a complex and dynamic matter as it is affected by multiple factors. This review has identified the range of multiple factors that have been found to affect non-adherence to TB medications in Ethiopia. The influence of these factors individually and in combination might vary from one social or geographic setting to the other. Healthcare managers need to consider the underlying factors for non-adherence to TB medication in the local setting (ideally using locally available evidence) when they design and implement an intervention.

Our literature review has found some similar influencing factors of non-adherence to TB treatment as those described in the previous two systematic reviews conducted in Ethiopia [8,9]. These factors were forgetfulness, inadequate knowledge about TB and its treatment regimen, psychological distress

(poor mental health condition), perceived barriers, long waiting time, drug side-effects, TB-HIV co-infection, being on the continuation phase of treatment, healthcare inaccessibility, and travelling costs. Adherence interventions such as providing health information about TB and its treatment regimen, dealing with side-effects, providing reminders, and other health system interventions could be used to resolve these factors.

However, in this review, we have found several additional factors of non-adherence to TB treatment that were not identified by the previous two systematic reviews. These factors were lack of social support, being busy with work, being away from home, perceived and experienced stigma and discrimination, beliefs such as perceived wellness/cured, perceived risk, financial constraints to buy food and medication cost other than anti-TB, poor healthcare provider–patient relationship such as communication gaps, disrespecting patients, quality of healthcare service, patient satisfaction, lack of health information/education, pill burden, the persistence of symptoms after initiation of treatment, and use of substances such as alcohol, smoking, and khat chewing. These factors and the possible interventions to overcome the factors are discussed below.

We have found that lack of social support can influence non-adherence to TB medication. Thus, providing social support such as financial assistance for transport costs, food assistance, and reminders for medication intake from families and neighbours may help the patient to adhere to TB medication. In the same way, not getting social acceptance to take medication from families, friends, and neighbours can lead to non-adherence. A systematic review in developing countries reported the same finding [42]. Similarly, the perceived stigma and discrimination were reported as factors for non-adherence to TB medication. These were higher especially among TB-HIV co-infected patients. The other new social factors were being busy with work and away from home for work and social-related activities. These factors influence non-adherence might be due to the patient forgetting to take their medication when they are busy and away from home. A reminder from family or through mobile SMS text could be considered as a solution for these factors. Beliefs related to TB and its treatment can also influence non-adherence. This might be due to the patient's perceived wellness or cure after taking some medications and thus interrupting their treatment. On the other hand, when the patient perceives that the disease is severe and the risk of discontinuing TB medication leads to poor health outcomes, their non-adherence to TB medication would be less likely. A systematic review conducted in developing countries also found that feeling well after the initiation of treatment was a factor for non-adherence to TB medication [42]. Providing patients with health information to change such wrong beliefs about the disease and its treatment could be considered as an adherence intervention to address these factors.

The financial constraints to get adequate food, transport cost, and medication cost other than anti-TB medication were found to influence non-adherence or loss to follow up from TB treatment. A systematic review conducted in developing countries also reported that the financial burden can cause TB medication non-adherence [42]. Financial assistance or support of food and transport and making all medications freely available to the patient may overcome this factor.

We also found that healthcare-system-related factors were other major factors for non-adherence to TB medication. Poor healthcare-provider relationship with communication gaps, disrespect of the patient, and lack of professional commitment influenced non-adherence to TB medication. A systematic review conducted in developing countries also found that poor patient–healthcare worker communication was a factor for non-adherence to TB medication [42]. The quality of health service as perceived by the patient and the patient satisfaction also influenced non-adherence to TB medication. It was also found that patients who did not receive health information/education were more likely to be non-adherent to TB medication. Therefore, health system interventions such as training for healthcare provider–patient communication and their relationships and health system strengthening to shorten waiting times and to raise the quality of health services could address these factors.

Pill burden was also a factor for non-adherence to TB medication both in TB and TB-HIV co-infected patients. TB-HIV co-infection has additional burden from the pills and drug side effects. Persistence of symptomatic conditions after initiation of TB treatment was another influence for non-adherence.

This might be due to the patient's belief in the curability of the disease becoming less when symptoms persist despite the treatment initiation. Health information about TB, its treatment, and side effects could reduce the influence of these factors. New drug investigations to reduce the drug side effect and to make a shorter treatment regimen could also be considered if it is possible.

Substance use such as alcohol use, cigarette smoking, and khat chewing was a factor for non-adherence to TB medication as reported by a few studies. The use of these substances might make the patient reluctant to follow the regular clinic appointment and follow up treatment. Other systematic reviews conducted in developing countries also showed that alcohol and tobacco were factors for non-adherence to TB medication [42]. Health information on how the use of substances affected treatment adherence and treatment outcome may help to resolve this factor.

5. Limitations

This review included studies conducted in Ethiopia; therefore the identified factors may not be generalizable to other settings. Adherence to TB medication is a complex problem as it is influenced by multiple factors so a single factor may not be shown as a cause–effect relationship.

6. Conclusions

This review describes more than 20 factors that influence adherence to TB treatment in Ethiopia, demonstrating that it is a complex problem that is affected by the interplay of multiple factors. We have found major additional factors for TB medication non-adherence or default or loss to follow up. These were social support from families and neighbours such as food support, reminders, and encouragement; being busy with work; being away from home; perceived and experienced stigma and discrimination; beliefs such as perceived wellness/cure; perceived risk; economic constraints for having adequate food and medication cost other than anti-TB medication; poor healthcare provider-patient relationships such as communication gaps, disrespecting patients, quality healthcare service, and patient satisfaction; health information/education, pill burden, the persistence of symptoms after treatment initiation; and use of substances. Healthcare managers, providers, and researchers need to address these underlying factors when they design and implement adherence interventions.

Definition of Term: Adherence to a medication regimen is defined by Osterberg and Blaschke (2005) as "the extent to which patients take medications as prescribed by their health care providers"(10).

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Appendix A

Table A1. Summary of reviewed articles showing factors or reasons linked with TB medication adherence or default or loss to follow up from TB treatment.

First Author (Year)	Region	Study Design	Sample Size	Population	Associated Factors of Non-Adherence to TB Medication and Loss to Follow up/Default from TB Treatment
Daba et al. (2019) [27]	Oromia	Prospective cohort	268	Active TB patients	Khat (herbal stimulant) and alcohol use was associated with non-adherence with TB medication. Educational and occupational status were also associated with non-adherence to TB medication.
Sahile et al. (2018) [13]	Addis Ababa	A qualitative study	10	Active TB patients	Forgetfulness is the factor of TB medication non-adherence. The perceived risk and perceived wellness were also associated with TB medication non-adherence.
Mekonnen et al. (2018) [14]	Amhara	Cross-sectional study	314	Active TB patients	Being in the continuation phase of treatment, the presence of more than one co-morbidity, inadequate knowledge of TB and its treatment, poor patient–provider relationships, and alcohol use were statistically associated non-adherence to TB treatment. Additionally, forgetting to take medication, being busy with work, and out of home/town were the reasons mentioned by patients for non-adherence.
Gube et al. (2018) [40]	SNNPR	Cross-sectional study	271	Active TB patients	Drug side effects, a far distance from the health facility, and prolonged wait time to get healthcare service were statistically associated with non-adherence.
Woimo et al. (2017) [22]	SNNPR	Cross-sectional study	261	Active pulmonary TB patients	Inadequate knowledge of TB and its treatment, health information at each medication refill visits, a far distance from a health facility (more than 10 km), transportation cost, and cost of medications other than anti-TB.

Table A1. *Cont.*

First Author (Year)	Region	Study Design	Sample Size	Population	Associated Factors of Non-Adherence to TB Medication and Loss to Follow up/Default from TB Treatment
Tola et al. (2017) [28]	Addis Ababa	Cross-sectional study	698	Active TB patients	Perceived barrier over and perceived benefits directly associated with non-adherence TB medication. Cue to action and psychological distress were indirectly influence non-adherence mediated through perceived barriers and benefits.
Tola et al. (2017) [29]	Addis Ababa	Cross-sectional study	698	Active TB patients	ART status, economic status, alcohol use, perceived barrier, and psychological distress were statistically associated with non-adherence to TB medication.
Gugsa et al. (2017) [36]	SNNPR	A qualitative study	22	Active TB patients	Lack of adequate food, poor communication between healthcare providers and patients, beliefs in traditional healing, unavailability of the healthcare service in nearby, drug side-effect and pill burden, stigma, and discrimination.
Getahun et al. 2017 [32]	Addis Ababa	Mixed method design	649	Active TB patients and healthcare provider	Among lost to follow-up patients inadequate information about TB, healthcare provider–patient relationship (respect and value to patients), lack of support such as transport and nutrition support, and less commitment of healthcare provider towards the patients were reported as reasons for lost to follow-up.
Ayele et al. (2017) [15]	Amhara	Cross-sectional study	154	Latent TB-HIV patients	Lack of information about isoniazid preventive therapy (IPT), drug side effect, forgetfulness, and being away from home were found as factors for non-adherence to isoniazid preventive therapy (IPT).
Diriba et al. (2016) [26]	Oromia	Cross-sectional study	67	Active TB patients	Lack of family support, a far distance from the health facility, drug side-effects, extremely ill, feeling better, education level, and being HIV positive were the factors that led to non-adherence to TB medication.

Table A1. *Cont.*

First Author (Year)	Region	Study Design	Sample Size	Population	Associated Factors of Non-Adherence to TB Medication and Loss to Follow up/Default from TB Treatment
Ayele et al. (2016) [37]	SNNPR	Prospective cohort	162	Latent TB-HIV patients	Patients experiencing a high level of HIV stigma and having opportunistic infections statistically associated with non-adherence to isoniazid preventive therapy (IPT).
Tesfahuneygn et al. 2015 [16]	Amhara	Cross-sectional study	200	Active TB patients	Forgetfulness, being away from home, drug side effects, being unable to go to the health facilities on the date of appointment, being hospitalized, TB-HIV infected, alcohol use, smoking, khat (herbal stimulant) chewing, unsatisfied with healthcare service, and long waiting time to get the health service were significantly associated.
Yasin et al. (2015) [17]	Oromia	Cross-sectional study	53	Active TB-HIV co-infected	Forgetfulness, a far distance from the health facility, and low income were the factors for non-adherence to TB medication.
Mindachew et al. (2014) [18]	Addis Ababa	A qualitative study	12	Latent TB-HIV patients	Forgetfulness, lack of patient information, knowledge about the disease and its treatment, mental health status make them reluctant to attend follow-up and clinic appointment, not disclosing their HIV status to their family members because of fear of stigma and discrimination and lack of support from family led them to non-adhere to isoniazid preventive therapy (IPT).
Kiros et al. (2014) [23]	Tigray	Cross-sectional study	278	Active TB patients	The drug side effect and knowledge about TB prevention were associated with non-adherence to TB medication.
Eticha et al. (2014) [19]	Tigray	Cross-sectional study	120	Active TB-HIV co-infected	Patients who do not have caregivers and people who do not have to remind them to take their medications more likely non-adhere to TB medications. Forgetfulness, feeling sick, and being far away from health facilities were the mention of the main reasons of the TB-HIV co-infected patients for missing medication.

Table A1. *Cont.*

First Author (Year)	Region	Study Design	Sample Size	Population	Associated Factors of Non-Adherence to TB Medication and Loss to Follow up/Default from TB Treatment
Berhe et al. (2014) [34]	Addis Ababa	Cross-sectional study	381	Latent TB-HIV patients	Patients who took their medication for ≥ 5 or months were highly likely to be adherent compared to those who took it for 1-2 months. Patients' friends' decision to take the medication made them less likely to be non-adherent to isoniazid preventive therapy (IPT).
Nezenega et al. (2011) [39]	SNNPR	Cross-sectional study	531	Active TB patients	Employment status, area of residence, perceived time spent with a healthcare provider, perceived accessibility, perceived waiting time, perceived professional care, and overall patient satisfaction were associated with non-adherence to TB medication.
Adane et al. (2013) [20]	Amhara	Cross-sectional study	280	Active TB patients	Forgetfulness, being in the continuation phase, HIV co-infection, and persistent symptoms of tuberculosis were the factors for non-adherence to TB medication.
Tadesse et al. (2013) [30]	Amhara	A qualitative	26	Active TB	Access to health facilities, financial burdens, quality of health services, and social support were the main reason for failing to fully adhere to TB medication.
Kebede et al. (2012) [21]	SNNPR	Cross-sectional study	24	Active TB-HIV co-infected	The educational status was associated with non-adherence to TB medication. Forgetfulness and transportation cost were mentioned as reasons for non-adherence to medication.
Mindachew et al. (2011) [35]	Addis Ababa	Cross-sectional study	319	Latent TB-HIV patients	Patients who did not receive information about IPT, patients not comfortable taking IPT in front of other people, patients who did not attend regular clinic appointments, and drug side effects were associated to non-adherence to isoniazid preventive therapy (IPT).

Table A1. *Cont.*

First Author (Year)	Region	Study Design	Sample Size	Population	Associated Factors of Non-Adherence to TB Medication and Loss to Follow up/Default from TB Treatment
Gebremariam et al. (2010) [31]	Addis Ababa	A qualitative study	38	Active TB-HIV co-infected and healthcare providers	Side effects, pill burden, economic constraints, lack of food, stigma with lack of disclosure, and lack of adequate communication with health professionals were barriers for adherence. While beliefs in the curability of TB, beliefs in the severity of TB in the presence of HIV infection and lack of support from families and health professionals influenced non-adherence to TB medication.
Mesfin et al. (2009) [38]	Tigray	Cross-sectional	237	Active TB patients	Lack of supervision and incapability of dealing with patients' illness more likely to interrupt and default from treatment.
Sagbakken et al. (2008) [33]	Addis Ababa	A qualitative study	50	Active TB patients, healthcare providers and relatives	Transportation costs, poor health status due to illness or slow progression, not having social support, and not managing to restore their health and social status were factors for non-adherence.
Shargie et al. (2007) [41]	SNNPR	Prospective cohort study	404	Active TB patients	Continuation phase of treatment, a far distance from the treatment centre, and necessity to use public transport were the factors for default from TB treatment.
Michael et al. (2004) [25]	Oromia	Cross-sectional study	114	Defaulted TB patients	Far distance from the health institution, transportation cost, and being unaware about TB were the major reasons contributing to defaulting.
Tekle et al. (2002) [24]	Oromia	Case-control	1367	Active TB patients	Being in the continuation phase of treatment, lack of family support, inadequate knowledge about treatment duration and drug side effects.

SNNPR–Southern Nations, Nationalities, and Peoples' Region, TB–Tuberculosis.

