Depression in people with tuberculosis:

Assessing the effectiveness of interventions for depression, and the barriers and facilitators for their implementation in Pakistan and other low-and-middle income countries

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Abstract

Background: Depression is a common comorbidity in people with tuberculosis (TB). Treating depression in people with other conditions often improves both physical and mental health outcomes. However, the impact of treating depression in people with TB on their mental health and TB-related outcomes remains unclear. Additionally, there is limited understanding of how to implement and deliver mental health interventions for depression for people with TB within existing TB services.

Aims: This thesis aims to assess the effectiveness of depression treatment for people with TB and explore the barriers and facilitators to implementing mental health interventions in TB services in low-and-middle-income countries (LMICs).

Methods: A meta-analysis was conducted to evaluate the effectiveness of depression interventions for people with TB. Barriers and facilitators to implementation were explored through a systematic review. Lastly, a qualitative case study of the implementation of a psychological mental health intervention in Karachi, Pakistan which aimed to integrate diagnosis and treatment for depression in people with drug-susceptible TB attending primary and tertiary care facilities for TB care.

Findings: Psychological interventions showed a small but positive effect on improving depression in people with TB, though the evidence quality was low. The most common interventions combined psychological and pharmacological approaches. All interventions required additional funding and training resources. The case study emphasized the importance of funding, training, and strong relational connections within TB facilities for successful implementation. Despite feasibility and evidence of effectiveness, none of the interventions described in this thesis have been sustained over time.

Conclusions: Psychological interventions can improve both mental health and TB-related outcomes for people with TB in LMICs. However, successful delivery requires adequate funding and training. Future research should prioritize sustainable integration of mental healthcare into existing TB services.

Glossary

cRCT: Cluster randomised clinical trial.

HIV: Human Immunodeficiency virus.

Implementation science: “the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practice into routine practice and, hence, to improve the quality and effectiveness of health services” (Eccles and Mittman, 2006).

Mental health: state of well-being where an individual can cope with the normal stresses of life, realize their own potential, learn well, work productively, and contribute to their community (WHO, 2025).

Mental healthcare: services and systems, formal and informal, that exist to provide therapeutic and social support to people with mental health illnesses. The goal of mental healthcare is to promote a positive mental health status of individuals and communities.

Morita therapy: Psychological therapy, initially developed for anxiety disorder, social phobia, and obsessive-compulsive disorder, and then used for other mental illnesses such as schizophrenia, depression, and other obsessive behaviours associated with mental or physical illness. Morita therapy has been mostly used in countries in Asia given the Eastern philosophies that underpin some of the programmatic approaches of the therapy. The therapeutic effectiveness of Morita therapy on mental health outcomes is unclear with one Cochrane review publishing that it may have some positive effects and a second Cochrane review concluding that there were not enough studies of sufficient methodological quality to draw conclusions on the effectiveness of the therapy (. Until 2014, all studies that reported and evaluated the use of Morita therapy for different mental health illnesses had been conducted in China (He. And Li., 2007; Wu., et al., 2015).

RCT: Randomised clinical trial

Table of Contents

Contents

List of Tables

List of Figures

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Author's declaration

I declare that this thesis is a presentation of original work and I am the sole author. This work has not previously been presented for a degree or other qualification at this University or elsewhere. All sources are acknowledged as references.

- The material in Chapter 3 has been partly published as a protocol in: Nava-Ruelas, R., Jarde, A., Elsey, H., Siddiqi, K., Todowede, O., Zavala, G., Siddiqi, N. *"Pharmacological and psychological interventions for depression in people with tuberculosis".* 2021. Cochrane Database of Systematic Reviews. Issue 5. Art. No.: CD014848. DOI: 10.1002/14651858.CD014848.
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- The material in Chapter 5 has been submitted for publication to the PLoS Global Public Health journal and is under review.

Chapter 1 - Introduction

People with tuberculosis (TB) can have comorbid conditions which,can influence the outcome of their TB treatment if untreated. Treating comorbid conditions in people with TB can improve their TB-related and general health outcomes. Depression is a common comorbidity in people with TB. Treating depression in people with TB at the same time that they are receiving TB care can improve the TB-related and mental health outcomes of people with TB.

It is unclear what the most effective way to treat depression in people with TB is. The overarching aim of my doctoral thesis was to explore the current evidence on interventions that aim to improve the TB and mental health outcomes for people with TB by delivering care for depression as part of TB programmes, or services, in low- and middle-income countries (LMICs). I also aim to explore the implementation context of a mental health intervention for people with TB in LMICs. The main research question of this thesis is to answer what are the most effective treatments for depression in people with TB, and what are the implementation experiences of countries who have tried to deliver depression care alongside TB care?

To address these aims and answer the research question of this thesis, I formulated the following research objectives:

1) To assess the effectiveness of interventions for treatment of depression in people with TB.
2) To identify the various interventions and approaches to deliver depression care as part of TB care which have been implemented in LMICs, and to analyse the barriers and facilitators for their implementation.
3) To identify a mental health intervention for depression implemented as part of a national TB program in a LMIC and explore the barriers and facilitators for its implementation.

This thesis will consist of two parts. The first part, addressing Objectives 1 and 2, will involve systematic reviews of available peer-reviewed literature. Objective 3 will be addressed through a qualitative case study focused on the implementation of an intervention for depression in people with TB in Pakistan. This two-pronged approach was based on the premise that evidence synthesis from international contexts can inform local contexts but must be complemented by a deep understanding of the local setting (Booth et al., 2019b). Gathering evidence on the effectiveness of depression interventions for people with TB

benefits from an international perspective to identify varying approaches and outcomes (Booth et al., 2019b). However, as highlighted in the implementation science literature (Booth et al., 2019a; Grol et al., 2007; Means et al., 2020), each health system is unique. Adequate consideration of the local context is essential in the design and evaluation of interventions, particularly those that include mental healthcare components (Rathod et al., 2017).

1.1 Thesis structure

The **Background** (Chapter 2) contains the literature review on the comorbidity of tuberculosis and depression, and it discusses the advantages of using implementation science approaches to explore the implementation of healthcare interventions for depression.

Chapter 3 contains a meta-analysis that assesses the effectiveness of treating depression in people with TB and its impact on TB and mental health outcomes.

Chapter 4 contains a systematic review exploring peer-reviewed literature describing the approaches used to implement mental health interventions for depression in people with TB in low- and middle-income countries (LMICs).

Chapter 5 contains a qualitative case study of the implementation experience of an intervention for depression in people with TB in Pakistan.

In the **Discussion** section (Chapter 6), I bring together the findings from the individual studies included in the thesis and I discuss links between them and their contributions to the research objectives, and to the wider field of depression comorbid with TB. I also discuss the limitations of the individual studies and the thesis.

In the **Conclusion** (Chapter 7), I summarize the key findings of this thesis and suggest ways to improve the thesis.

Chapter 2 - Background

Chapter Summary

This chapter starts by providing the definitions of TB and depression, and it continues by describing the literature on their co-occurrence and comorbidity. Lastly, it provides a rationale for assessing the effectiveness and exploring the implementation context of interventions to improve mental health and mental healthcare-related outcomes in people with TB and depression.

2.1 Definitions

Tuberculosis (TB)

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. The World Health Organisation (WHO) estimates that approximately 25% of the global population has been or is infected with TB (WHO, 2023a). The COVID-19 pandemic influenced the incidence, prevalence, and mortality rates of TB. For example, the latest Global Tuberculosis Reports mentions that TB was the second largest cause of death from a single infectious agent after COVID-19, causing more deaths than HIV/AIDS (WHO, 2023a:p17). In 2019, TB affected between 25% and 30% of people worldwide, with around 97% of reported cases until then occurring in low- and middle-income countries (LMICs) (WHO, 2019a). In 2023, more than 8 million people were newly diagnosed with TB, which is the highest number recorded since 1995, and an increase of more than half a million cases than detected in 2022 (WHO, 2024a). The disease is especially prevalent among vulnerable populations, including those in prisons and individuals living in overcrowded conditions (WHO, 2023a). Given the increase in detection rates, the increase in viable TB, and the aftermath of the COVID-19 pandemic and its impact on health systems, TB is a critical global health priority that merits renewed efforts to address (Schwalb, et al., 2024).