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Article 2: Protocol of a parallel group Randomised Control Trial (RCT) for Mobile-assisted Medication Adherence Support (Ma-MAS) intervention among Tuberculosis patients

PLOS ONE

STUDY PROTOCOL

Protocol of a parallel group Randomized Control Trial (RCT) for Mobile-assisted Medication Adherence Support (Ma-MAS) intervention among Tuberculosis patients

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Abstract

Background

Non-adherence to Tuberculosis (TB) medication is a serious threat to TB prevention and control programs, especially in resource-limited settings. The growth of the popularity of mobile phones provides opportunities to address non-adherence, by facilitating direct communication more frequently between healthcare providers and patients through SMS texts and voice phone calls. However, the existing evidence is inconsistent about the effect of SMS interventions on TB treatment adherence. Such interventions are also seldom developed based on appropriate theoretical foundations. Therefore, there is a reason to approach this problem more rigorously, by developing the intervention systematically with evidence-based theory and conducting the trial with strong measurement methods.

Methods

This study is a single-blind parallel-group design individual randomized control trial. A total of 186 participants (93 per group) will be individually randomized into one of the two groups with a 1:1 allocation ratio by a computer-generated algorithm. Group one (intervention) participants will receive daily SMS texts and weekly phone calls concerning their daily medication intake and medication refill clinic visit reminder and group two (control) participants will receive the same routine standard treatment care as the intervention group, but no SMS text and phone calls. All participants will be followed for two months of home-based self-administered medication during the continuation phases of the standard treatment period. Urine test for the presence of isoniazid (INH) drug metabolites in urine will be undertaken at the random point at the fourth and eighth weeks of intervention to measure medication adherence. Medication adherence will also be assessed by self-report measurements using the AIDS Clinical Trial Group adherence (ACTG) and Visual Analogue Scales (VAS) questionnaires, and clinic appointment attendance registration. Multivariable regression model analysis will be employed to assess the effect of the Ma-MAS intervention at a significance level of P-value < 0.05 with a 95% confidence interval.

trial implementation, analysis, and interpretation of the findings. All trial information is the responsibility of the authors.

Competing interests: The authors declared that they have not any competing interests.

Discussion

For this trial, a mobile-assisted medication adherence intervention will first be developed systematically based on the Medical Research Council framework using appropriate behavioural theory and evidence. The trial will then evaluate the effect of SMS texts and phone calls on TB medication adherence. Evidence generated from this trial will be highly valuable for policymakers, program managers, and healthcare providers working in Ethiopia and beyond.

Trial registration

The trial is registered in the Pan-Africa Clinical Trials Registry with trial number PACTR202002831201865.

Background

Non-adherence to Tuberculosis (TB) treatment is a risk factor for further transmission, treatment failure, relapse, acquired multi-drug resistance, or extensively drug-resistant TB and death [1–3]. In Ethiopia, non-adherence to TB treatment, specifically a medication regimen involving a combination of antibiotics, is a serious threat to TB prevention and control programs. A recent systematic review and meta-analysis conducted in Ethiopia found that the pooled prevalence of non-adherence to TB medication was 21.3% [4].

Non-adherence to TB treatment is influenced by many interconnected factors. These include patient-centred-related factors, economic-related factors, social-related factors, health system-related factors, therapy-related factors, geographical access-related factors and lifestyle-related factors [5, 6]. The major factors affecting TB treatment adherence in Ethiopia are patient-centred-related factors such as knowledge about TB, its treatment duration and consequence of non-adherence [7–9], educational status [7, 10], psychological state of the patients like forgetfulness [10–13] and psychological distress [7, 14] and social-related factors such as social support, stigma and discrimination, perceived risk, perceived wellness/cure, and perceived barriers over the benefits [7, 14].

The World Health Organization (WHO) recommended Direct Observation of Treatment (DOT) by a trained supervisor; a health worker or a treatment supporter watches the patient take their antibiotics every day to ensure adherence [15]. However, evidence shows that DOT does not necessarily provide a reliable solution to poor TB treatment adherence [16, 17]. In Ethiopia, implementing DOT is also very challenging for patients as it requires patients' daily visits to the health facility, which has undesired implications in their work, social life and high transportation cost [18, 19]. The current WHO recommendations are to consider DOT implementation with different administration options including conventional DOT, video-observed treatment (VOT), and non-daily DOT [20]. The non-daily DOT has been implemented in Ethiopia, in which during the first two months of the intensive phase of treatment patients take their daily medications with the supervision of the healthcare provider, and from two to six months in the continuation phase of treatment patients take all their medications at home and visit a clinic weekly to refill their medications [11, 19]. However, the non-daily DOT schedule has been interrupted by the COVID-19 pandemic [21].

Digital health interventions through mobile health can create new opportunities for healthcare improvements, especially in situations with limited infrastructure, expertise, and human

resources in the healthcare system [22–25]. Digital health interventions that enhance TB medication adherence are seen as a promising option to bring health benefits to the community [26]. The growth in popularity of mobile phones provides opportunities to address adherence challenges related to DOT, as mobile health can facilitate direct communication between healthcare providers and TB patients through SMS and voice calls along with DOT or non-daily DOT [27, 28]. Along with SMS text reminders, phone calls are also suggested to improve a patient's clinic attendance and treatment outcomes, and can also be used to make the SMS text intervention interactive [29, 30]. In Ethiopia, access to mobile phones is expanding widely: according to the Ethiopia Demography Health Survey (EDHS) 2016, 88% of urban households and 47% of rural households have mobile phone access [31]. This is substantial growth over 5 years when compared to the EDHS 2011, which indicated 65% of urban households and 13% of rural households had mobile phone access [32].

There is some evidence that interventions that rely on communications, like educating and counselling the patient, or medication monitoring and reminders, can improve treatment adherence and success [28, 33–35]. In Ethiopia, for example, a randomized trial in 2016 found that psychological counselling and educational intervention can significantly improve a patient's treatment adherence [36]. Another trial in Ethiopia in 2019 has investigated the effect of a daily SMS text and weekly medication refill reminders on patient's medication adherence [37]. However, the combination of SMS text and phone calls (as in the intervention proposed here) based on the application of formal behavioural theories and behavioural techniques has not been previously designed and tested. This trial will also apply a combination of direct and indirect methods of adherence measurements for outcomes assessment. The mobile-assisted medication adherence support intervention will be developed systematically based on the Medical Research Council model, incorporating appropriate theory and evidence. The intervention design will be informed through qualitative in-depth interviews with different stakeholder groups such as patients, healthcare providers and healthcare managers, and the SMS content will be validated with experts in behavioural science, healthcare system, pulmonary disease and digital health, using a Delphi technique and will be revalidate by health professionals working at ground level.

Methods

Hypothesis

We plan to test whether our Mobile-assisted Medication Adherence Support (Ma-MAS) intervention using mobile SMS text reminders and phone calls will improve Tuberculosis medication adherence in addition to routine standard non-daily DOT care.

Trial design

A parallel-group individual randomized controlled trial (RCT) with two groups will be employed to investigate the effect of Ma-MAS intervention on TB medication adherence. Participants will be individually randomized into one of the two groups (one intervention and one control group) in a 1:1 allocation ratio (Fig 1).

Study setting

The study will be conducted at the primary public health facilities of Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia, and the city has 11 administrative sub-city regions. Based on population projection the estimated total population of Addis Ababa in 2017 was 3,433,999 with 1,624,999 Males and 1,809,000 Females [38]. In Ethiopia, a DOT program has

Study Period					
	Enrolment	Allocation	Post-allocation		close-out
Timeline	- t1	t0	t1	t2	t3
	Week 1	Week 12	Week 16	Week 20	week 21
Enrolment					
Eligibility screening	X	X			
Informed consent	X	X			
Allocation	X	X			
Intervention					
Daily SMS text			↔	↔	
Weekly Phone calls			↔	↔	
Assessment					
Baseline					
Socio-demographic	X	X			
Clinical characterstics	X	X			
Substance Use-related information	X	X			
Health Service-related information	X	X			
Adherence measured by AIDS Clinical Trial Group adherence questionnaire	X	X			
Adherence measured by Visual Analogue Scales (VAS)	X	X			
Outcome					
Adherence measured by IsoScreen test				X	X
Adherence measured by AIDS Clinical Trial Group adherence questionnaire					X
Adherence measured by Visual Analogue Scales (VAS)					X
Adherence measured by clinic appointment attendance			↔	↔	

Fig 1. Timeline for Ma-MAS intervention trial (SPIRIT figure).

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been implemented in two phases, "intensive" and "continuation". In the intensive phase (daily DOT), a patient takes their medication in front of the healthcare worker every day at a health facility. In the continuation phase (non-daily DOT), a patient is given the responsibility to take

the medication at home and come to a health facility weekly for health checking and medication refilling [39].

Participants

Adult Tuberculosis patients who are receiving anti-TB treatment at primary public health facilities of Addis Ababa, Ethiopia will be prospective participants for the trial.

Eligibility

Inclusion criteria. To be included in the trial:

- participants must be enrolled in a primary public health facility for anti-TB treatment and have attained their first two months of the intensive phase of treatment
- participants must be aged 18 years and above
- participants must be able to read and understand SMS text that is written in the national official language (Amharic) of Ethiopia
- participants must have their own mobile phone, or
- participants who do not have a mobile phone can be included if they have a shared mobile phone in the household with a collaborative agreement; (i.e. a voluntary agreement between the patient and family member living in the same household).

Exclusion criteria. Participants will be excluded from the trial under the following conditions:

- participants whose anti-tuberculosis treatment has been underway for more than six months.
- participants who are enrolled or have agreed to enroll in any other interventional study at the same time as this study is conducted.

Intervention group

The intervention will be given in arm-1 (intervention) group participants will receive a daily SMS text and weekly phone calls for medication intake and medication refill visit reminders. All participants will receive the intervention at a similar time for two months during the continuation phase of anti-TB treatment (Fig 2).

Control group

The control group (Arm-2) participants will receive the same routine standard treatment care as the intervention group, but no SMS text and phone calls intervention. Patients in the control group will be followed for the same two-month period as the intervention group during the continuation phase of their treatment.

Intervention development procedure

The mobile SMS text messages will be developed systematically with the best available evidence in the context area and with the application of appropriate behavioural theory and technique. The intervention will be developed and evaluated based on the Medical Research Council

Fig 2. Mobile-assisted Medication Adherence Support (Ma-MAS) intervention diagram.

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(MRC) framework for complex interventions in healthcare (Table 1) [40]. The non-sequential development stage of the framework as adapted by Bleijenberg et al. (2018) will be used as a more specific guide for the intervention design [41]. This has seven different phases:

Phase 1: problem definition (identification and analysis)

Phase 2: systematically identifying the evidence

Phase 3: identifying and developing a theory

Phase 4: determining the needs (patients and/or providers)

Phase 5: examining the practice

Phase 6: modeling process and outcome and

Phase 7: intervention design.

Table 1. Mobile-assisted medication adherence support intervention development process using an adapted development phase of MRC framework and the associated methods.

Development phases	Methods
Phase 1: Problem identification and definition	• Review of literature • Qualitative research
Phase 2: Identifying the evidence base	• Review of literature • Qualitative research • Quantitative Survey research
Phase 3: Identifying and/or developing theory	• Review of literature
Phase 4: Determine the need	• Review of literature • Qualitative research
Phase 5: Examine current practice and context	• Qualitative research
Phase 6: Modeling process and outcome	• Modeling a prototype of intervention components • Identity interrelation with the outcome • Experts opinion through Delphi method and survey
Phase 7: Intervention design	• Experts opinion • Refine the intervention

https://doi.org/10.1371/journal.pone.0261758.t001

Phase 1: Problem identification and definition. The problem of non-adherence to the anti-TB medication has been identified and defined through a literature review. The literature review is published in the title of "Factors Influencing Patient Adherence to Tuberculosis Treatment in Ethiopia? A Literature Review" [6]. This review will be further supported by qualitative research using in-depth interviews with TB patients and healthcare providers.

Phase 2: Identifying the evidence base. Evidence has been collected through a review of literature, to identify the effectiveness of mobile health SMS interventions including acceptability, feasibility, and characteristics of the intervention. Acceptability and feasibility survey will be conducted before the trial is implemented. This phase aims to identify previous interventions and their effectiveness and to assess the acceptability and feasibility of the target groups of the interventions, as well as the success and failure factors (S1 and S2 Tables).

Phase 3: Identifying and/or developing theory. The theories or models that can best explain the proposed intervention mechanism and action have been selected through a review of the literature. This phase of development aims to identify the theory or model that can best explain the intervention mechanism of action. We have selected an information motivation behavioural skill model [42], and have shown the relationship between the model construct of information, motivation and behavioural skills with adherence behaviour based on the factors affecting TB medication adherence identified in phase one (Fig 3).

Phase 4: Determine the needs. The needs, preferences, perceptions, and capacities of the patient and healthcare providers with the identified problems and proposed solutions will be determined through a review of the literature and qualitative research by using in-depth interviews. This will generate information about which characteristics of the intervention are likeable and adaptable, and how the SMS texts can be tailored regarding language, content, frequency, length, and time of the day.

Phase 5: Examine current practice and context. Identification of barriers and facilitators of mobile health interventions through examining the current practice and context from the patient's and healthcare provider's perspectives will be made. This would help the functionality of the proposed mobile health intervention best fits with the existing practice and context. This activity will be done through qualitative research by using in-depth interviews.

Phase 6: Modelling process and outcome. Modeling the active component of the mobile health intervention and its relationship with outcomes will be refined with multidisciplinary team involvement. The initial SMS text content will be refined using the taxonomy of evidence-based behaviour change [43]. The Delphi technique will be employed to validate the content of the SMS text further. Eight experts from different professional backgrounds of behavioural science, healthcare system, pulmonary disease, and digital health experts will be involved in this process. A survey will be conducted among health professionals who working as TB focal persons and communicable disease control officers from health facilities and health offices in Addis Ababa, Ethiopia.

Phase 7: Intervention design. A full prototype mobile SMS text intervention will be developed and will be given to experts for their feedback to make final refinements. The experts will be asked to comment on the timing and frequency of information, clarity, and arrangement of the SMS text messages. Based on the expert's comments the final SMS text message set will be prepared.