TB can affect any organ in the body, and it is classified into pulmonary and extrapulmonary infections. Pulmonary TB affects the lungs, lung parenchyma, or tracheobronchial tree; extrapulmonary TB affects organs other than the lungs, such as lymph nodes, pleura, abdomen, skin, joints, bones, meninges, or genitourinary tract (WHO, 2020). The characteristics of TB infection also include the drug-susceptibility of the strain, active or latent status of the infection, and presence of HIV comorbidity (WHO, 2020). The prognosis of TB infection depends on all these characteristics of the infection, with the most important variation being the drug-susceptibility or resistance displayed by the bacteria. Drug-resistant TB (DR-TB) often requires more complex and prolonged treatment than drug-susceptible TB

(DS-TB), which can be more burdensome and is associated with a higher risk of treatment attrition and adverse effects (Cohen, Meghji, & Squire, 2018). The treatment success rates for DS- and DR-TB reflect this: for DS-TB treatment success rate is 88%, while it is 63% for DR-TB (WHO, 2023a).

A person infected with *Mycobacterium tuberculosis* does not necessarily develop TB. The number of people who develop active TB after infection was estimated to be 2.0% in 2022; after the COVID-19 pandemic that estimated number increased to between 4.9% and 7.7% (Scwhalb, et al., 2024). That means that only a small proportion of people who get infected with TB actually develops the disease and symptoms (active TB) and are therefore contagious. TB is contagious when people who are sick expel the bacteria into the air by coughing, for example (WHO 2024b). Latent TB is the name used to refer to TB infection that does not cause symptoms and is not contagious, although it can become active in the future

TB infection is curable with established treatment plans using different anti-TB drugs depending on the drug-susceptibility of the strain. Without treatment, active TB infection has a high mortality (WHO, 2023a). Successful treatment of TB is defined as a combination of treatment completion and cure:this means that a person with TB has a successful treatment when they have completed the course of anti-TB drugs and their last sputum test is bacteriologically negative (WHO, 2023a). Successful treatment and treatment completion, depend on adequate adherence to the treatment regime (WHO, 2020; WHO 2023a). The guidelines on TB treatment were updated in 2022 to reflect recent learnings on drug susceptibility, drug resistance, and treatment length. People with drug-susceptible TB (pulmonary and extrapulmonary), should follow a 6-month treatment plan of isoniazid, rifampicin, ethambutol, and pyrazinamide; the last two months of treatment should comprise only isoniazid and rifampicin (WHO, 2024b).

Some of the factors that influence adherence to treatment are age, nutritional status, alcohol consumption, smoking, and gender of the person with TB (Chaves-Torres, et al., 2019; WHO, 2020). Following infection, the risk of developing active TB disease is highest in the first 2 years, after which it decreases; depending on the mediating factors (e.g., smoking, HIV positive status, undernutrition, diabetes, and alcohol consumption) the risk of developing active TB can increase and remain high after 2 years (WHO, 2024b).Comorbidities also influence treatment adherence, often negatively (Samuels, et al., 2018). There is a growing body of evidence examining how other physical and mental health comorbidities affect TB outcomes (Ruiz-Grosso, et al., 2020; Tegegne, et al., 2018).

Depression

Depression is one of the most prevalent mental health comorbidities in people with TB (Koyanagi, et al., 2017; Van Rensburg, et al., 2020). Major depressive disorder, or depression is characterised by low mood (e.g. sadness, irritability, emptiness) or loss of pleasure, accompanied by other cognitive, behavioural, or neurovegetative symptoms that significantly affect the person's ability to function. The Diagnostic and Statistical Manual (DSM-5) describes depression as experiencing at least five of the following symptoms listed below in the presence of depressed mood, or loss of interest or pleasure, for at least two weeks, every day or nearly every day (APA, 2013):

- A persistently low or depressed mood for most of the day, nearly every day, as observed by others or self-reported.
- Markedly diminished interest or pleasure in all, or almost all, activities most of the day.
- Significant weight loss when not dieting, weight gain, or decrease or increase in appetite.
- Insomnia or hypersomnia (excessive sleeping).
- Feelings of fatigue or loss of energy nearly every day.
- Feelings of worthlessness or excessive guilt.
- Diminished ability to think or concentrate, or indecisiveness.
- Recurrent thoughts of death, suicidal ideation, or a suicide attempt.

These symptoms refer to adult populations only, or those over 18 years of age.

2.2 Tuberculosis and depression comorbidity

Depression is one of the four primary mental health comorbidities associated with TB in LMICs (Van Rensburg et al., 2020). While the exact causes of depression in people with TB remain unclear, contributing factors may include treatment-induced depression, direct effects of the illness (e.g., organic depression), psychological responses to the disease and its associated stigma, or random co-occurrence (Doherty, 2013; Sweetland et al., 2017). Furthermore, metabolic pathways triggered by both depression and TB may interact synergistically, exacerbating each condition in what is known as a syndemic, or bidirectional, relationship (Doherty et al., 2013; Sweetland et al., 2017; Hayward, et al., 2022, Zhang, et al., 2019).

It is unclear what is the risk and prevalence of depression in people with TB across settings. According to data from the World Health Survey (2002–2004), an estimated 23.7% of people with TB experience depression, compared to 6.7% of those without TB (Koyanagi et al.,

2017). This study estimated the prevalence of depression among people with drug-susceptible TB (DS-TB) to be between 6.8% and 23.7% (Koyanagi et al., 2017). Another study estimated similarly wide range in prevalence of depression among people with drug-resistant TB, of 25% (14–39%, 95% CI) (Alene et al., 2018). A study based in East African countries found that the prevalence of depression in people with TB was 43.03%, based on a sample size of 2,838 individuals (Alemu & Zeleke, 2023). Other study based in the United States including only people of non-US origin found that prevalence of mental disorders in people with TB was 34% (21.1% - 49.5%, 95% CI) (Njie & Khan, 2022). A large cohort study of over 32,000 people found that individuals with depression have a 2.63 times higher risk of developing TB (1.74–3.95, 95% CI), with the risk potentially increasing with the severity of the depressive disorder (Oh et al., 2017). Depression also raises the risk of active TB, with an effect size of 1.52 (1.29–1.79, 95% CI) (Hayward et al., 2022). What these studies help illustrate is the increasing awareness of the significant prevalence of depression and mental health illness in people with TB while also highlighting the lack of a global estimate that reflects the findings of these individual studies carried out in different countries. Thus, the real prevalence of depression in people with TB, its severity, and its impact remain unknown.

The impact of depression on TB health outcomes can be significant and multifaceted. Systematic reviews have reported a loss of self-esteem and increased mortality risk among individuals with both TB and depression compared to those without depression (Van Rensburg et al., 2020; Koyanagi et al., 2017; Ugarte-Gil et al., 2013). Depression and TB comorbidity can lead to higher mortality rates and increased loss to follow-up during TB treatment (Lee et al., 2020; Ruiz-Grosso et al., 2020). Depression is also strongly associated with poor adherence to TB treatment, particularly during the early stages of diagnosis and treatment when mental health needs are most critical (Van Rensburg et al., 2020). people with TB with depression exhibit the fastest and most pronounced decline in self-assessed health status compared to those without depression (Koyanagi et al., 2017).