Outcome

The outcome of the trial is the medication adherence of the patient, measured by both direct and indirect methods of measurement. The primary outcome will be measured using an Iso-Screen test (GFC Diagnostics Ltd, Bicester, England) for the presence of isoniazid (INH) drug

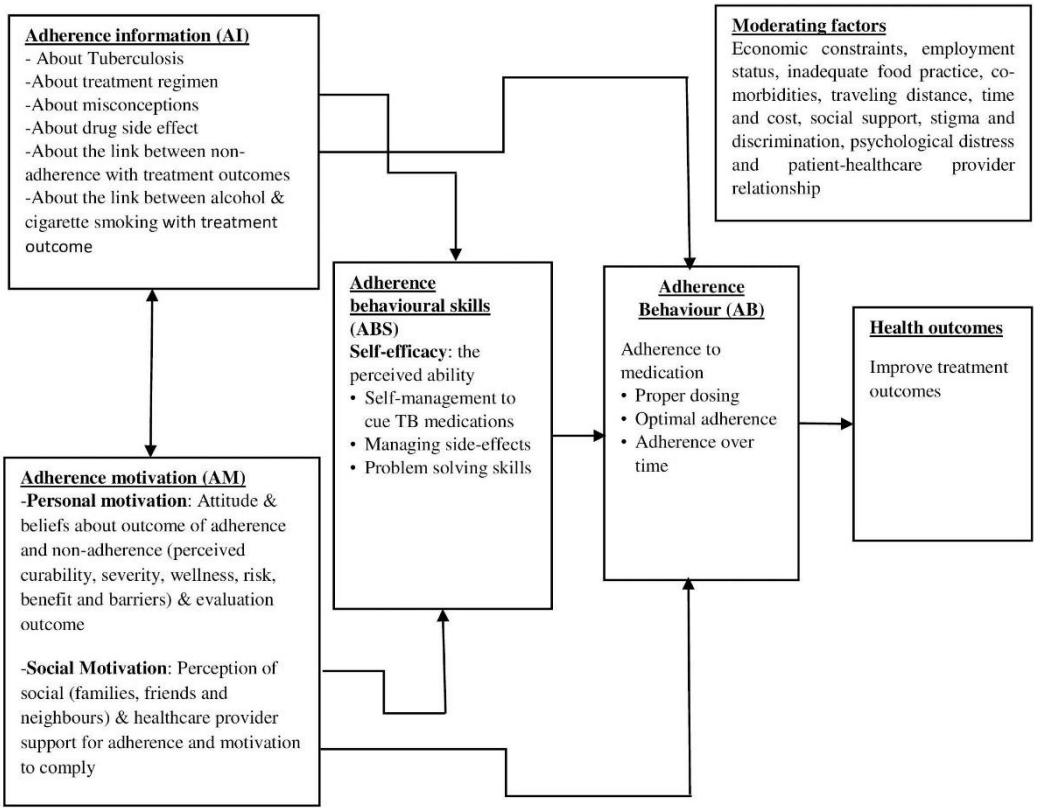

Fig 3. Information, motivation and behavioural skills model to Tuberculosis medication adherence adapted from Fisher et al. 2006 [42].

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metabolites in urine in accordance with the vendor-supplied user manual. The IsoScreen test result is negative when there is no colour change (i.e. the strip remains yellow) after 5 minutes, and the test result is positive when the colour changes to dark purple, or blue/ green in that time, depending on the concentration of the medication (i.e. if the medication was taken in the last 24 hours or 48 hours respectively) [44, 45]. The IsoScreen test will be done at the fourth and eighth weeks of the intervention. The proportion of adherence measured by the IsoScreen test at the eighth week of the intervention (primary end point) will be used as the primary interest of analysis. The proportion of adherence measured by the IsoScreen test at the fourth week of the intervention will be used as the secondary interest of analysis.

The secondary outcome will also be measured by self-report of medication adherence using the adapted AIDS Clinical Trial Group adherence questionnaire (ACTG) [46], Visual Analogue Scales (VAS) [47], and by clinic appointment attendance registration [48]. The adapted version of ACTG has three sections: section B (social support), section C (possible reasons for non-adherence) and section D (adherence behaviour). Participant scores less than "somewhat satisfied" to any questions in section B or other than "never" to any questions in sections C

and D are considered as non-adherence [48]. VAS is a single adherence scale that requires a patient to estimate their adherence level from 0% to 100%: 0% means the patient has taken no medication, 50% means the patient has taken half of their prescribed medications, and 100% means the patient has taken all of their prescribed medications, for the last 30 days. Participant scores less than 90% for VAS are considered as non-adherence [36, 49]. Clinic appointment attendance registration for weekly medication refills visits will also be used for adherence measurement. Patients who delay for at least one medication refill visit are considered as non-adherence [48]. The ACTG and VAS questions will be asked at bassline assessment and end of two months of intervention (Fig 1). The proportion of adherence measured by self-report and clinic appointment attendance registration at the eighth week of the intervention will be used as the secondary interest of analysis.

Sample size

A STATA code *power twoproportions* was used to calculate the sample size considering the trial outcome of anti-TB medication non-adherence. The rate of anti-TB medication non-adherence in Ethiopia varies considerably in the literatures, ranging from 10% to 26% depending on the patient's treatment phase and different settings [8, 11, 14]. It was found specifically that the rate of non-adherence was 25.6% (po = 0.256) during the continuation phase of treatment from a recent study conducted at Addis Ababa, Ethiopia [14] in the control group. We used a 15% absolute reduction of non-adherence due to a mobile SMS text intervention found in a similar study [37] to estimate a non-adherence rate of 10.6% (pa = 0.106) in the intervention group. Considering that we are using a simple randomized controlled trial parallel-group design, choosing a 95% confidence level (alpha = 0.05), 80% power (beta = 0.80) and a one-sided p-value of 0.025 for the initial sample size would yield n = 81 participants per arm. Assuming an attrition rate of 15%, the final sample size would be a total of n = 186 with each of the 2 arms having n = 93. From 10 sub-cities in Addis Ababa, a total of 36 primary public health facilities will be included in the trial study by random selection, based on the assumption that on average 6 patients per public health facility will be available to be included in the study.

Recruitment

Patients enrolled in the intensive phase of anti-TB treatment will be recruited by the research support team of healthcare professionals from each health facility, based on the eligibility and exclusion criteria. The recruitment will be continued until the required sample size is obtained. All the recruitment process details will be recorded on paper forms and kept securely by the facilities until the project is completed.

Randomization and allocation

Participants will be centrally randomized into one of the two groups using simple randomization in computer-generated algorithm, with an equal allocation ratio (1:1), by members of the research support team, who will not be involved in measuring the outcome (Fig 4).

Follow up

Both the intervention and control groups' patients will be followed for an equal period of 2 months. Intervention group participants will receive a total of 60 daily SMS text reminders and 8 phone calls for medication intake and refill visits reminders.

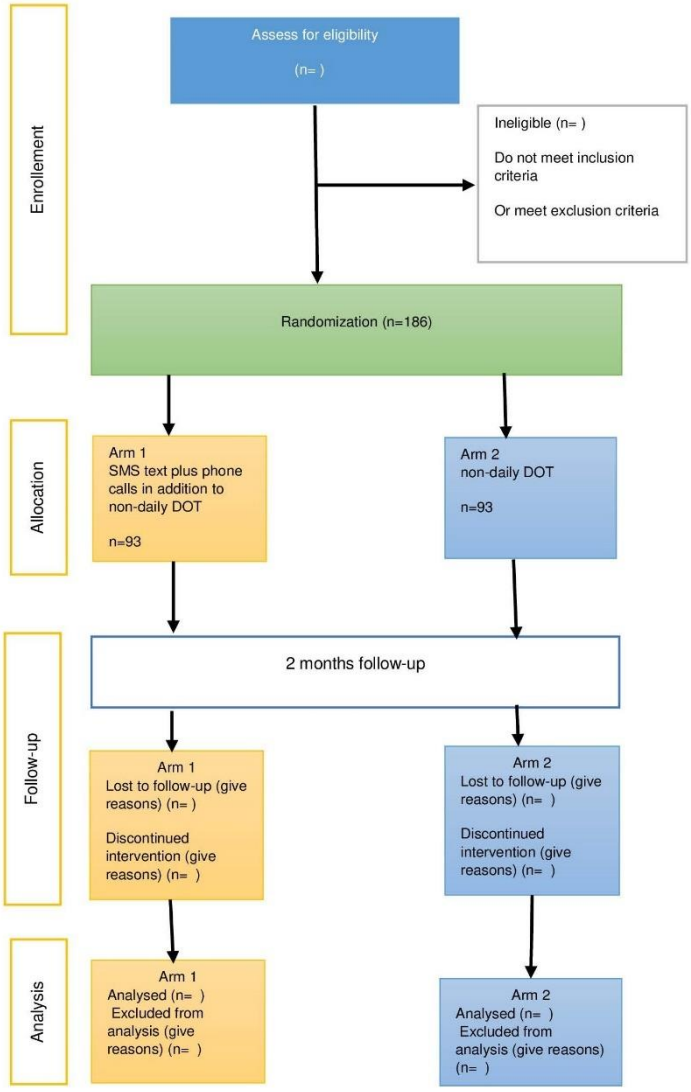

Fig 4. Flow diagram for Ma-MAS intervention trial.

https://doi.org/10.1371/journal.pone.0261758.g004

Blinding

Single-blinding will be applied to avoid bias in outcome measurement, by differentiating the person who measures the outcome from the person who randomizes and provides the intervention. Thus, the person who measures the outcome will be blinded as to which group

participants are assigned. Due to the nature of the trial intervention participants will not be blinded to which group they are assigned.

Implementation

All patients assigned to any group will get the same standard treatment based on the Ethiopia National Tuberculosis Treatment guideline which is rifampicin, isoniazid, pyrazinamide and ethambutol for two months followed by rifampicin and isoniazid for four months [50]. Patients screening, enrolment, consenting and randomization will be undertaken by the research support team, who have health professional backgrounds. An open SMS automation software platform will be used to store, monitor, and send SMS texts. Global system for mobile (GSM) sim card and short code SMS credit will be used to send the SMS texts. SMS text traffic will be managed and monitored in one centralised computer database server by trained IT personnel. The maximum size of an SMS text will not be more than 160 characteristics. A weekly phone calls will be made to the intervention group participants from the health facility by delegated members of the research team. A checklist of questions will be recorded at each time the weekly phone calls are made to the participants (S2 Checklist). Bothe the SMS text and Phone calls intervention will be made using the national official language which is Amharic. For patients who do not answer phone calls, three repetitive attempts will be made at five-minute intervals. All SMS texts and phone calls will be delivered at a similar time in the morning before the actual medication time. The message delivery reports will be continuously monitored to ensure the participants have received the SMS texts as planned. Participants will also be asked whether they are receiving the SMS text every week through phone calls and when they come for their medication refill visit. Participants will be briefed on the duration, frequency, and timing of SMS text and phone calls intervention and advised to turn on their mobile in the morning. Participants will be informed about the intervention and instructed not to tell and/or share the SMS texts or phone calls with other people. If participants lose or change their phone numbers, the new phone number will be replaced immediately after they have informed a support team member. The trial will be audited with participant enrolment, consent, allocation, and during the intervention period.

Data collection and management

A trained healthcare professional team will collect and supervise the data collection. Data collection will be made after the patient has received the routine non-daily DOT services in a different room from the TB clinic room, to ensure the confidentiality and privacy of the patient's information. The data will be collected electronically using a smart mobile app through a questionnaire coded using Open Data Kit (ODK). Data will be collected from the primary source through interviews and sample urine collection, and secondary source by a review of the health facility attendance registration book to confirm the patient's medication refill visit attendance. All interviews will be conducted after the patients finish the non-daily DOT service. Interviews will be conducted in a different room from the TB clinic to be convenient for discussion and privacy.

To ensure the security of the patients' information, all data will keep in Open Data Kit (ODK) database, principal investigator laptop computer, and backup file with password protectors. All identifiable information will be removed and replaced by code. All hard-copy research documents will be locked in a cabinet.

Statistical analysis

The electronically collected data will be exported to STATA and cleaned using STATA coding programing language. Descriptive statistics of mean, standard deviation, median, and range will be used for continuous variables and frequency and percentage for categorical variables.

Intention to treat (ITT) analysis will be performed for all randomized participants according to their group. A chi-square test for binary outcomes and Student's t-test for continuous outcomes will be used as appropriate. For primary and secondary interest of analysis, multivariable regression model analysis will be employed to adjust confounding factors in the statistical effect. A P-value of less than 0.05 will be used as a cut-off point to show a statistically significant association between Ma-MAS intervention and medication adherence with a 95% confidence interval.

Ethical considerations

The research proposal has been approved by the Southern Adelaide Clinical Health Research Ethics committee (SAC HREC) on April 8, 2020, with Office for Research (OFR) number: 23.20. The proposal has also be approved by the Addis Ababa Health Bureau ethics committee on August 21, 2020, with reference number A/A/H/930/227 and an official permission letter is provided from Addis Ababa Health Bureau to respective sub-city and health facilities. Each participant will complete a written informed consent form after being informed about the research objectives, procedures, anticipated risks, and benefits of the research. The research team will be confirming or renegotiating consent with participants for additional data. The principal investigator will be ensuring participants are confirming their consent to participation. Participants have the right to withdraw from the study at any time when they feel uncomfortable or unable to continue in the study, and they will be informed of its limitations or consequences on the research during consent requests. Any change in the study protocol and participant informed consent will be submitted to SAC HREC before implementing the change. This trial has no forms of inducement, coercion and the study does not bring any risks that incur compensation in cash or kind.

Publication and dissemination of the result

The trial findings will be reported based on the Consolidated Standard of Reporting Trials (CONSORT) guidelines. The research outcomes will be published in an international peer-reviewed open access journal. The research outcomes will also be presented at selected national and international conferences. The principal investigator is responsible for disseminating the finding to Health facilities, Addis Ababa Health Bureau, Federal Ministry of Health (FMOH), Flinders University, national and international conferences. The participants will be asked whether they wish to get a summary of the research work, and if so in what form, and will be informed about how they can access the research results. In the case of a formal request for further research purposes, non-identifiable secondary data may be granted to others. A participant's identifiable information will be removed and replaced by code to protect the anonymity of the participants. Identifiable data and/or information will not be accessed or granted to others.

The trial is registered in the Pan-Africa Clinical Trials Registry with trial number PACTR202002831201865.

Discussion

An adherence intervention needs to address the underlying factors that cause medication non-adherence [26]. Medical Research Council (MRC) guidelines recommend using appropriate theory and evidence when developing an intervention [40]. However, most adherence interventions are developed without a strong theoretical base, which might be one of the reasons they have not been effective [51]. In this randomized controlled trial, the Mobile-assisted

Medication Adherence Support (Ma-MAS) intervention will be developed systematically using the MRC conceptual framework with an appropriate selection of behavioural theory.