Socioeconomic factors and gender further influence the risk of depression in people with TB. Poor mental health in people with TB can also be influenced by individual and societal level factors that are “inextricably linked to poverty” (Mainga, et al., 2022b). Women, in particular, consistently report poorer mental health outcomes following TB diagnosis and during treatment (WHO, 2023a). Lower educational attainment also increases the likelihood of depressive symptoms in people with TB (Van Rensburg et al., 2020). Other significant risk factors for depressive episodes in people with TB include older age, low income, smoking, and diabetes (Koyanagi et al., 2017). Additionally, the social stigma associated with both TB and mental illness in LMICs plays a major role in heightening the risk of depression (Rathod

et al., 2017). This stigma may cause individuals to delay seeking care for either TB or depression, exacerbating both conditions and increasing the risk of transmission, particularly in shared living environments and negative treatment outcomes (Koyanagi et al., 2017).

2.3 Treating depression in people with TB

Treating depression in people with TB can lead to significant improvements in mental health, TB-related outcomes, and overall health. Studies show that integrating mental healthcare, such as psychotherapy or group counselling, into TB treatment enhances adherence to TB treatment (Acha et al., 2007; Janmeja et al., 2005). In people with drug-resistant TB, counselling has been shown to boost cure rates by nearly 30% compared to those who do not receive counselling (Baral et al., 2014). Addressing psychosocial factors in people with TB is crucial for improving treatment outcomes and supporting global efforts to eradicate TB (Walker et al., 2017). For instance, providing non-clinical support to the families of people with TB in LMICs has been found to improve both cure rates and treatment adherence (Oliosi et al., 2019). Primary care services are the settings where TB care is delivered and represent a feasible opportunity to integrate the provision of mental healthcare for TB(Sweetland, et al., 2018).

While treatment guidelines for TB are well established, guidelines for managing depression, especially as a comorbidity in people with TB, are less defined. A systematic review demonstrated the positive impact of psychological and socioeconomic interventions on TB treatment outcomes, showing that these approaches benefit people across various settings (van Hoorn et al., 2016). Some interventions, such as providing food or economic support to people with TB, target the socioeconomic aspects of the disease. However, these efforts had limited or no effect on TB treatment outcomes or adherence (van Hoorn et al., 2016). Other reviews found that mental health interventions for people with TB require a psychological component to be effective (Farooq et al., 2021; Van Rensburg et al., 2021).

2.4 Implementing mental health interventions for people with TB

In most LMICs, TB control programs are primarily funded by multilateral and bilateral donors, while their operational capacity lies with national governments through national TB programs (NTPs) (WHO, 2021). These programs are typically structured as vertical interventions, focused on a specific disease, with financing, monitoring, and service delivery targeting TB exclusively (Atun et al., 2010). A notable example is the Global Fund to Fight AIDS, Tuberculosis, and Malaria, which allocates over $4 billion annually to 140 countries, accounting for more than 70% of external TB funding in LMICs (Dieleman et al., 2017; The Global Fund, 2018). Despite their success in controlling TB, the single-disease focus of

vertical programs can limit their integration with broader health systems, particularly in addressing comorbid conditions like depression.

Although depression is a common comorbidity in people with TB, it remains largely unaddressed in TB programs. The World Health Organisation (WHO) and the Global Fund have included vague references to mental health in their TB strategies, but no clear guidelines exist for diagnosing or treating depression in people with TB (WHO, 2021; The Global Fund, 2019). This gap reflects broader challenges in mental healthcare in LMICs, where funding is insufficient, human resources are scarce, and services are often concentrated in urban areas (Rathod et al., 2017). Mental health spending in LMICs remains less than 1% of GDP, despite evidence suggesting that mental health interventions could yield substantial societal benefits (WHO, 2018b).

There is growing recognition of the need to integrate mental healthcare into TB programmes, as demonstrated by initiatives like the WHO's Mental Health Gap Action Programme (mhGAP)(WHO, 2016)..However, the best approaches to delivering depression care alongside TB services remain unclear. Evidence on the clinical effectiveness of depression interventions in people with TB is limited, and no systematic reviews have assessed the relative impact of pharmacological, psychological, or combined interventions. Moreover, while some interventions, such as person-centred approaches, have been piloted in LMICs, their effectiveness and sustainability are yet to be fully explored. Further research is needed to identify the most effective and scalable interventions for treating depression in people with TB and to assess their real-world impact.

In conclusion, addressing the depression-TB comorbidity in LMICs will require comprehensive strategies that go beyond evaluating the clinical effectiveness of existing interventions. The strategies for integrating mental health and TB treatment delivery must account for local health system characteristics, funding limitations, and broader socioeconomic factors. A systematic assessment of existing evidence of the delivery of depression interventions in TB care is crucial to inform future policies and ensure that mental healthcare is integrated sustainably into TB control efforts.

There is a research gap on understanding the impact of treating depression in TB and how to deliver depression care for people with TB. The following sections aim to address this gap in the literature by addressing the research objectives outlined in Chapter 1- Introduction. The following chapters correspond to one research objective each.

Chapter 3 - Pharmacological and psychological interventions for depression in people with tuberculosis: a systematic review.

Chapter Summary

In this chapter, I describe the methods I used to review studies that had evaluated the effectiveness of interventions for depression in people with tuberculosis. The protocol for this study was published in Issue 5 of Cochrane Database of Systematic Reviews in 2021 (Nava-Ruelas *et al.,* 2021). I first submitted the full review for publication on 6th August 2022, and then a revised manuscript on 24th March 2023.

3.1 Introduction

In Chapter 2 – Background, I described the rationale for researching the approaches used to treat depression in people with TB. The clinical effects of treating depression in people with TB have been addressed in other systematic reviews which varied in methodological design and inclusion criteria such as the types of intervention used to treat depression, the types of participants included, and the types of outcomes assessed in the studies. When I started writing the protocol for this review in 2021, there were few reviews about the effectiveness of pharmacological and psychological interventions for treating depression in people with TB, and their impact on TB-related and mental health outcomes. Moreover, there were no systematic reviews that explore the use of antidepressants (with or without psychological interventions) to treat depression in people with TB and their effect on TB-related health outcomes.

3.1.1 Review aim and objectives

The purpose of this review was to begin to determine whether treating depression in people with TB is effective for improving mental and physical health outcomes by summarising the existing evidence on pharmacological and psychological interventions. I also aimed to assess the effect of treating depression on other outcomes of interest, such as health-related quality of life.

To do this, I had as an objective to conduct a systematic review that focused on assessing the effectiveness of pharmacological and psychological interventions for the treatment of

depression in people with tuberculosis (TB) by assessing the impact of these interventions on depression and health-related quality of life in people with TB.

3.2 Methods

3.2.1 Protocol and registration

I undertook this systematic review and meta-analysis following the Cochrane guidelines for systematic reviews of interventions (Higgins, et al., et al., 2019d). The methods I used are documented in a protocol published in the Cochrane Database of Systematic Reviews (Nava-Ruelas *et al.,* 2021).

3.2.2 Eligibility criteria

This was the inclusion criteria for TB and depression I followed to identify eligible studies:

Types of study design

I included randomised controlled clinical trials (RCTs), crossover trials, and cluster-randomized trials (cRCT) that evaluated interventions to treat depression in people with tuberculosis (TB).

Types of participants

- Diagnostic criteria (TB): I included adults aged 18 years and over, living with all forms of TB. For the purposes of this review, I defined a diagnosis of TB as any person who presents signs or symptoms suggestive of TB, or who has a confirmed laboratory or clinical diagnosis of TB. I included people with latent, drug-susceptible, or drug-resistant TB from all countries and from all clinical settings, including community-based care, primary care, secondary care, and TB programmes.
- Diagnostic criteria (depression)**:** I included participants with a diagnosis of depression co-occurring with tuberculosis. The categories of depression diagnosis included in this review were mild, moderate, or severe depressive disorders, either as a single or recurrent episode. I included studies where depression was diagnosed using the criteria from the World Health Organisation International Classification of Diseases (ICD) for mental and behavioural disorders (e.g. ICD-10: F32, F33, F34.1) (WHO 2004), the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA, 2013), and a combination of or measures based on these. If a study includes the analysis of people with and without a diagnosis of depression, I included it if it discloses the outcome measurement data at all

timepoints for people with TB and depression diagnosis separately from those with TB without depression diagnosis.