Some evidence has shown that interactive SMS texts may have a better impact than using simple SMS text reminders in improving medication adherence [52, 53] although there is also inconsistent evidence found in some two-way [30, 54] and one-way SMS text studies among TB patients [55, 56]. This trial was designed to test an intervention with a combination of daily SMS text and weekly phone calls for medication intake and medication refill visit reminders during the continuation phase of treatment for a two months period, which was not studied previously.

When testing an intervention with randomized trials, correctly measuring outcomes in the same way for both the intervention and control groups is crucial. The accuracy of adherence measurement is very important to assess the true effect of an adherence intervention. Here the adherence outcome will be measured through the combination of a direct method (IsoScreen test) and several indirect methods (VAS, ACTG, and clinic attendance registration) of measurement. This will help to avoid bias in outcome measurement. Therefore, this research would provide evidence to help healthcare managers and policymakers to develop strategies that improve Tuberculosis medication adherence and treatment outcomes in general.

Supporting information

S1 Checklist. SPIRIT 2013 checklist: Recommended items to address in a clinical trial protocol and related documents*.
(DOC)

S2 Checklist. English version checklist for phone calls intervention.
(PDF)

S1 Table. SMS text messaging interventions for TB treatment support.
(DOCX)

S2 Table. SMS interventions for TB: Acceptability and feasibility study design.
(DOCX)

S1 File. Participant information sheet/consent form intervention and post-intervention participants.
(PDF)

S2 File. Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis patients: Adoption of intention, effectiveness, and experiences in Addis Ababa, Ethiopia.
(PDF)

S3 File. Pan African Clinical Trials Registry.
(PDF)

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Article 3: Mobile-assisted medication adherence support intervention among Tuberculosis patients: a parallel group randomised control trial (Conference Abstract)

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Mobile-assisted medication adherence support intervention among tuberculosis patients: a parallel group randomized control trial

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More details

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Article (PDF)

ABSTRACT

Background:
There is conflicting evidence regarding the efficacy of SMS texts to promote TB medication adherence. Thus, we developed a mobile-assisted medication adherence support (Ma-MAS) intervention using the medical research council (MRC) framework based in a local context targeting audience needs and the effectiveness of this intervention evaluated in a sample of TB patients in Addis Ababa, Ethiopia.

Methods:
A parallel group randomized control trial design was used to evaluate the effectiveness of Ma-MAS intervention. In total, 186 adult TB patients (93 per group) were randomly assigned 1:1 to one of the two groups. Participants in the Ma-MAS group received daily SMS texts and weekly phone calls regarding their daily medication intake and reminders to attend clinic visits for 8 weeks. Participants in the control group did not receive SMS texts or phone calls but received the same routine standard care as the Ma-MAS group. The primary outcome was the proportion of adherence measured by urine tests for isoniazid (INH) metabolites at the end of the 4th and 8th week of follow-up period. Analysis of a multivariable binomial generalized linear model was employed to evaluate the effect of Ma-MAS at P value< 0.05.

Results:
Ma-MAS significantly improved adherence to TB medications by 15.25% (95%CI: 5.38, 25.12; P-value=0.0065) after 8 weeks of intervention compared to the standard care alone in the control group. At the end of the 8 weeks follow-up period, the predicted probability of adherence to TB medication in the Ma-MAS group was 86% (95%CI: 81, 93), and in the control group was 70% (95%CI: 61, 79). Ma-MAS also improved adherence to TB medication by 15.30% (95%CI: 6.68, 23.90; P-value=0.0022) after 4 weeks of intervention compared with the control group.

Conclusion:
Ma-MAS intervention based on information-motivation-behavioural skills model and behavioural change techniques is useful to improve adherence to TB medication.

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APPENDIX NINE: QUESTIONNAIRE

In-depth Interview Guide for Ma-MAS Intervention Development

Introduction

Hello my name is_____. I am going to ask you a few questions regarding your perceptions and experiences on mobile SMS text and phone calls intervention development for TB adherence support during your treatment follow-up.

Section 1: Participant characteristics

S. No	Characteristics	Response
1	Sex	
2	Age	
3	Educational status	
4	Occupational status	

Section 2: In-depth interview guide questions

1. Is non-adherence to TB medication is a problem in Addis Ababa, Ethiopia? (Probe: why that?)
2. What interventions are available to address the problem of non-adherence? (Probe: what current and past interventions have been implemented?)
3. Are mobile SMS text and/or phone call-based interventions a possible solution for non-adherence to TB medications? (Probe: how?)
4. How can mobile SMS text and/or phone call-based interventions be designed to make them desirable and culturally appropriate? (Probe: content, frequency, length of intervention, time of day?)
5. How can mobile SMS text and/or phone call be made more interactive and engaging? (Probe: two-way SMS? phone call conversation?)
6. Would a daily programme of mobile SMS text and/or phone call-based reminders to improve TB medication adherence be desirable? (Probe: how? what do you suggest in the programme?)
7. Would a weekly programme of mobile SMS text and/or phone call-based reminders to encourage medication refill visits improve a patient's clinic attendance? (Probe: how? what do you suggest?)
8. Is a mobile SMS text and/or phone call-based intervention compatible with the current non-daily DOT service? (Probe: what opportunities and challenges are there?)
9. What would be the challenges if mobile SMS and/or phone call interventions are being implemented? (Probe: to system level, healthcare provider, patient, and any risk associated)
10. Would mobile SMS text and/or phone call intervention help healthcare professionals in delivering better care services? (Probe: how?)

Feasibility and Acceptability Questionnaire

Identification
Sub-city Name: _____
Health facility Name: _____
Participant registration code: _____
Date of interview _____ Time started_____ Time finished_____
Data collector's name _____Signature _____ Date ___
Supervisor's name _____Signature _____ Date _____

Section 1: Socio-Demographic Characteristics Information

S. No	QEUSTION	Response	Code
101	Your sex	1= Male 2=Female	|___|
102	Your age in years		|___|
103	Your marital status	1=Married 2=Divorced/separated 3=Widowed 4=Never Married	|___|
104	Your educational status	1=No formal education 2=Primary 1-8 3=Secondary 9-10 4=Technical/Vocational 11-12 5= Higher Education 12+	|___|
105	Your occupational status	1=Governmental employee 2=Daily labourer 3=Merchant 4=Housewife 5=Student 6=Driver 7=Guard 8=Pensioner 9= Unemployment Other (specify----------)	|___|
106	What is the family size of your household (include all related persons residing there)		|___|
107	What is the average monthly household income (sum of incomes contributed by all family members)		|___|
108	How much time does it take you on average to travel to this health facility?		|___|
109	Which kind of transportation do you use to travel to this health facility?	1=Taxi 2=Public Transport/Bus 3=Bajaj 4=Bicycle/ Motor bicycle 5=Walk Other (specify----------=----)	|___|
110	If you paid for your transportation here, how much Ethiopian birr did you pay per visit?		|___|

Intervention description

Mobile-assisted medication adherence support (Ma-MAS) intervention is a systematically developed behavioural intervention that is delivered through mobile SMS text and phone calls to improve a TB patient's medication adherence and clinic appointment attendance. Mobile SMS text and phone calls will be sent to remind patients to take their medication at home and to collect refills of their medication during the TB treatment. I will ask you a few questions based on this intervention.

Section 2: Feasibility and Acceptability of Mobile-assisted Medication Adherence Support (Ma-MAS) Intervention

S.NO	Question	Response	Code
200	Do you have your own Mobile phone?	1=Yes 2=NO	|___|
201	Type of mobile phone	1=Smart phone (install and use applications) 2. Basic (only used for voice and text messages)	
202	Do you have a trusted family or caregiver in the house that can share their mobile phone with you?	1=Yes 2=NO	|___|
203	Are you confident using your mobile phone to receive and open SMS text?	1=Yes 2=NO	|___|
204	Are you confident to read an SMS text message on your mobile phone?	1=Yes 2=NO	|___|
205	Are you confident using your mobile phone to send an SMS text?	1=Yes 2=NO	|___|
206	Are you confident using your mobile phone to make a phone call?	1=Yes 2=NO	|___|
207	Are you confident using your mobile phone to set a reminder?	1=Yes 2=No	|___|
208	Are you confident using your mobile phone to send a "Please Call Me"?	1=Yes 2=NO	|___|
209	Are you confident using your mobile phone to add a contact?	1=Yes 2=NO	|___|
210	Are you willing to receive SMS reminders to take your medications?	1=Yes 2=NO	|___|
211	Are you willing to receive SMS reminders to your clinic appointments?	1=Yes 2=NO	|___|

212	Are you willing to receive a phone call reminder to take your medications?	1=Yes 2=NO	|___|
213	Are you willing to receive a phone call reminder to your clinic appointment?	1=Yes 2=NO	|___|
214	Are you willing to receive a SMS text reminder to take your medications on a trusted family member's shared mobile phone?	1=Yes 2=NO	|___|
215	Are you willing to receive SMS text reminder to your clinic appointment on a trusted family member's shared mobile phone?	1=Yes 2=NO	|___|
216	Are you willing to receive a phone call reminder to take your medications on a trusted family member's shared mobile phone?	1=Yes 2=NO	|___|
217	Are you willing to receive a phone call reminder to your clinic appointment on a trusted family member's shared mobile phone?	1=Yes 2=NO	|___|
218	Total cost for SMS text message (from record review)		|___|
219	Total cost for a phone call (from record review)		|___|
220	Total cost for Ma-MAS intervention (from record review)		|___|

Section 3: Disease-related Information (from record review)

S.NO	Question	Response	Code
300	TB diagnosis category?	1=Smear positive pulmonary TB 2=Smear Negative pulmonary TB 3=Extra Pulmonary TB	|___|
301	TB HIV co-infection?	1=Yes 2=No	|___|
302	Any concurrent non-communicable disease?	1=Diabetes 2=Cancer 3=Hypertension 4=Other (specify……)	|___|
303	History of Tuberculosis?	1=New case 2=Failure 3=Relapsed case 4=Default	|___|

Ma-MAS Intervention Trial Questionnaire

Identification
Sub-city Name: _____
Health facility Name: _____
Participant registration code: _____
Participant Phone no 1:_____ Phone no 2: _____
Date of interview _____ Time started_____ Time finished_____
Data collector's name _____Signature _____ Date _____
Supervisor's name _____Signature _____ Date _____

Section 1: Socio-Demographic Characteristics information

S.NO	Question	Response	Code
101	Your sex	1= Male 2=Female	|___|
102	Your age in years		|___|
103	Your marital status	1=Married 2=Divorced/separated 3=Widowed 4=Never Married	|___|
104	Your educational status	1=No formal Education 2=Primary 1-8 3=Secondary 9-10 4=Technical/Vocational 11-12 5=Higher Education 12+	|___|
105	Your occupational status	1=Governmental employee 2=Daily laborer 3= Merchant 4=Housewife 5=Student 6=Driver 8=Guard 7=Pensioner Other (specify----------)	|___|
106	What is the family size of your household (include all related persons residing there)		|___|
107	What is the average monthly household income (sum of incomes contributed by all family members)		|___|
108	How much time does it take you on average to travel to this health facility?		|___|
109	Which kind of transportation do you use to travel to this health facility?	1=Taxi 2=Public transport/Bus 3= Bajaj 3=Walk Other (specify----------)	|___|
110	If you paid for your transportation here, how much Ethiopian birr did you pay per visit?		|___|
111	Do you have access to adequate food?	1=Yes 2=No	|___|
112	Do you get food support from any other source?	1=Yes 2=No	|___|
113	Do you get financial/social support from any other source?	1=Yes 2=No	|___|
114	Does your family member or caregiver remind you to take your medications?	1=Yes 2=No	|___|

115	Does your family member or caregiver remind you to attend your clinic appointment?	1=Yes 2=No	|___|
116	Have you experienced any stigma and/or discrimination because of your disease?	1=Yes 2=No	|___|

Section 2: Disease-related information

S.NO	Question	Response	Code
200	TB diagnosis category	1=Smear positive pulmonary TB 2=Smear Negative pulmonary TB 3=Extra Pulmonary TB	|___|
201	TB HIV co-infection	1=Yes 2=No	|___|
202	Any other co-morbidity?	1=Diabetes 2=Cancer 3=Hypertension 4=Other (specify ……..)	|___|
203	History of Tuberculosis	1=New case 2=Failure 3=Relapsed case 4=Default	|___|

Section 3: Substance Use-related information

S.NO	Question	Responses	Code
300	Have you ever drunk alcohol?	1=Yes 2=NO (Skip Q 301)	|___|
301	If yes for Q. 300, do you drink alcohol currently?	1=Daily 2=Weekly 3=Occasionally	|___|
302	Have you ever smoked cigarettes?	1=Yes 2=NO (Skip Q 303)	|___|
303	If Yes for Q. 302, do you currently smoke cigarettes?	1=Daily 2=Weekly 3=Occasionally	|___|
304	Do you ever chew khat?	1=Yes 2=NO (Skip Q 305)	|___|
305	If yes for Q. 304, do you chew khat currently?	1=Daily 2=Weekly 3=Occasionally	|___|
306	Do you ever use any other substance like shisha, ganja?	1=Yes (specify…….) 2=NO (Skip Q 307)	|___|
307	If yes for Q. 306, do you use it currently?	1=Daily 2=Weekly 3=Occasionally	|___|

Section 4: Health Service-related information

S.NO	Question	Response	Code
400	Is the waiting time to get the health service acceptable?	1=Yes 2=No	|___|
401	How do you judge your relationship with health care providers?	1=Very good 2=Good 3=Poor 4=Very poor	|___|
402	How do you judge the quality of health service you obtained from this facility?	1=Very good 2=Good 3=Poor 4=Very poor	|___|

Section 5: Treatment adherence questionnaire

Instructions: **Please answer the following questions by placing a "√" in the appropriate box.**

A. **The following questions ask about your medication.** *(Please check one box for each question*.)

	Not at all Sure	Some what Sure	Very Sure	Extremely Sure
1. How sure are you that you will be able to take all or most of the medication as directed?	□	□	□	□
2. How sure are you that the medication will have a positive effect on your health?	□	□	□	□
3. How sure are you that if you don't take this medication exactly as instructed, the TB in your body will become resistant to TB medications?	□	□	□	□

B. **The following questions ask about your social support.** *(Please check one box for each question*.)

	Very Dissatisfied	Somewhat Dissatisfied	Somewhat Satisfied	Very Satisfied
1. In general, how satisfied are you with the overall support you get from your friends and family?	□	□	□	□
2. To what extent do your friends or family members help you remember to take your medication?	□	□	□	□

C. If you have NOT taken any medication <u>within the past month</u>, please check this box and skip to section D: □

People may miss taking their medication for various reasons. Here is a list of possible reasons why you may have missed taking medication. *(Please check one box for each question*.)