Types of interventions

I described the types of psychological and pharmacological interventions for depression according to the guidelines of the Cochrane Group for Common Mental Disorders (Cochrane Collaboration, 2024). I described eligible interventions as follows:

- Psychological interventions refer to any type of group or individual therapy used to treat depression. I considered psychological therapies if they involved direct person-professional interaction, face-to-face interaction, interventions in which face-to-face therapy was augmented by telephone or internet-based support, as well as interventions delivered entirely online (e.g., through web pages or e-mail) or through mobile applications (i.e., applications (apps) via computers or mobile devices. Examples of eligible psychological interventions are behaviour therapy (e.g., behaviour modification), cognitive behavioural therapy (including third wave cognitive behavioural therapies, such as behavioural activation), psychodynamic therapies (e.g., group therapy, interpersonal therapy, or psychoanalytic therapy), and other types of psychological therapy (e.g., family therapy). All interventions must have had a psychological component – talking, listening, support, advice – and be delivered by somebody with recognised training in, and supervision of, therapies, and were directed at helping people develop their social problem-solving skills.
- Pharmacological interventions referred to the use of any type of antidepressant (e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and other antidepressant medications) commonly used to treat depression.
- Psychological and pharmacological interventions (e.g., combined treatment).

Comparator intervention

For studies with pharmacological interventions with or without psychological interventions, comparator interventions must have included placebo, no intervention, or routine or usual care. For studies with psychological interventions, comparators must have included no intervention, or routine or usual care. For the purposes of this review, I considered routine or usual care as the care delivered for people with TB in accordance with the local or national TB guidelines.

Type of outcome measures

I included studies that assessed either of the following primary outcomes:

Primary outcomes

- Treatment effectiveness was defined as improvement in or recovery from depression, when compared to a pre-intervention baseline assessment, or as defined in the study, measured at study end. I defined this as changes in depression scores (i.e. continuous outcomes), measured using the Patient Health Questionnaire, Hamilton Depression Rating Scale, the Montgomery Åsberg Depression Rating Scale, the Beck Depression Inventory, the Hospital Anxiety and Depression Scale, the General Health Questionnaire, the Generalised Anxiety Disorder test, the Hamilton Anxiety Scale, the Beck Anxiety Inventory, the Hospital Anxiety and Depression Scale, or any other scale validated for the measurement of depression, provided that measures are taken with the same scale at baseline and end of treatment.
- Adverse events (for all forms of TB):
    - Self-reported adverse events were defined as any adverse effects expressed by the participant, related to interventions for treating depression, TB, or both.
    - Diagnosed adverse events were defined as adverse events diagnosed using blood tests, audiometry, vision tests, or electrocardiogram (ECG). Examples of these are toxicities, audiological complaints, hearing loss, and QT prolongation.

I included studies that measured the outcomes of interest at baseline and at the end of the intervention, as defined in the included study, and used the same measurement instrument for all time points.

Secondary outcomes

I also included studies if they assessed the following secondary outcomes in addition to the primary outcomes described above:

- Effect on TB was defined as changes in TB-related outcomes (i.e., dichotomous outcomes (WHO 2020):

    - Cure was defined as a person who initially had a positive diagnosis of TB and has a negative sputum smear test in the last month of treatment, or at least on one previous occasion.
    - TB treatment failure was defined as a person with a positive sputum test after five months or more of treatment.
    - Treatment completed was defined as a person who completed the anti-TB pharmacological treatment, without evidence of failure, with no record of

negative sputum or culture test at the end of treatment, due to either unavailability of the test or results.

- Loss to follow-up was defined as a person with a confirmed diagnosis of TB who did not start treatment, or whose treatment was interrupted for at least two consecutive months.
- Relapse was defined as a person who has been previously treated for TB, has been declared cured or completed treatment, and is now diagnosed with a recurrent episode of TB (either by re-infection or by true relapse).
- Mortality was defined as death by any cause during the intervention or the anti-TB treatment.

- Changes in health-related quality of life were defined as outcomes measured using composite scales, such as the Short Form Health Survey (36- or 12-item version), Quality of Life Scale, or any other scale validated for the measurement of health-related quality of life, provided that measures are taken with the same scale at baseline and end of treatment. I considered this a continuous outcome.

3.2.3 Search strategy

I conducted searches between 19th May 2021 and 19th August 2021. I did not apply any restriction on date, language, or publication status to the searches.

I searched a total of 20 electronic databases. These consisted of international trial registers, grey literature databases, and theses databases:

- Cochrane Common Mental Disorders Controlled Trials Register (CCMDCTR; all available years). Search date: 09th July 2021.
- Cochrane Central Register of Controlled Trials (CENTRAL; current issue). Search date: 22nd May 2021.
- MEDLINE Ovid (1946 onwards). Search date: 19th May 2021.
- Epistemonikos. Search date: 30th July 2021.
- Health Evidence. Search date: 24th August 2021.
- Embase Ovid (1974 onwards). Search date: 19th May 2021.
- Database of promoting health effectiveness reviews (DoPHER). Search date: 18th August 2021.
- National Institute for Health and Care Research Publications Library (NIHR). Search date: 19th August 2021.

- EPPI Centre Publications. Search date: 19th August 2021.
- PsycINFO Ovid (all years). Search date: 19th May 2021.
- ProQuest. Search date: 13th August 2021.
- ProQuest Theses and Dissertations Database. Search date: 13th August 2021.
- Web of Science Social Science Citation Index (SSCI; all years). Search date: 24th May 2021.
- Scopus (all years). Search date: 24th May 2021.

I searched ClinicalTrials.gov (search date: 30th July 2021), and the World Health Organisation (WHO) International Clinical Trials Registry Platform (ICTRP; all years; search date: 30th July 2021) to identify ongoing or unpublished trials.

I also searched the following grey literature databases:

- Open Grey. Search date: 13th August 2021.
- ProQuest Dissertations & Theses Global. Search date: 13th August 2021.
- DART-Europe E-theses Portal. Search date: 13th August 2021.
- EThOS – the British Libraries e-theses online service. Search date: 13th August 2021.
- Networked Digital Library of Theses and Dissertations (NDLTD). Search date: 18th August 2021.
- Open Access Theses and Dissertations (OATD). Search date: 18th August 2021.

An example of the search strategy used for Medline is included in Appendix 1.

3.2.4 Data collection and analysis

Data collection

Selection of studies

I worked with a second reviewer (Dr Gerardo Zavala) to independently screen titles and abstracts during the first screening stage. I retrieved the selected full texts, and we screened them
independently. For studies excluded during the full-text screening stage, we recorded a reason for exclusion. We resolved discrepancies through recourse to a third review author (Prof Najma Siddiqi). I requested full versions of the texts that were not available directly

from the authors. I recorded our decision process in a PRISMA flowchart (Page, et al., 2021).

Data extraction and management

For included studies, I worked with a different second reviewer (Dr Olamide Todowede) to independently extract key study, participant, and intervention characteristics, as well as a outcomes data. We used a standard pre-piloted data extraction form from the Cochrane collaboration (Li, et al., 2022). Disagreements were resolved by discussion or, if required, by a third reviewer (Dr Alexander Jarde). We extracted the following data:

- General information: authors of study or report, year of publication, citation.
- Study design: year of study, study duration, recruiting and sampling procedures, trial design, sequence generation, unit of analysis, funding sources, and author affiliations.
- Participants' information: population description, sample size, TB diagnosis information, depression diagnosis information, other comorbidities, age, gender, country, and socioeconomic status (if available).
- Intervention: description of the intervention, frequency, length, and dose of intervention, length of follow-up, mode of delivery of the intervention, description of co-intervention (if applicable):
- For pharmacological interventions: class of drug used, dose, frequency, duration.
- For psychological interventions: description of the intervention, provider or mode of delivery of the intervention, theoretical approach, or content of the intervention (or both), intensity (length, frequency, and duration of sessions.
- Comparison interventions: description of comparator or control groups, data on routine or usual care, and no intervention comparators
- Outcomes (Higgins, et al., 2019b):
    - In RCTs:
        - For dichotomous (binary) data (e.g., mortality), we planned to extract the number of events and participants randomised for each intervention group. If these numbers were not available, we would extract the reported effect estimate (odds ratio (OR) or risk ratio) with its uncertainty measure (95% confidence interval (CI), standard error, or exact P value).