In the **<u>past month</u>**, how often have you missed taking your medication because you:

	Never	Rarely	Sometimes	Often
1. Were away from home?	□	□	□	□
2. Were busy with other things?	□	□	□	□
3. Simply forgot?	□	□	□	□
4. Had too many pills to take?	□	□	□	□
5. Wanted to avoid side effects?	□	□	□	□
6. Did not want others to notice that you were taking medication?	□	□	□	□
7. Had a change in daily routine?	□	□	□	□

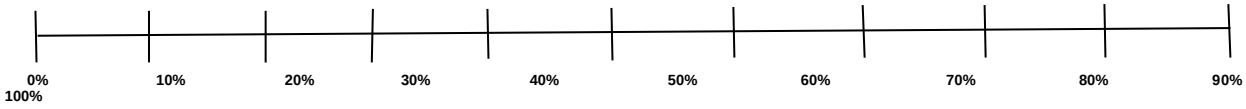
8. Felt like the drug was toxic/harmful?	□	□	□	□
9. Fell asleep/slept through dose time	□	□	□	□
10. Felt sick/ill	□	□	□	□
11. Felt depressed/overwhelmed?	□	□	□	□
12. Had problem taking pills at specified times (with meals, on empty stomach, etc.)?	□	□	□	□
13. Ran out of pills	□	□	□	□
14. Felt good	□	□	□	□

D. When was the last time you missed taking any of your medication? *(Please check only one box)*

1. Within the past week	□
2. 1-2 weeks ago	□
3. 2-4 weeks ago	□
4. Never skip medication or not applicable	□

Visual Analogues scale

Put a cross on the line below at the point showing your best guess about how much of your TB medication you have taken (baseline) in the past one month. For example, 0% means you have taken no medication, 50% means you have taken half of your prescribed medications, and 100% means you have taken all of your prescribed medications.



Section 6: Isoscreen test (Urine test)

S.No	Urine Test	Test result	Code
600	At the fourth week of the study assessment	1=Purple 2=Blue 3=Green 4=Yellow	|___|
601	At the eighth week of the study	1=Purple 2=Blue 3=Green 4=Yellow	

Adoption Intention of Ma-MAS Intervention Questionnaire

Identification
Sub-city Name: _____
Health facility Name: _____
Participant registration code: _____
Date of interview _____ Time started_____ Time finished_____
Data collector's name _____Signature _____ Date ___
Supervisor's name _____Signature _____ Date _____

Section 1: Socio-Demographic Characteristics Information

S.No	QEUSTION	Response	Code
101	Your sex	1= Male 2=Female	|___|
102	Your age in years		|___|
103	Your marital status	1=Married 2=Divorced/separated 3=Widowed 4=Never Married	|___|
104	Your educational status	1=No formal education 2=Primary 1-8 3=Secondary 9-10 4=Technical/Vocational 11-12 5= Higher Education 12+	|___|
105	Your occupational status	1=Governmental employee 2=Daily labourer 3=Merchant 4=Housewife 5=Student 6=Driver 7=Guard 8=Pensioner 9= Unemployment Other (specify----------)	|___|
106	What is the family size of your household (include all related persons residing there)		|___|
107	What is the average monthly household income (sum of incomes contributed by all family members)		|___|
108	How much time does it take you on average to travel to this health facility?		|___|
109	Which kind of transportation do you use to travel to this health facility?	1=Taxi 2=Public Transport/Bus 3=Bajaj 4=Bicycle/ Motor bicycle 5=Walk Other (specify----------=----)	|___|
110	If you paid for your transportation here, how much Ethiopian birr did you pay per visit?		|___|

Section 2: Disease-related Information (from record review)

S.NO	Question	Response	Code
200	TB diagnosis category?	1=Smear positive pulmonary TB 2=Smear Negative pulmonary TB 3=Extra Pulmonary TB	|___|
201	TB HIV co-infection?	1=Yes 2=No	|___|
202	Any concurrent non-communicable disease?	1=Diabetes 2=Cancer 3=Hypertension 4=Other (specify……)	|___|
203	History of Tuberculosis?	1=New case 2=Failure 3=Relapsed case 4=Default	|___|

Intervention description

Mobile-assisted medication adherence support (Ma-MAS) intervention is a systematically developed behavioural intervention that is delivered through mobile SMS text and phone calls to improve a TB patient's medication adherence and clinic appointment attendance. Mobile SMS text and phone calls that sent to you to remind you to take their medication at home and to collect refills of their medication during TB treatment. I will ask you a few questions based on your experience to this intervention.

Section 3: Intention to adopt Mobile-assisted Medication Adherence Support (Ma-MAS) intervention

S.NO	Items	Strongly disagree	Disagree (2)	Neutral (3)	Agree (4)	Strongly Agree (5)
PE	**Performance expectancy**					
PE1	Using mobile SMS and calls would help me to remember my daily medication intake.					
PE2	Using mobile SMS and calls would help me to remember my refill medication visits at the scheduled date.					
PE3	Mobile SMS and calls would be very useful to my follow-up treatment.					
PE4	Mobile SMS and calls would provide very useful services and information to me.					
EE	**Effort of expectancy**					
EE1	Learning to operate mobile SMS and calls would be easy for me.					
EE2	I would find the mobile SMS and calls easy to use.					
EE3	My interaction with health professionals through mobile SMS and calls would be clear and understandable.					

EE4	It will be easy for me to become skillful at sending, receiving, reading and interpreting mobile SMS text.					
SI	**Social Influence**					
SI1	People who are important to me think that I should use mobile SMS and calls.					
SI2	People who influence my behaviour think that I should use mobile SMS and calls.					
SI3	The health professionals of this health facility have been helpful in explaining the use of mobile SMS and calls.					
SI4	The health facility has indicated that it would support the use of mobile SMS and calls for my treatment follow-up					
FC	**Facilitating Conditions**					
FC1	I have the resources necessary to use mobile SMS and calls.					
FC2	I have the knowledge necessary to use mobile SMS and calls.					
FC3	I believe I can get reliable help from health professionals when I have difficulties using mobile SMS and calls.					
FC4	The mobile SMS and calls are not compatible with other services I use.					
ATT	**Attitude**					
ATT1	Using mobile SMS and calls is a good idea for medication reminders					
ATT2	I believe that mobile SMS and calls can be utilized to improve my medication intake adherence and refill visits					
ATT3	Mobile SMS and calls are easy to work					
ATT4	I would enjoy using mobile SMS and calls					
BI	**Behavioural Intention**					
BI1	I predict I will use mobile SMS and calls in the next months for my treatment follow-up					
BI2	I will always try to use mobile SMS and calls in my daily life for continued health services					
BI3	I prefer to use mobile SMS and calls to remember medications intake and refill visits					
BI4	I intend to use the mobile SMS and calls for my treatment follow-up when it is available					
BI5	I plan to inform my friends and relatives about using mobile SMS and calls for treatment follow-up					

In-depth Interview Guide for Post-Ma-MAS Intervention Experiences

Introduction

Hello my name is_____. I am going to ask you a few questions regarding your perceptions and experiences on mobile SMS text and phone calls that you received in the past two months during your treatment follow-up.

Section 1: Participant characteristics

S.No	Characteristics	Response
1	Sex	
2	Age	
3	Educational status	
4	Occupational status	

Section 2: In-depth interview questions

1. Were the daily mobile SMS texts and/or weekly phone calls beneficial? (Probe: to remind you to take your medications and attend your refill visits, how? What? Why?)
2. Were the mobile SMS texts and/or phone calls easy to understand? (Probe: What? Why?)
3. Were there any difficulties or challenges for you in receiving the mobile SMS texts and/or phone calls? (Probe: What? Why?)
4. Did the mobile SMS text and/or phone calls give you any risk or make you feel uncomfortable? (Probe: What? Why?)
5. Was the frequency of the mobile SMS texts and/or phone calls enough? (Probe: What? Why?)
6. Was the timing of the mobile SMS texts and/or phone calls appropriate? (Probe: What? Why?)
7. Was the duration of the mobile SMS texts and/or phone calls intervention enough? (Probe: What? Why?)
8. Was the content of messages good for you? (Probe: What? Why?)
9. What would you recommend in the use of mobile SMS texts and/or phone calls in the future? (Probe: What? Why?)

APPENDIX TEN: INFORMED CONSENT FORM

Participant Information Sheet/Consent Form
In-depth Interview Participants

Health/Social Science Research - Adult providing own consent

Title	Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention in Addis Ababa, Ethiopia.
Sub-title	Mobile-assisted Medication Adherence Support intervention development using the Medical Research Council (MRC) framework
Short Title	Ma-MAS intervention development using the MRC framework
Protocol Number	[NA]
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal Investigator	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon; Dr Lua Perima-Lewis, Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project for mobile-assisted medication adherence support Intervention development. You have been invited because you are in one of the groups of interest to the project: Tuberculosis-infected persons, Health care providers at Tuberculosis (TB) clinic, health care system service providers experts and managers. Your contact details were obtained by/from the Addis Ababa Health Bureau.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the processes involved in taking part. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or local health worker.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read

• Consent to take part in the research project
• Consent to be involved in the research described
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The research aims to systematically develop a mobile-assisted medication adherence support intervention for Tuberculosis patients (objective 1). In Ethiopia, past interventions of this type using SMS text and phone calls have not been not well developed using locally available evidence and appropriate behavioural theory. This research will develop an intervention systematically for those aspects, to provide new evidence that could help health care managers and policymakers to improve Tuberculosis medication adherence. The mobile-assisted medication adherence intervention will be tested for feasibility, effectiveness and adoption intention in the next stages of this research project (see Figure 1). The research findings will also be used as a base for future research and serve as educational material.

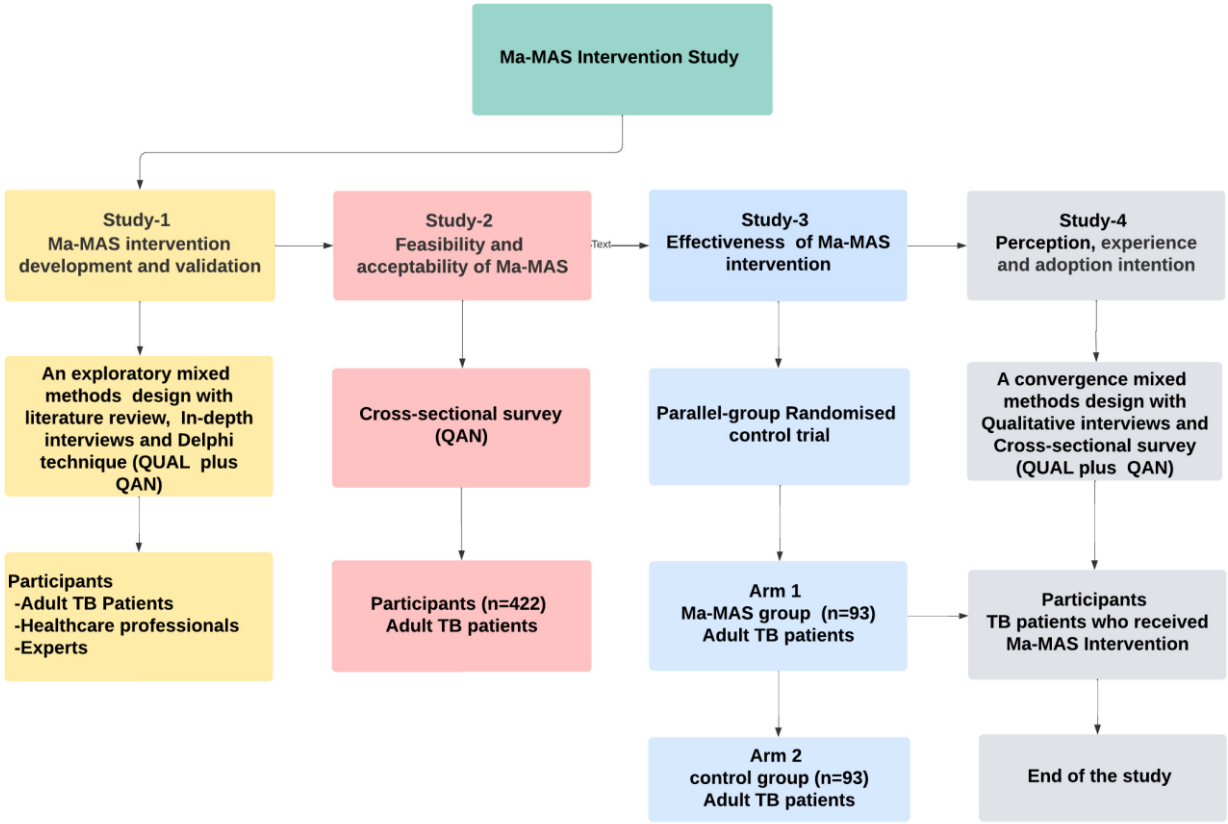


Figure 1: The flow of the study objectives

This research is conducted by collaboration between Flinders University and Addis Ababa Health Bureau. The research results will be used in the study programme for the Doctor of Philosophy degree being undertaken by the candidate Mr Zekariyas Sahile at Flinders University, Australia.

3 What does participation in this research involve?

If you consent to participate in the research project, you will first complete an initial screening questionnaire taking approximately 5 minutes which will determine if you are eligible to take part. You will then take part in an In-depth Interview by one or more members of the research team which will take approximately 60 minutes. You will be asked only for a one-time interview. This interview will be made in a quiet place that is convenient for privacy and confidentiality. The research team

will record the interview discussion by using a digital audio recorder. Your information provided will be kept confidential and used only for research purposes, and your personal and identifiable information will not be presented, reported, or published.

If the screening questionnaire shows that you meet the requirements, then you will be able to start the research project. If the screening questionnaire shows that you cannot be in the research project, the research coordinator will discuss other options with you.

This research project has been designed to make sure the researchers interpret the results fairly and appropriately and to avoid the study team or participants jumping to conclusions. There are no costs associated with participating in this research project, nor will you be paid.

4 Other relevant information about the research project

This study is conducted at Addis Ababa, Ethiopia. Participant groups such as TB-infected persons, Health care providers at TB clinic, health care system service providers experts and managers at Addis Ababa health Bureau, and sub-city will participate in the study. This study does not affect regular care and/or service provided. You will be interviewed at a convenient place for privacy and confidentiality. Once you voluntarily agreed to be involved in the study, you will be interviewed about the intervention development process. After developing this intervention, it will be tested for acceptability and effectiveness in the different participants.

5 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part in this research, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part in this research, or to take part and then withdraw, will not affect your routine care, your relationship with healthcare professional staff or your relationship with this health facility.