        - For numerical or continuous outcomes (e.g., depression scores), we planned to extract the mean value, the standard deviation, and the number of participants in each group. If these numbers were not available, we would extract the reported effect estimate (difference in means) with its uncertainty measure (95% CI). If a study reported the same outcome using different depression scores (e.g., improvement in Patient Health Questionnaire and Beck Depression Inventory), we would extract both.
    - In cluster-RCTs:
        - For studies that took into account the cluster design in their analyses (e.g., multi-level analysis), we would extract the effect estimate (e.g., OR for dichotomous data) and its confidence interval.
        - For studies that did not take into account the cluster design, we planned to extract the outcome data for the total number of participants (e.g., the number or proportion of participants with events, or means and standard deviations for continuous data), the average (mean) size of each cluster, and if available, an estimate of the intracluster (or intraclass) correlation coefficient (ICC).
    - In cross-over trials:
        - For studies using a cross-over design, we planned to only use data from the first active treatment phase to minimise the risk of carry-over effects.
- Adverse events: if reported, we planned to extract these verbatim from the study report.
- Study or author's conclusions

Management of time points

I planned to summarise and categorise post-treatment outcomes, and outcomes at each reported follow-up point as follows: at the end of treatment (zero to four weeks after treatment), short-term (up to three months post-treatment), medium-term (six months post-treatment), and long-term (longer than 12 months post-treatment).

Management of studies in different languages

For included studies that were not in the English language, I identified a health services researcher with working knowledge of English and the language of the included study.

Data analysis

Measures of treatment effect

The plan was to express dichotomous data as odds ratios (OR) or risk ratios (RR), with 95% confidence intervals (CI). I would express continuous data as mean differences (MD) with 95% CIs (Higgins, et al., 2019b). If the same outcome of interest was measured using different instruments (i.e., depression scales) across studies, we would address this by using the standardised mean difference (SMD) and do different meta-analyses including the different instruments used to measure the outcome of interest (See Sensitivity analysis**),** as long as the difference lay in the instrument used to measure the outcome, and not in the population (Higgins,et al., 2019b). It was also planned to separate severe depression data from mild and moderate depression data, if available.

Unit of analysis issues

To address this, I considered the level at which randomisation occurred, such as cross-over trials, cluster-randomised trials, and multiple observations for the same outcome (Deeks, Higgins, & Altman, 2020). To correct this unit of analysis error and analyse both studies as cRCTs, I used the inflated standard error method, as suggested in the Cochrane Handbook. This method of analysis is useful to explore the effect of the intervention at the individual level, and it helps to correct for unit of analysis errors in cRCTs (Higgins, et al., 2019a). This correction consists of multiplying the standard error of the effect estimate from the analyses (ignoring clustering) by the square root of the design effect. In cases where there were other issues with the unit of analysis, I had planned to approach them according to the Cochrane handbook guidance (Higgins, et al., 2019b).

For studies with more than two interventions (multiple-arm studies), consisting of either different types of interventions or different doses of medication, I planned to avoid any possible bias caused by multiple comparisons with one control group by combining the groups to create a single pair-wise comparison.

Dealing with missing data

I planned to deal with missing data in line with the guidelines provided by the Cochrane Handbook for Systematic Review of Interventions (Deeks, Higgins, & Altman, 2020):

- I would collect and document information on missing data. I would contact the original study authors to obtain relevant missing data. I would also document all correspondence with authors, and report which authors had responded, and what methods they (might) have used for inputting data (such as multiple imputations).
- When it could be assumed that data are 'missing at random' (due to available information), I would only analyse the available data. If it could be assumed that data were 'not missing at random', I would assume that participants who dropped out after randomisation had a negative outcome; I would also conduct our analyses according to the principle of intention-to-treat (ITT) in this scenario.
- I planned to conduct sensitivity analyses to assess the impact caused by missing data.
- I planned to thoroughly discuss with the other reviewers the potential impact of missing data on the findings in the full review.

Assessment of heterogeneity

I assessed heterogeneity using the I^2 statistic, as stated in the Cochrane Handbook for Systematic Reviews of Interventions (Deeks, Higgins, & Altman, 2020). In the event of substantial clinical, methodological, or statistical heterogeneity, I planned to not report study results as the pooled effect estimate in a meta-analysis. I planned to identify heterogeneity by using a standard Chi^2 test or I^2 statistic, which quantifies inconsistency across studies, to assess the impact of heterogeneity on the meta-analysis. If applicable, I planned to determine potential reasons for heterogeneity by examining individual study and subgroup characteristics. I considered heterogeneity as significant if the value of I2 was between 75% and 100%, in line with the recommendations of the Cochrane Handbook (Deeks, Higgins, & Altman, 2020).

Assessment of reporting biases

I planned to use funnel plots to assess bias in reporting of effects when 10 or more studies report on the same outcome of interest, according to the Cochrane Handbook for Systematic Reviews of Interventions (Page, Higgins, & Sterne, 2020).

Data synthesis

I combined data in a meta-analysis if the study designs, interventions, and participant

characteristics are sufficiently similar. To aid this assessment, I considered statistical heterogeneity – which can be a consequence of clinical or methodological diversity, or due to unexplained factors – of 75% or higher, as quantified by the I^2 statistic, as substantial.

I used Revman Web as software to aid with the analyses (Revman Web, 2022). I used a random-effects model for the meta-analyses, using the generic inverse-variance method (DerSimonian & Laird, 1986). For cluster-RCTs that reported outcomes without considering the cluster design, I carried out the analysis using the inflated standard error method before pooling the results with the remaining studies (Higgins, et al., 2019a).

Subgroup analysis and investigation of heterogeneity

I had planned to carry out the following subgroup analyses, based on the characteristics of the population or intervention that might influence the primary outcomes:

- Type of TB (i.e., drug-susceptible, drug-resistant, or extensively drug-resistant). I considered this information relevant as there might be a correlation between the severity of the TB illness and the severity and prevalence of depression, anxiety, and psychosis (Duko, Bedaso, & Ayano, 2020).
- Age and gender. I considered this relevant as there is some evidence of the correlation between female sex and older age with the prevalence of depression symptoms (Koyanagi, *et al.,* 2017).
- Intervention duration (less than three months versus three months or more, as the length of follow-up and outcome measure points can provide information about relapses in depression symptoms (Cuijpers, et al., 2020).
- Length of follow-up (less than three months versus three months or more; this is likely to influence the detection of outcomes).
- Presence of other comorbidities (if applicable, specify which). The presence and treatment of comorbidities can have a bidirectional synergy with the presence and treatment of depression (Arnaud, et al., 2023).

I also planned to explore the impact that the severity of depression had on the effectiveness of the intervention if data was available. I planned to separate severe depression data from mild and moderate depression data.

Sensitivity analysis

I planned to carry out the following sensitivity analyses for primary and secondary outcomes of interest:

- Effect of trial size: I would exclude trials with a sample size smaller than 50.
- Effect of choosing the most prevalent measurement scale outcome when studies report the same outcome using different scales. If multiple instruments were used in the same study to report the same primary outcome, I would re-do the meta-analysis using the SMD measured with the less prevalent instrument in the pool of studies.
- Effect of study quality (risk of bias; low risk of bias versus uncertain or high risk of bias).

Summary of findings and assessment of the certainty of evidence

I created a summary of findings table (Table 3.2) in line with the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions (Schünemann, *et al.,* 2020). I created it using the GradePRO GDT software (GRADEpro GDT, 2015). I planned to present data on absolute and relative effects with 95% CI, risk for treatment and for usual care, the number of participants and studies for each outcome, and the quality assessment of the evidence, using the GRADE approach for each outcome. For each outcome, I planned to analyse the factors that can limit the quality of evidence according to the GRADE handbook: limitation in study design or execution, inconsistency of results, indirectness of evidence, imprecision, and publication bias (Schünemann, *et al.,* 2013). I explained the reasons for downgrading the certainty of the evidence in the footnotes. I planned to show the results for outcomes of the following comparisons:

- Psychological intervention versus no intervention or usual care
- Pharmacological intervention versus placebo, no intervention or usual care
- Psychological and pharmacological intervention versus placebo, no intervention or usual care

I planned to report on these outcomes in the summary of findings tables:

- Treatment effectiveness for depression
- Adverse events for all forms of TB, self-reported and diagnosed,
- TB treatment success (cured),
- TB treatment failure,
- TB treatment completion,

- Loss to follow-up, and
- Changes in health-related quality of life.

I planned to fully describe these outcomes in the table, including information on thresholds and values for outcomes that are assessed using scales, such as depression scores, if the information were available.

3.2.5 Assessment of risk of bias in included studies

I worked with a third reviewer to independently assess the risk of bias of each included study. We resolved disagreements by consensus, or by consultation with a third party. We assessed risk of bias using version 2 of the Cochrane tool for assessment of risk of bias (RoB 2) (Higgins, et al., 2019c). We assessed the following domains for risk of bias:

- bias arising from the randomization process
- bias due to deviations from intended interventions
- bias due to missing outcome data
- bias in measurement of the outcome
- bias in selection of the reported result.

We judged the risk of bias criteria as low risk, high risk, or unclear risk, and evaluated individual bias items as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins, et al., 2019c). We reached a consensus by discussing our views or consulting with a third party. I created a risk of bias graph figure with the assessments for the included studies for the outcomes of interest (see Figure 3.4).

3.3 Results

3.3.1 Search strategy results

I identified 2,613 results: 2,508 from electronic, grey literature, and theses databases, and 105 from trial registers. The results of all searches are reported in a PRISMA flow diagram in Figure 3.1 (Page, et al., 2021).

I removed 492 duplicate records. A second reviewer helped me to screen the titles and abstracts of 2,121 records.12 records met eligibility criteria for full-text screening. The same second reviewer helped to screen the full texts of these 12 records. For every excluded record, we also wrote down the reason for exclusion. We resolved discrepancies through discussion and by consulting a third reviewer. For the full-text records I could not find, I

asked the authors directly. I recorded our decision process in a PRISMA flowchart (see Figure 3.1).

3.3.2 Included studies

Two studies were included in the review and analysis (Li, *et al.,* 2019; Zhang, *et al.,* 2021). Both were cluster randomised trials (cRCT) in which the interventions were psychological (cognitive behavioural therapy [CBT] and Morita therapy) compared to routine care. Both studies are described in Table 3.1.

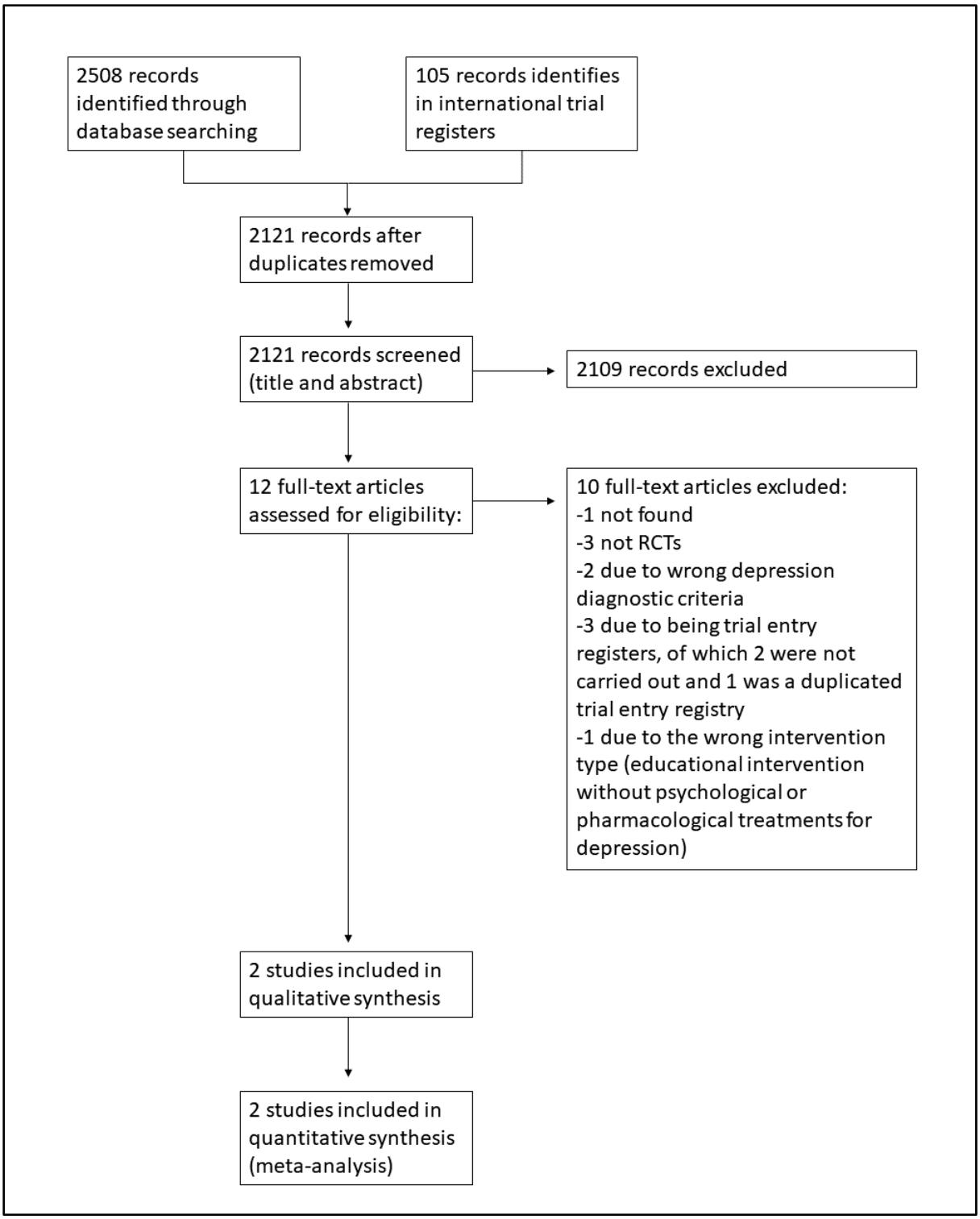

Figure 3.1 PRISMA guidelines for systematic reviews, Cochrane review. Adapted from (Page, et al., 2021).

Study	Li 2019	Zhang 2021
Study design	cRCT; parallel design	cRCT; parallel design
Setting (country, city, year)	China, Hubei province, 2016	China, Pizhou, 2018
Length of study	6 months	3 months
Participant characteristics		
Allocation to intervention and control groups	201 total participants randomised. n=69 allocated to intervention group; n=132 allocated to control group	461 total participants randomised. n=233 allocated to intervention group; n= 228 allocated to control group
Age (as reported in study)	Only participants >65 years of age were eligible to participate. The mean age of the intervention group was 71.8 (SD 5.5). The mean age of the control group was 71.9 (SD 5.4).	The mean age of the intervention group was 41.31 (SD 10.27) . The mean age of the control group was 41.94 (SD 9.69).
Gender*	In the control group 61.4% were male. In the intervention group 55.7% were male.	In the intervention group, 66.5% were male. In the control group, 67.4% were male.
TB status	TB diagnosis was done according to the WHO 2010 guideline. Type of pulmonary TB was not recorded. Data on the phase of participants' TB treatment was recorded (i.e., if people were in the initial stages of treatment or the intensive management phases).	Methods for TB diagnosis were not reported. Type of TB was not reported. Stage of treatment was not reported.