6 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research, however, possible benefits may include the evidence produced from this study which may be helpful to systematically develop mobile-assisted medication adherence support interventions based on the needs of the local population and the culture, that will be tested for effectiveness in near future. The study mobile-assisted medication adherence support intervention may be scaled up if it found to be effective. Further, the study will serve as educational material and could be a base for future research.

7 What are the possible risks and disadvantages of taking part?

You may feel that some of the questions we ask you are stressful or upsetting. If you do not wish to answer a question, you may skip it and go to the next question, or you may stop immediately. If you become upset or distressed as a result of your participation in the research project, the research team will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research team. This counselling will be provided to you free of charge.

8 What if I withdraw from this research project?

If you do consent to participate, you may withdraw at any time. If you decide to withdraw from the research project, please notify a member of the research team before you withdraw. A member of

the research team will inform you if there are any special requirements linked to withdrawing. If you do withdraw, you will be asked to complete and sign a 'Withdrawal of Consent' form; this will be provided to you by the research team.

If you decide to leave the research project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want your data to be included, you must tell the researchers when you withdraw from the research project.

9 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as decisions made by local regulatory/health authorities or by research sponsors.

10 What happens when the research project ends?

Participants will be asked whether they wish to get a summary of the research work and if so in what form and will be informed about how they can access the research results. The research outcomes will be disseminated to the Federal Ministry of Health, Addis Ababa Health Bureau, and respective health facilities for decision making for the purpose of program improvement and informing future research directions.

Part 2 How is the research project being conducted?

11 What will happen to information about me?

By signing the consent form, you consent to the research team collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Our discussion will be recorded the audio when you interview with the research team is conducting. All participant's information or data will keep in the University server and investigators computers and backup file with protected password and will be locked in cabinet storage for hard-copy document file. All identifiable information will be removed and replaced by code. Participant's identifiable information or data will not be reported or transferred to third party. Your information will only be used for the purpose of this research project, and it will only be disclosed with your permission, except as required by law. The personal information that the research team collects, and uses is information from interview questionnaires. The interview discussion will be used only for this research purpose. The non-identifiable transcription information will be reported.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, the information will be provided in such a way that you cannot be identified, except with your express permission. Your identifiable information or data will not be presented, reported or published.

You have the right to request access to the information about you that is collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please inform the research team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project and for any future research described that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

12 Complaints and compensation

If you suffer any distress or psychological injury as a result of this research project, you should contact the research team as soon as possible. You will be assisted with arranging appropriate treatment and support.

13 Who is organising and funding the research?

This research project is being organised by Zekariyas Sahile and the research is being conducted through Flinders University. It is being financially supported by Flinders University, Australia and NIH/Fogarty International Centre Global Infectious Disease.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages). The research investigators declare that have no conflict of interest.

14 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Southern Adelaide Clinical Human Research Ethics Committee and Addis Ababa Health Bureau Human Research Ethics Committee, Ethiopia.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

15 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any problems which may be related to your involvement in the project, you can contact the researcher on +251911072963 or any of the following people:

Research contact person

Name	Zekariyas Sahile
Position	Principal Investigator
Telephone	+2519 11072963
Email	zekariyas.nezenega@flinders.edu.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	
Position	
Telephone	
Email	

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Addis Ababa Health Bureau Human Research Ethics Committee
HREC Executive Officer	Dr Yohannes Channea
Telephone	
Email	yoha2wok@yahoo.com

Local HREC Office contact

Name	Dr Yohannes Channea
Position	HREC co-ordinator Addis Ababa Health Bureau, Ethiopia
Telephone	
Email	yoha2wok@yahoo.com

Consent Form - *Adult providing own consent*

Title	Mobile-assisted medication adherence support intervention design for Tuberculosis patients using the Medical Research Council (MRC) framework
Short Title	Ma-MAS intervention design using the MRC framework
Protocol Number	[NA]
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal Investigator	Zekariyas Sahile
Associate Investigator(s)	Professor Paul Arbon, Dr Lua Perinmal-Lewis, Professor Anthony Maeder
Location	Addis Ababa, Ethiopia

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures, and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Researcher†

I have given a verbal explanation of the research project, its procedures, and risks and I believe that the participant has understood that explanation.

Name of Researcher† (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

It is recommended that this form NOT be included as part of the PICF itself, but that it be developed at the same time and made available to researchers for later use, if necessary.

Title	Mobile-assisted medication adherence support intervention design for Tuberculosis patients using MRC framework
Short Title	Ma-MAS intervention design using MRC framework
Protocol Number	[NA]
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal Investigator	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon, Dr Lua Perinmal-Lewis, Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine care, or my relationships with the researchers.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Senior Researcher must provide a description of the circumstances below.

Declaration by Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Researcher (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.

Participant Information Sheet/Consent Form
Feasibility and Acceptability Participants

Health/Social Science Research - Adult providing own consent

Title	Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention in Addis Ababa, Ethiopia.
Sub-title	Feasibility and acceptability and of Mobile-assisted Medication Adherence Support intervention
Short Title	Feasibility and acceptability of Ma-MAS intervention
Protocol Number	[NA]
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal Investigator	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon; Dr Lua Perima-Lewis, Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project for assessing feasibility and acceptability of a Mobile-assisted Medication Adherence Support intervention. You have been invited because you are following anti-Tuberculosis treatment at this health facility. Your contact details were obtained by/from the health facility.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the processes involved in taking part in this research project. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part in this research, you might want to talk about it with a relative, friend or local healthcare professional.

Participation in this research is voluntary. If you don't wish to take part, you don't have to.
If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing the consent form you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to be involved in the research described
• Consent to the use of your personal and health information as described.
You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The research aims to assess the acceptability and feasibility of mobile-assisted medication adherence support intervention (objective 2). These aspects have not previously been well investigated. The mobile-assisted medication adherence intervention has been systematically developed and will be evaluated for effectiveness in the next stage of this research project (see Figure 1). This research, therefore, must be tested for the acceptability and feasibility of intervention to provide evidence for health care managers and policymakers to develop strategies to improve Tuberculosis medication adherence. The research findings will also be used as a base for future research studies and used for educational material.

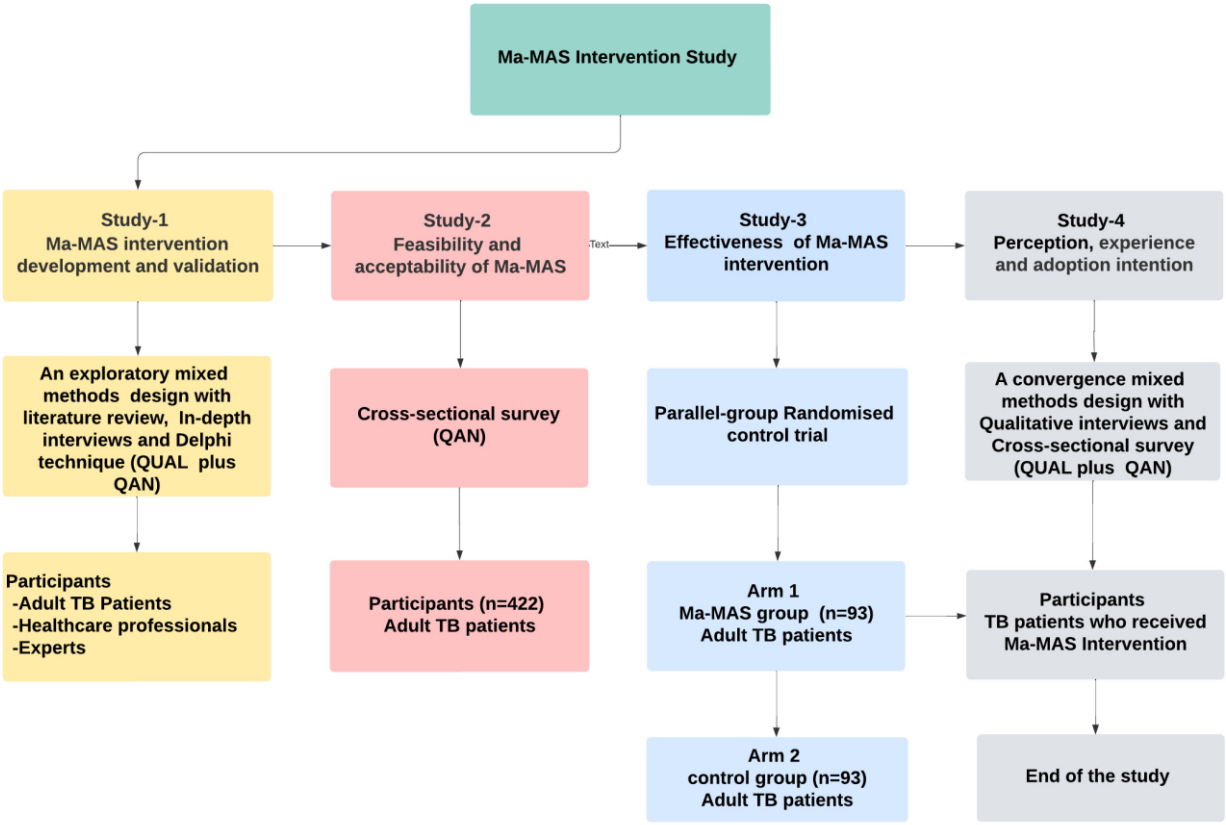


Figure 1: The flow of the study objectives

This research is conducted by collaboration between Flinders University and Addis Ababa Health Bureau. The research results will be used in the study programme for the Doctor of Philosophy degree being undertaken by the candidate Mr Zekariyas Sahile at Flinders University, Australia.

3 What does participation in this research involve?

If you decide to participate in the research project, you will first complete an initial screening questionnaire taking approximately 5 minutes which will determine if you are eligible to take part in this research project. In this research, only TB-infected persons who are undergoing anti-TB treatment will participate. You will then take part in a survey by interview conducted by one or more members of the research team which will take approximately 20 minutes. You will be asked only for a one-time interview. The interview will be made in a quiet place that is convenient for privacy and confidentiality. The research team will record your answers to the survey questions given during the interview on a form. Your information provided will be kept confidential and used only for research purposes, and your personal and identifiable information will not be presented, reported, or published.

If the screening questionnaire shows that you meet the requirements, then you will be able to start the research project. If the screening questionnaire shows that you cannot be in the research project, the research coordinator will discuss other options with you.

This research project has been designed to make sure the researchers interpret the results fairly and appropriately and to avoid study doctors or participants jumping to conclusions. There are no costs associated with participating in this research project, nor will you be paid.

4 Other relevant information about the research project

This study is conducted at Addis Ababa, Ethiopia, Public Health Facilities. A total of 36 public health centers that are providing the Tuberculosis (TB) treatment service will be enrolled for this study. All adult TB-infected participants who are following anti-TB treatment for a six-month period will be eligible for this study. This study does not affect your regular anti-TB treatment care provided or your relationship with a health facility. Once you voluntarily agree to be involved in the study, you will be asked questions about acceptability and feasibility of the intervention.

5 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part in this research, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage. If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep with you.

Your decision whether to take part or not to take part in this research, or to take part and then withdraw, will not affect your routine care, your relationship with professional staff or your relationship with this health facility.

6 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include the evidence produced from this study which may be helpful to improve a mobile-assisted medication adherence support intervention, that will be tested for effectiveness in near future. The study will also generate evidence for health care managers and policymakers on ways of improving TB medication adherence interventions and strategy. Further, the study will serve as educational material and could be a base for future research.

7 What are the possible risks and disadvantages of taking part?

You may feel that some of the questions we ask are stressful or upsetting. If you do not wish to answer a question, you may skip it and go to the next question, or you may stop immediately. If you become upset or distressed as a result of your participation in the research project, the research team will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research team. This counselling will be provided free of charge.

8 What if I withdraw from this research project?

If you do consent to participate, you may withdraw at any time. If you decide to withdraw from the project, please notify a member of the research team before you withdraw. A member of the research team will inform you if there are any special requirements linked to withdrawing. If you do withdraw, you will be asked to complete and sign a 'Withdrawal of Consent' form; this will be provided to you by the research team.

If you decide to leave the research project, the researchers will not collect additional personal information from you, although personal information already collected will be retained to ensure that

the results of the research project can be measured properly and to comply with the law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want your data to be included, you must tell the researchers when you withdraw from the research project.

9 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include a reason such as decisions made by local regulatory/health authorities or by research sponsors.

10 What happens when the research project ends?

Participants will be asked whether they wish to get a summary of the research work and if so in what form and will be informed about how they can access the research results. The research outcomes will be disseminated to the Federal Ministry of Health, Addis Ababa Health Bureau, and respective health facilities for decision making for the purpose of program improvement and informing future research directions.

Part 2 How is the research project being conducted?

11 What will happen to information about me?

By signing the consent form, you consent to the research team collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. All participant's information or data will keep in the University server and principal investigator laptop computer and backup file with a protected password and will be locked in the cabinet storage for hard-copy document files. All identifiable information will be removed and replaced by code. All participant information will be encrypted. Participant's identifiable information or data will not be reported or transferred to others. Your information will only be used for this research project, and it will only be disclosed with your permission, except as required by law. The personal information that the research team collects, and uses is information from interview questionnaires. The interview discussion will be used only for this research purpose. The non-identifiable transcription information will be reported.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, the information will be provided in such a way that you cannot be identified, except with your express permission. Your identifiable information or data will not be presented, reported or published.

You have the right to request access to the information about you that is collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please inform the research team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project and for any future research described that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

12 Complaints and compensation

If you suffer any distress or psychological injury as a result of this research project, you should contact the research team as soon as possible. You will be assisted with arranging appropriate treatment and support.

13 Who is organising and funding the research?

This research project is being organised by Zekariyas Sahile and the research is being conducted through Flinders University. It is being financially supported by Flinders University, Australia and NIH/Fogarty International Centre Global Infectious Disease.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages). The research investigators declare that have no conflict of interest.

14 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the South Adelaide Clinical Human Research Ethics committee and Addis Ababa Health Bureau, Ethiopia.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

15 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any problems which may be related to your involvement in the project, you can contact the researcher on +251911072963 or any of the following people:

Research contact person

Name	Zekariyas Sahile
Position	Principal Investigator
Telephone	+251911072963
Email	Zekariyas.nezenega@flinders.edu.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	
Position	
Telephone	
Email	

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

This person should be someone independent of the research, such as the Executive Officer of the reviewing HREC that approved the project. Contact your local HREC administrator for the requirements at your institution.

Reviewing HREC approving this research and HREC Executive Officer details

Local HREC Office contact

Reviewing HREC name	Addis Ababa Health Bureau Human Research Ethics Committee
HREC Executive Officer	Dr Yohannes Channea
Telephone	
Email	yoha2wok@yahoo.com

Name	Dr Yohannes Channea
Position	HREC co-ordinator Addis Ababa Health Bureau, Ethiopia
Telephone	
Email	yoha2wok@yahoo.com

Consent Form - Adult providing own consent

Title	Patient's acceptability and feasibility of mobile-assisted medication adherence support (Ma-MAS) intervention
Short Title	Feasibility and acceptability of Ma-MAS intervention
Protocol Number	[NA]
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon; Dr Lua Perinmal-Lewis, Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Researcher† (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

It is recommended that this form NOT be included as part of the PICF itself, but that it be developed at the same time and made available to researchers for later use, if necessary.

Title	Feasibility and acceptability of mobile-assisted medication adherence support intervention
Short Title	Feasibility and acceptability of Ma-MAS intervention
Protocol Number	[NA]
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal Investigator	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon; Dr Lua Perinmal-Lewis, Professor Anthony Maeder
Location	Addis Ababa, Ethiopia

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine care, or my relationships with the researchers.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Senior Researcher must provide a description of the circumstances below.

Declaration by Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Researcher (please print) _____

Signature _____ Date _____

† An appropriately qualified member of the research team must provide information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.

Participant Information Sheet/Consent Form
Intervention and post intervention Participants

Interventional Study - Adult providing own consent

Title	Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention in Addis Ababa, Ethiopia.
Sub-title	Mobile-assisted Medication Adherence Support Intervention Effectiveness: Randomised control Trial (RCT)
Short Title	Ma-MAS intervention Effectiveness: RCT
Protocol Number	PACTR202002831201865
Project Sponsor	Flinders University, South Australia
Coordinating Principal Investigator/ Principal	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon; Dr Lua Perima-Lewis, Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project because you have been following your anti-Tuberculosis treatment at this health facility. The research project is testing a new behavioural intervention for Tuberculosis medications adherence. The new behavioural intervention is called Mobile-assisted Medication Adherence Support (Ma-MAS).

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and behavioural intervention involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your doctor or Health care provider.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible healthcare whether or not you take part in this study.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing the consent form you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests and behavioural intervention that are described
• Consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The research aims to measure the effectiveness of a mobile-assisted medication adherence support intervention on patients' treatment adherence. This is an experimental behavioural intervention that is given through mobile SMS texts and phone calls in Ethiopia. The mobile-assisted medication adherence intervention has been developed systematically and tested for feasibility, and acceptability in previous stages of this research project (see Figure 1).

At present, there is a lack of well-investigated knowledge on how behavioural interventions using mobile SMS and phone calls could be effective for Tuberculosis medication adherence. This research, therefore, would provide evidence that would help healthcare managers and policymakers to develop strategies to improve Tuberculosis medication adherence. The research findings will also be used as a basis for future research and used for educational purposes.

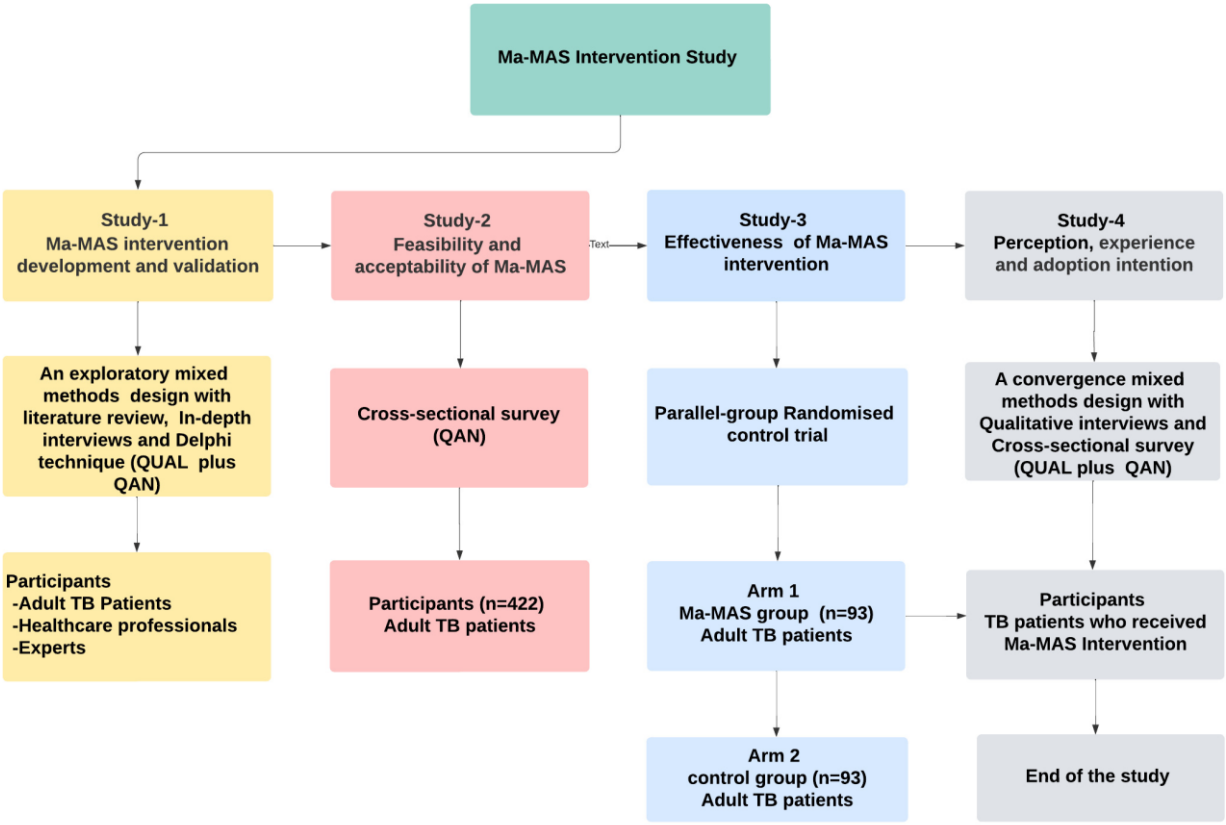


Figure 1: The flow of the study objectives

This research is conducted by collaboration between Flinders University and Addis Ababa Health Bureau. The research results will be used in the study programme for the Doctor of Philosophy degree being undertaken by the candidate Mr Zekariyas Sahile at Flinders University, Australia.

3 What does participation in this research involve?

To be involved in this research, you must agree voluntarily before any assessment or interview is made, by signing the consent form. You cannot be involved in this study unless you fulfil all the following conditions:

- participants are adult (age 18 years and above)
- participants will be following their anti-Tuberculosis treatment for six months
- participants are at the intensive phase of treatment during the screening
- participants can read and understand the national official language (Amharic)

- Participants have their own mobile phone, however, participants who don't have their own mobile phone may be included if they have a trusted family member's mobile phone in the household with a collaborative agreement

However, you will not be involved if you are deemed not to have the capacity to decide reasonably to participate, or if you are enrolled in other behavioural interventions.

You will be participating in a randomised controlled research project. Sometimes we do not know which behavioural intervention is best for treating a condition. To find out, we need to compare different behavioural interventions. We put people into groups and give each group a different behavioural intervention which may use mobile SMS text messages and phone calls (see Figure 2). The results are compared to see if one intervention is better. To try to make sure the groups are unbiased, each participant is put into a group by chance (random). If you agree to participate in the study, you will be assigned into one of two groups.

1. Group one participants will receive daily SMS text messages and weekly phone calls for daily medication intake and medication refill visit reminders
2. Group two participants will receive the standard treatment as group one but not receive an additional intervention on a mobile phone.

You will know which of the group you have to be assigned, but you cannot choose yourself.

Figure 2: Mobile-assisted Medication Adherence Support (Ma-MAS) intervention

You are asked to participate in this research because the information found from this study can help the improvement of Tuberculosis treatment services. Moreover, your participation is confirmed by the probability sampling technique which provides an equal chance of selection. You have a 50% chance to participate in the intervention group and a 50% chance of being in the control group. If you are assigned to the intervention group, you will receive a daily SMS text and weekly phone calls reminder of medication intake and refill visit reminders for 8 weeks while you are on anti-Tuberculosis treatment during the continuation phase of treatment. If you have a local doctor or health care provider, we strongly recommend that you inform them of your participation in this research project.

This research project has been designed to make sure the researchers interpret the results fairly and appropriately and avoid study researchers or participants jumping to conclusions. If you agree to participate in this research, the following procedures will be undertaken:

- One or more members of the research team will interview you about a few socio-demographic, health service, and disease-related questions at the beginning of the study. This interview takes about 20 minutes and will be conducted in your usual clinic session.

- At subsequent clinic visits for your medication refills, the data collector will assess your medications adherence level by asking you questions about your medication usage and by taking a sample of urine for testing at a random point after 4 and 8 weeks follow up time. The maximum amount of time you will spend in contact with data collectors for this purpose is 10 minutes for each time of assessment. All adherence assessments will be made immediately after you have finished your regular treatment services.
- After 8 weeks of intervention and follow up period, if you have participated in the intervention group listed above, you will also be asked to participate in another study and you may be a part of an in-depth interview and survey interview to assess the adoption, perceptions and experiences of mobile-assisted medication adherence support. The average time needed for this one-time In-depth interview and survey interview is 60 and 15 minutes, respectively.

The information obtained from this study will be used for research proposes only to inform possible solutions to improve future anti-Tuberculosis medication adherence. Your identifiable information will not be disclosed in the presentation, report, or publication and will not be stored after completion of the study. The information that you give us in this study will be kept confidential within the study research team. For ensuring your privacy, all discussions that we will have with you will be held in a safe place where no one can hear what we are discussing. Your daily SMS text messages and weekly phone calls, to be delivered for 8 weeks, will not be accessed by anybody other than the study research team and our record of your phone number will be deleted after the study is completed. In your medication refill visits to the clinic, a research team member will ask you whether you are receiving the intervention regularly if you are assigned into the intervention group.

There are no additional costs to you associated with participating in this research project, nor will you be paid. All SMS and phone calls within the intervention and tests required as part of the research project will be provided to you free of charge.

4 What do I have to do?

All participants in the study will follow their regular anti-Tuberculosis treatment for six months period as per standard care, in whichever study group they assigned. Once you have voluntarily agreed to be involved in the study and been assigned into the intervention group, you will accept to receive the daily SMS text and weekly phone calls medications intake and refill visits reminders for 8 weeks. If you are assigned to the no-intervention (control) group, you will still be monitored for those 8 weeks.

You will need to disclose your own mobile phone number to the research team to receive an SMS text or phone calls. If you don't have your own mobile phone, you will need to be able to use your trusted family member's mobile phone number in the household with a collaborative agreement, to receive the intervention. Participants are expected to read and answer the daily and weekly medications intake and refill visits reminders of SMS text message and phone call, and regularly fellow the information as directed by mobile SMS text or phone calls. Participants need to report to the research team if they change their mobile phone or lose their mobile phone, to immediately replace the old mobile phone number by the new one. You must not forward, tell or show your mobile SMS text and phone call information to other participants as this will affect the study.

5 Other relevant information about the research project

A total of 36 government health centres from Addis Ababa, Ethiopia will be included in the study and a total of 186 participants will be expected to be involved in the study. Of 186 participants, 93 participants will be assigned in the intervention group (SMS text plus phone call reminders). This intervention has been systematically developed through the involvement of different participants such as Tuberculosis infected person, health care providers, health care managers, and Tuberculosis prevention and control experts. It has also been evaluated for the acceptability and feasibility of the intervention.

6 Do I have to take part in this research project?

Participation in this research project is voluntary. If you do not wish to take part in this study, you do not have to. If you decide to take part in this study and later change your mind, you are free to withdraw from the project at any stage. If you do decide to take part in this study, you will be asked to sign this Participant Information and Consent Form and you will be given a copy to keep with you. Your decision whether to take part in this study or not to take part in this study, to take part and then withdraw, will not affect your routine standard treatment care, your relationship with healthcare professionals treating you or your relationship with this health facility.

7 What are the alternatives to participation?

This is an additional behavioural intervention delivered through mobile SMS text and phone call that evaluates the effectiveness of medication adherence improvement. It is not an alternative treatment to standard care. Your study healthcare provider will discuss this aspect with you before you decide whether or not to take part in this research project.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; however, possible benefits may include participants receiving additional information through daily SMS text messages and weekly phone calls, to remind you to take your daily medications and to attend your medications refill visits. The study may provide relevant evidence for program managers and policymakers to improve Tuberculosis treatment adherence in the future.

9 What are the possible risks and disadvantages of taking part?

This research has no anticipated risk for you, or your family, or your Tuberculosis treatment services you get in future from this health facility. The research has no intention to cause any physical harm, social discrimination, psychological trauma and economic loss. You may feel that some of the questions we ask are stressful or upsetting. If you do not wish to answer a question, you may skip it and go to the next question, or you may stop immediately. If you become upset or distressed as a result of your participation in the research, the study healthcare professional will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling service will be provided to you free of charge.

10 What will happen to my test samples?

The proposed sample urine test is part of the medication adherence assessment and will be taken at a random point after 4 and 8 weeks of follow up. You will receive information how sample of urine collected before a urine test is made. You will also receive medical advice from the research team after a urine test is completed. Your urine sample will be individually re-identifiable when the test procedure is undertaken, but it will not be stored or transferred for further tests. This study will also collect data from your health record about your treatment adherence. Only non-identifiable information or data about you will be stored for the study. Thus, your urine test and treatment adherence results will be confidential, known only by you and the person who has tested your urine. Signing the consent form means that you agree to have this testing; it will not be done without your consent.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the intervention that is being studied. If this happens, your study healthcare provider will tell you about it and discuss with you whether you want to continue in the research project. If you decide to continue in the research project, you will be asked to sign an updated consent form. On receiving new information, your study health care provider might consider it to be in your best interests to withdraw you from the research project. If this happens, he/she will explain the reasons and arrange for your regular standard of healthcare to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to a part of any other behavioural interventional research. It is important to tell your study healthcare provider and the study staff about if you are already enrolled or may want to enrol in another research project.

13 What if I withdraw from this research project?

If you decide to withdraw from this research project, please notify a member of the research team before you withdraw. This notice will allow that the research supervisor to discuss with you about any health risks or special requirements linked to withdrawing If you do withdraw your consent during the research project, the study healthcare provider and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with the law. You should be aware that data collected by the research team up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell the research team when you withdraw from the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as decisions made by local regulatory/health authorities or by the project sponsor.