Study	Li 2019	Zhang 2021
Depression diagnosis or symptom severity assessment	Study used the Zung Self-rating depression scale (SDS). All eligible participants could receive the intervention, regardless of their depression symptom score at baseline.	Study used the PHQ-9. People were eligible to participate in the intervention if they had a depression score ≥ 5 points in PHQ-9.
Other comorbidities	The study collected demographic data on participants' comorbidities: 26 participants in the intervention group had comorbidities; 55 participants in the control group reported comorbidities. The data on the type and frequency of comorbidities in participants was not reported at the participant level.**	The study collected demographic data associated with comorbidities: • body-mass index, • smoking (68 participants in the intervention group; 65 participants in the control group) • alcohol use (83 participants in the intervention group; 81 participants in the control group)
Intervention characteristics		
Type of intervention	Psychological. The study described the use of Morita therapy, (which they categorised as a type of CBT).	Psychological. The study described the use of CBT as the intervention.
Dose and frequency	The length of the intervention delivered to people is not reported, and it is unclear how many sessions people received in total. Each psychotherapy session lasted around 30 minutes, and they were delivered twice-a-month.	Each session lasted 40 minutes or more. Their frequency was not described.
Length of intervention	6 months	1 month

Study	Li 2019	Zhang 2021
Mode of intervention delivery (as described in the study)	Intervention sessions were delivered in a one-to-one setting. The study mentioned that people also received home visits by community administrators and health workers, but their frequency and length were not reported.	The delivery of the intervention was face-to-face.
Intervention components (as described in the study)	Intervention sessions were delivered by trained therapists from the Tongji Research Centre of Mental Health. The sessions consisted of routine health education, psychotherapy, home visit, peer support, and psychoeducational workshops.	The study described the training that practitioners received prior to the delivery of the intervention. 20 community general practitioners (GPs) received 8 hours of training on cognitive behavioural therapy over 3 days. The content of the training included cognitive behavioural therapy skills, relaxation training, and supportive therapy skills.
Comparator (control group) characteristics		
Definition of comparator intervention	The study described the comparator intervention as routine care for TB. This was defined as routine health education. The contents of routine health education included basic knowledge of TB, healthy diet, and lifestyle, as well as information on the treatment process and side effects of drugs. It also included psychological coping skills such as methods to overcome stigma.	The study described the comparator intervention as routine care for TB. Routine care was described as TB treatment according to the requirements of the national directly observed treatment short course. In the control group, people were monitored daily by community GPs or nurses to adhere to their TB treatment.
Outcomes		

Study	Li 2019	Zhang 2021
Outcomes measured in the study (instrument used to measure)	The outcomes measured in the study were changes in depression symptom scores, measured using the Zung self-rating depression scale. Participants who died, dropped out, or had poor compliance were excluded from the analysis. They also measured anxiety symptoms, using the Zung Self-rating Anxiety Scale. Outcomes were reported for all the time-point measurements for all groups using mean and standard deviations, as well as Cohen's d for effect size.	The outcomes measured in the study were changes in depression symptom severity. They used PHQ-9 to measure depression symptom severity. They also measured changes in anxiety symptom severity using the GAD-7 scale, and the health-related quality of life using the SF-36 scale. These outcomes were measured for all participants. People who were lost to follow-up or did not adhere to the intervention were excluded from the analysis. The outcomes were reported using mean and standard deviations and reported their *t* and *p* values.
Time points measured in the study	Measurements were taken at baseline, first month, third month, and sixth month of the study.	Measurements were taken at baseline and at the end of the intervention.
Participants lost to follow-up (and reasons)	18 in total (8 intervention group; 10 control group)	7 in total (3 intervention group; 4 control group).
Footnotes: SD: Standard deviation *These values are as reported in the studies, i.e., only percentages of male participants were reported in the studies. ** In this study, comorbidities were grouped into one category. This category was defined as including hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, coronary heart disease, tumour, and arthritis.		

Study	Li 2019	Zhang 2021
cRCT: cluster-randomized clinical trial PHQ-9: Patient Health Questionnaire, 9 items GAD-7: Generalised anxiety disorder assessment, 7 items SF-36: Short-Form 36 Health Survey Questionnaire CBT: cognitive-behavioural therapy The study funding sources for Li *et al.,* 2019 was supported by National Social Science Fund of China under Grant 15BSH118; Innovation Research Fund of Huazhong University of Science and Technology under grant 2013TS004. The study funding sources for Zhang, *et al.,* 2021 were not declared.		

Table 3.1. Characteristics of included studies

General information of included studies

One study was published in 2021 in Mandarin (Zhang, *et al.,* 2021). Only the abstract was available in English, and I translated the full text article to English using Google translate. The translation was checked by a researcher fluent in Mandarin and English and there were no significant discrepancies found. This study was conducted in the Jiangsu province between September 2018 and November 2018 (Zhang, *et al.,* 2021). The authors were affiliated to the Centre for Disease Control and Prevention of the Pizhou province and the Oriental People's Hospital in Xuzhou (Zhang, *et al.,* 2021).

The other included study was published in 2019 in English (Li, et al., 2019). This study was carried out in the Hubei province in China between November 2015 and April 2016. The authors were affiliated to the Centre for Disease Control and Prevention of the City, and the Huazhong University of Science and Technology. This study was funded by the National Social Science Fund of China and the Innovation Research Fund of Huazhong University of Science and Technology (Li, et al., 2019).

Study design of included studies

Both studies were cluster randomised controlled trials in which groups of people with TB were randomly allocated to control or intervention groups. Both studies reported their sample size calculation methods and made reference to peer-reviewed articles from which they drew the parameters necessary to calculate their sample size.

- In Zhang, the research objective was "to explore the effect of cognitive-behavioural therapy on psychological stress and quality of life in people with pulmonary tuberculosis." (Zhang, *et al.,* 2021). The sample size was calculated according to a previous study that explored the effectiveness of cognitive-behavioural therapy on people with type 2 diabetes mellitus (Zhang, *et al.,* 2021). This study estimated that intervention and control groups each needed at least 210 to satisfy their statistical parameters for significance and to account for a 10% rejection to participation rate. In both groups, this minimal number of participants was met. The total number of participants was 454, with 230 in the intervention group and 224 in the control group. It is unclear how participants were recruited but the paper mentions that participants registered at the community health service of Pizhou city were eligible to participate.
- In (Li, et al., 2019) the research objective of the study was "to assess the effects of comprehensive interventions on the anxiety and depression experienced by elderly people with TB" (Li, et al., 2019). The authors reported that they calculated their sample size according to the repeated measures formula (Liu & Wu, 2005). They

estimated that they needed 195 participants, but it is unclear if this was in total or in each group. The number of participants in total in this study was 183, with 61 in the intervention group and 122 in the control group. In this study, the process of randomisation and allocation of clusters is clearly described. The study mentions that multistage random sampling was used to select study cities and communities from the Hubei province. Once a city was allocated to control or intervention, 12 communities in the city were randomly selected (Li, et al., 2019). None of the participants were blinded to the cluster allocation; participants and recruiters knew they were being allocated and recruited to participate in the intervention or study cluster of the study. The researchers who analysed the data, however, were blinded to the groupings (Li, et al., 2019). It is unclear how participants were recruited in the trial; however, all community-dwelling participants who were diagnosed with TB according to the WHO 2010 guideline were invited to participate (Li, et al., 2019).

Types of participants of included studies

TB diagnosis:

Both studies included participants who were diagnosed with pulmonary TB.