15 What happens when the research project ends?

You will finish the study after 8 weeks of intervention period. You will be asked whether you wish to get a summary of the research work and be informed about how you can access the research results. The research outcomes will be also disseminated to the Federal Ministry of Health, Addis Ababa Health Bureau, and respective government health facilities for decision making for programme improvement and informing future research directions.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form, you consent to the study research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. All participant's information or data related to the research project will keep in the university server and investigators computer and backup electronic file with a protected password and lock cabinet storage for the hard-copy document file. All identifiable information will be removed and replaced by code. All participant information or data will be encrypted. All participant's identifiable information or data will not be reported or transferred to others. Non-identifiable information will be stored for 5 years after the study in Flinders University repository server and will be destroyed after that period. Your

information will only be used for this research project, and it will only be disclosed with your permission, except as required by law.

Your health records and any information obtained during the research project are subject to inspection (to verify the procedures and the data) by the relevant authorities and authorised representatives of the project sponsor [Flinders University], by the institution relevant to this Participant Information Sheet, [South Adelaide clinical HREC], or as required by law. By signing the Consent Form, you authorise the release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, the information will be provided in such a way that you cannot be identified, except with your permission. Your identifiable information or data will not be reported or published. Any information obtained for this research project and for the future research described in Section 16 that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

You have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

17 Complaints and compensation

If you suffer any distress or psychological injury as a result of this research project, you should contact the research team as soon as possible. You will be assisted with arranging appropriate counselling support.

18 Who is organising and funding the research?

This research project is being conducted by Zekariyas Sahile, a Doctor of Philosophy candidate of Flinders University. It is being financially supported by Flinders University, Australia and NIH/Fogarty International Centre Global Infectious Disease.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages). The research investigators declare that have no conflict of interest.

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the South Adelaide Clinical Human Research Ethics Committee and Addis Ababa Health Bureau HREC, Ethiopia.

This project will be carried out according to the Australian National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal investigator on +251911072963 or any of the following people:

Clinical contact person

Name	[Name]
Position	[Position]
Telephone	[Phone number]
Email	[Email address]

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Zekariyas Sahile
Position	Associate Investigator
Telephone	+251911072963
Email	Neze0002@flinders.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Addis Ababa Health Burea Human Research Ethics Committee
HREC Executive Officer	Dr Yohannes Channea
Telephone	
Email	yoha2wok@yahoo.com

Local HREC Office contact (Single Site Research Governance Officer)

Name	Dr Yohannes Channea
Position	HREC-coordinator Addis Ababa Health Bureau, Ethiopia
Telephone	
Email	yoha2wok@yahoo.com

Consent Form - Adult providing own consent

Title	Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention in Addis Ababa, Ethiopia.
Sub-title	Mobile-assisted medication adherence support (Ma-MAS) Intervention Effectiveness among Tuberculosis patients
Short Title	Ma-MAS intervention Effectiveness among Tuberculosis patients
Protocol Number	PACTR202002831201865
Project Sponsor	Flinders University, Australia
Coordinating Principal Investigator	Zekariyas Sahile
Associate	Prof. Paul Arbon; Dr Lua Perinmal-Lewis Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand. I understand the purposes, procedures and risks of the research described in the project.
I give permission for my doctors, other health professionals, health facility to release information to Flinders University concerning my disease and treatment for the purposes of this research project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my current or future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project. Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

It is recommended that this form NOT be included as part of the PICF itself, but that it be developed at the same time and made available to researchers for later use, if necessary. Note that a participant's decision to withdraw their separate consent to the use and storage of tissue will need to be documented separately and linked to the PICF used for that purpose.

Title	Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Effectiveness, Experiences and Adoption Intention in Addis Ababa, Ethiopia
Sub-title	Mobile-assisted medication adherence support (Ma-MAS) Intervention Effectiveness among Tuberculosis patients
Short Title	Ma-MAS intervention Effectiveness among Tuberculosis patients
Protocol Number	PACTR202002831201865
Project Sponsor	Flinders University, Australia
Coordinating Principal Investigator/ Principal Investigator	Zekariyas Sahile
Associate Investigator(s)	Prof. Paul Arbon; Dr Lua Perimal-Lewis, Prof. Anthony Maeder
Location	Addis Ababa, Ethiopia

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine standard care treatment, my relationship with those treating me or my relationship with this health facility.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project, and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.

APPENDIX ELEVEN: ETHICS APPROVAL

Office for Research
Flinders Medical Centre
Ward 6C, Room 6A219
Flinders Drive, Bedford Park SA 5042
Tel: (08) 8204 6453
E: Health.SALHNOfficeforResearch@sa.gov.au

Government of South Australia

Health
Southern Adelaide
Local Health Network

Final Approval for Ethics Application

8 April 2020

Professor Anthony Maeder
College of Nursing and Health Sciences
Flinders University

Dear Professor Maeder,

OFR Number: 23.20
Project title: Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Adoption of Intention, Effectiveness, and Experiences in Addis Ababa, Ethiopia.
Chief Investigator: Professor Anthony Maeder

Ethics Approval Period: 8 April 2020 – 8 April 2023

The Southern Adelaide Clinical Human Research Ethics Committee (SAC HREC) (EC00188) has approved this application, which was first reviewed at the 2 March 2020 full committee meeting, through the greater than low risk pathway, and provided approval which meets the requirements of the *National Statement on Ethical Conduct in Human Research (2007, updated 2018)*.

You are reminded that this letter constitutes **Ethics** approval only. **Ethics approval is one aspect of the research governance process**.

You must not commence this research project at any SA Health sites listed in the application until a Site Specific Assessment (SSA), or Access Request for data or tissue form, has been approved by the Chief Executive or delegate of each site.

The below documents have been reviewed and approved:

Document	Version	Date
Human research ethics application form	AU/1/DF3B316	24 March 2020
Project description	3	23 March 2020
Objective 1 in depth interview participant information sheet and consent form	-	23 March 2020
Objective 2 feasibility and adoption participant information sheet and consent form	-	23 March 2020
Objective 3 & 4 intervention and focus group participant information sheet and consent form	-	23 March 2020
Leaflet	-	23 March 2020
Eligibility screening tool for objective 1	-	-

Eligibility screening tool for objective 2	-	-
Eligibility screening tool for objective 3	-	-
Objective 1 in depth interview guide	-	22 March 2020
Objective 2 participant feasibility questionnaire	-	22 March 2020
Objective 3 participant monitoring questionnaire	-	22 March 2020
Objective 3 compliance follow up	-	22 March 2020
Objective 4 participant focus group discussion guide	-	22 March 2020
Sample prototype SMS text	-	22 March 2020
Letter of support from Ethiopian Ministry of Health	-	23 March 2020

TERMS AND CONDITIONS OF ETHICS AND GOVERNANCE APPROVAL

The Principal Investigator must ensure this research complies with the National Statement on Ethical Conduct in Human Research (2018) & the Australian Code for the Responsible Conduct of Research (2007 updated 2018) by immediately reporting to the Office for Research (OFR) anything that may change the ethics or scientific integrity of the project. Final approval is granted subject to the researcher agreeing to meet the following terms and conditions:

1. **This approval is subject to local Addis Ababa Health Bureau IRB approval.**
2. Confidentiality of research participants MUST be maintained at all times.
3. If the research involves the recruitment of participants, a signed copy of the 'Consent Form' must be given to the participant. Any changes to the Participant Information Sheet/Consent Form must be approved by the lead HREC prior to being used.
4. No promotion of a study can commence until final ethics and SALHN executive approval has been obtained. All advertisements/flyers need to be approved by the committee and media contact should be coordinated through the FMC media unit.
5. Non-SA Health researchers viewing confidential SALHN data are required to complete and sign a SALHN Confidentiality Disclosure Deed
6. All approved requests for access to medical records at any SALHN site must be accompanied by this approval letter.
7. If your study involves a tertiary institution, contact the University to ensure compliance with University requirements prior to commencement of this study. This includes any insurance and indemnification.
8. The PI must adhere to Monitoring and Reporting requirements for both ethics and governance which are available on the SALHN Research Website.
9. The PI must immediately report to SAC HREC anything that may change the ethics or scientific integrity of the project
10. An annual report must be submitted to the SAC HREC and SALHN governance on each anniversary of the date of final approval. Please visit the Office for Research website for the current template.
11. Non-SA Health researchers coming onsite at SALHN must provide evidence of a recent (<3 years) screening check. It is the responsibility of the Principal Investigator to ensure any non-SA Health personnel who conducts or monitors research meets SA Health screening requirements as per the SA Health Criminal & Relevant History Screening Policy Directive before they access any SA Health site. The cost of any such screening is the responsibility of the individual accessing the site or their employer.
12. Any reports or publications derived from the research should be submitted to the Committee at the completion of the project.

13. Once the research project has concluded, any new product/procedure/intervention cannot be conducted in the SALHN as standard practice without the approval of the SALHN New Medical Products and Standardisation Committee or the SALHN New Health Technology and Clinical Practice Innovation Committee (as applicable). Please refer to the relevant committee link on the SALHN intranet for further information.
14. SALHN site-monitoring of authorised studies - this approval/authorisation is subject to participation in this monitoring process. You will be notified in advance if your site has been selected for an inspection.

Please visit the SALHN Research website regularly and comply with all submission requirements as they may change from time to time.

For any queries about this matter, please contact The Office for Research on (08) 8204 6453 or via email to Health.SALHNOfficeforResearch@sa.gov.au

Yours sincerely,

Professor Bill Heddle
Chair
Southern Adelaide Clinical Human Research Ethics Committee

አዲስ አበባ ከተማ አስተዳደር ጤና ቢሮ
City Government of Addis Ababa Health Bureau

Ref.No. A/A/H/950/227
Date 11/12/12

TO:

- **Addis Ketema Sub- city Health Office**
- **Arada Sub- city Health Office**
- **Bole Sub- city Health Office**
- **Akaki-kality Sub- city Health Office**
- **Kirkos Sub- city Health Office**
- **Gulelle Sub- city Health Office**
- **Nefas Silk Lafto Sub- city Health Office**
- **Kolfe Keranio Yeka Sub- city Health Office**
- **Lideta Sub- city Health Office**
- **Yeka Sub- City Health Office**

Addis Ababa

Subject: Request to access Facilities to conduct approved research

The letter is to support **Zekariyas Sahile to** conduct research, which is entitled as **"Mobile-assisted Medication Adherence Support (Ma-MAS) Intervention for TuberculosisPatients: Adoption of Intention, Effectiveness and Experiences Based in Addis Ababa, Ethiopia.''** The study proposal was duly reviewed and approved by Addis Ababa Health Bureau IRB, and the principal investigator is in formed with a copy of this letter to report any changes in the study procedures and submit an activity progress report to the Ethical Committee as required. Therefore we request the facility and staffs to provide support to the principal investigator.

With Regards

Ethical Clearance Committee

Cc

- **Zekariyas Sahile**
- **To Ethical Clearance Committee**

SAC HREC amendment approval - 23.20

Health:SALHN Office for Research <Health.SALHNOfficeforResearch@sa.gov.au>

Wed 7/04/2021 11:09 AM

To: Zekariyas Nezenega <zekariyas.nezenega@flinders.edu.au>

Cc: Paul Arbon <paul.arbon@flinders.edu.au>;Lua Perimal-Lewis <lua.perimal-lewis@flinders.edu.au>;Anthony Maeder <anthony.maeder@flinders.edu.au>

Dear Zekariyas,

OFR reference: 23.20
Title: Mobile-assisted Medication Adherence Support (Ma-MAS) intervention for Tuberculosis Patients: Adoption of Intention, Effectiveness, and Experiences in Addis Ababa, Ethiopia.
Principal Investigator: Professor Paul Arbon

The amendment to the above study has been reviewed and approved by the SAC HREC.

Approval period: 8 April 2020 – 8 April 2023

The following documents have been reviewed and approved:

Document	Version	Date
Project amendment form	-	5 March 2021
Project description	4	5 March 2021
PICF	4	5 March 2021

The terms and conditions of ethics and governance approval remain unchanged from the original approval. Please note a formal approval letter will not be provided. Please retain a copy of this email as evidence of approval.

Kind Regards,

Dominic How

On behalf of

Professor Bill Heddle
Chair
SAC HREC

APPENDIX TWELVE: CONFERENCE PRESENTATIONS CERTIFICATES

ASA
AMERICAN STATISTICAL ASSOCIATION
Promoting the Practice and Profession of Statistics®
732 North Washington Street, Alexandria, VA 22314-1943
(703) 684-1221 ▪ www.amstat.org ▪ asainfo@amstat.org
www.facebook.com/AmstatNews www.twitter.com/AmstatNews

January 18, 2023

Zekariyas Sahile Nezenega
Flinders University
PhD candidate
2-4 Gladstone
Fullarton, 5063
Australia

Dear Zekariyas Sahile Nezenega,

Thank you for attending the 2023 American Statistical Association International Conference on Health Policy Statistics (ICHPS) which was held January 9-11, 2023. This letter is to verify that you were present at the conference and that you presented a poster presentation entitled "Mobile-assisted Medication Adherence Support intervention among Tuberculosis Patients: A Parallel Group Randomized Control Trial" on Tuesday, January 10, 2023, from 7:30 p.m. – 8:30 p.m.

We hope that you enjoyed the conference and will be able to join us at ICHPS 2025.

Sincerely,

Clarissa Davis
Customer Services Manager

ጤና ሚኒስቴር - ኢትዮጵያ
MINISTRY OF HEALTH-ETHIOPIA

Hawassa University

Sidama Health Bureau

የተሳትፎ የምስክር ወረቀት
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ለ _____

የፌዴራል ጤና ሚኒስቴር፣ ሐዋሳ ዩኒቨርሲቲ እና ሲዳማ ክልል ጤና ቢሮ ከመጋቢት 13-15 ቀን 2014 ዓ.ም. ባዘጋጁት የ16ኛው የቲቢ ምርምር ጉባኤና በ2014 ዓ/ም የዓለም ቲቢ ቀን በዓል ላይ በመገኘት ላቀረቡት የቲቢ ምርምር ውጤት ይህ የምሥጋና ምስክር ወረቀት ተሰጥቶዎታል።

Certificate of participation awarded to

Zekariyas Sahile

In recognition of your participation and presentation of **Tuberculosis Research Findings** on the 16th TB research annual conference and 2022 World TB Day organized by Federal Ministry of Health, Hawassa University and Sidama Regional Health Bureau held from March 22-24, 2022

Hiwot Solomon
Disease Prevention and Control Directorate Director

Dr. Ayano Berasso
TB Research Advisory Committee Chairperson

Dr. Selamawit Mengesha
Sidama Regional Health, Bureau Head