- In (Zhang, *et al.,* 2021), it is not mentioned how the TB diagnosis was done or verified. It is only mentioned that people with TB registered and managed by eligible TB community centres (those with >50 people with TB in their registers) were included in the study. It is not mentioned what type of pulmonary TB participants had, if drug-susceptible or drug-resistant, or what was the stage of their treatment.
- In (Li, et al., 2019) it is mentioned that TB diagnosis was done according to the WHO 2010 guideline. It was not mentioned what type of pulmonary people with TB had, as in if they were drug-susceptible or drug-resistant. However, (Li, et al., 2019) recorded data on the phase of participants' TB treatment and it was recorded if people were in the initial stages of treatment or the intensive management phases, for both control and intervention clusters (Li, et al., 2019).

Depression diagnosis:

- In (Zhang, *et al.,* 2021) depression was assessed with the PHQ-9. People were eligible to participate in the intervention if they had an anxiety score ≥ 5 on the GAD scale or depression score ≥ 5 points in PHQ-9, as well as clear consciousness and were able to communicate normally. People who had other serious or comorbid

chronic diseases, were receiving treatment for psychological conditions, or refused to be assessed, were excluded. At baseline, the PHQ-9 scores in the intervention group were 8.13 ± 6.01; in the control group they were 8.00 ± 5.84.

- In (Li, et al., 2019) depression was assessed with the Zung self-rating depression scale (SDS). All eligible participants could receive the intervention, regardless of their depression symptom score at baseline. People who were unable to communicate normally, had cognitive impairment, or participated in other studies were excluded. At baseline, the SDS score in the intervention group was 59 ± 7.49; in the control group it was 57 ± 9.66.

Total number of participants included in the study:

- In (Zhang, *et al., 2021*) the initial number of participants randomised into control, or intervention groups was 461. The number of participants in each cluster in this study was similar (see table 3.1). Age was similar in the control and intervention groups for this study (see table 3.1). Gender proportions were also similar in the intervention and control groups. In the intervention group, 66.5% were male, and in the control group, 67.4% were male. Other relevant demographic characteristics collected in this study were years of education, body-mass index, smoking (cases, %), and alcohol use (cases, %).
- In (Li, *et al., 2019*) the initial number of participants randomised into control or intervention groups was 201. These participants consisted of people with TB of 65 years of age or older as this was the goal of their study. The number of participants in each cluster varied (see table 3.1). Age was similar in both clusters: 71.8 ± 5.5 in the intervention group, and 71.9 ± 5.4 in the control group (see table 3.1). There was a slightly higher proportion of males in the control group (61.4%) as compared to the intervention group (55.7%). Other relevant demographic characteristics were education level, occupation before TB diagnosis, comorbidities, and participants' TB-related knowledge.

Type of interventions of included studies

Both studies described the use of psychological interventions (cognitive-behavioural therapy-CBT) to improve depressive symptoms in people with TB (Li, et al., 2019; Zhang, et al., 2021). There were no co-interventions in any of the included studies.

- The study by (Zhang, *et al.,* 2021) used CBT as the psychological intervention. This study mentions that, prior to the delivery of the intervention to the participants, 20 community general practitioners (GPs) received 8 hours of training on cognitive behavioural therapy over 3 days. The content of the training included cognitive behavioural therapy skills, relaxation training, and supportive therapy skills. The number of participants that received the intervention was 233. The length of the intervention was 2 months, and each session lasted 40 minutes or more, but their frequency was not described. The delivery of the intervention was face-to-face, and the sessions were recorded by mobile phone and then analysed by the research team to ensure the integrity of delivery. The video recording was uploaded by the GP delivering the intervention and the research team would evaluate the fidelity by analysing the recording for every session. GPs also assigned homework to people after each session, and the homework would be discussed with the people at the beginning of the next session for 10-15 minutes.
- (Li, et al., 2019) described the psychological intervention they delivered to their participants as Morita therapy, which they described as a type of cognitive-behavioural therapy. Morita therapy is a psychological intervention developed by Shoma Morita in Japan, in the early 1900s. The therapy involves a structured programme of progressive exposure to external stimuli with the objective of increasing social function and promote acceptability, mainly used for treating anxiety and mental illness that included obsessive behaviours (He. And Li., 2007; Wu., et al., 2015). The number of participants who were randomised to the intervention group was 69, but the results report the data for 61 participants. 8 participants were not included in the data analysis due to attrition, poor adherence to the intervention, or death. The length of the study was 6 months, but the length of the intervention delivered to people is not reported, and it is unclear how many sessions people received. The sessions consisted of routine health education, psychotherapy, home visit, peer support, and psychoeducational workshops, twice a month, in a one-to-one setting. Each psychotherapy session lasted around 30 minutes. In the study, it is mentioned that sessions were delivered by trained therapists from the Tongji Research Centre of Mental Health. People were asked to complete a diary to help therapists assess the effect of the intervention. The researchers asked people about how the intervention was being delivered to ensure quality. In this study, it is mentioned that people also received home visits by community administrators and health workers, but the frequency and length of these visits were not reported.

Types of comparison interventions of included studies

Both studies compared the intervention with routine care (Li, *et al*., 2019; Zhang, *et al*., 2021).

- In (Zhang, *et al.,* 2021) routine care was described as TB treatment according to the requirements of the national directly observed treatment short course. 228 participants received the control intervention. In the control group, people were monitored daily by community GPs or nurses to consume their TB treatment.
- In (Li, et al., 2019) routine care was defined as routine health education. 132 participants were assigned to receive the control intervention. The study reports the outcome data for 122 participants. 10 participants' data were not included due to poor adherence, loss to follow-up, or death. The contents of routine health education included basic knowledge of TB, healthy diet, and lifestyle, as well as information on the treatment process and side effects of drugs. It also included psychological coping skills such as methods to overcome stigma.

Types of outcomes measured in included studies

Both studies measured improvement in depression symptom severity compared to baseline measurements in intervention and control groups. There was no missing outcome data for this outcome (we considered missing data to be missing at random).

<u>Improvement in depression symptom severity:</u>

- In (Zhang, *et al.,* 2021) the PHQ-9 was used to measure the symptoms at the end of the intervention. This scale has 9 items, and the scoring ranges between 0 and 27. According to the authors of the PHQ-9, a score of 0-4 meant no depression, 5-9 meant mild depression, 10-14 meant moderate depression, 15-19 meant moderately severe depression, and 20-27 meant severe depression. On this scale, the higher the score, the more severe the depression symptoms are. Measurements were taken at baseline and at the end of the intervention.
- In (Li, et al., 2019) the outcomes were changes in depression symptom scores, measured using the Zung self-rating depression scale. This scale has 20 items and people can be scored between 25 and 100. Each item is scored on a Likert-type scale of 1 to 4, where 1 means the item is present a little of the time, 2 means it is present some of the time, 3 means it is present a good part of the time, and 4 means it is present most of the time. The total score is calculated by adding up all the scores of all items and then multiplying by 1.25. A higher score means the depression

symptoms are more severe. In the analysis, outcomes are reported for 61 participants in the intervention group and 122 participants in the control group. Participants who died, dropped out, or had poor compliance were excluded from the analysis. Measurements were taken at baseline, first month, third month, and sixth month of the study. Outcomes were reported for all the time-point measurements for all groups using mean and standard deviations, as well as Cohen's d for effect size. Outcomes were also reported in multilevel analysis in which they constructed five models which accounted for group variables, the interaction effect between group and time, and other sociodemographic variables.

Improvement in anxiety symptom severity:

- In (Zhang, *et al.,* 2021) they also measured the changes in anxiety symptom severity using the GAD-7 scale, and the health-related quality of life using the SF-36 scale on the same groups of participants. In the analysis, people who were lost to follow-up or did not adhere to the intervention were excluded. The outcomes were reported for 230 participants in the intervention group and 224 participants in the control group. The outcomes were reported as the mean values and standard deviations for both groups and for both outcomes. Further analyses were performed to observe the changes in depression and anxiety scores in people according to the severity of their depression and anxiety symptoms at baseline. Measurements were taken at baseline and at the end of the intervention. The chi-squared test was also presented to account for comparisons between clusters; paired t-test was used to compare groups before and after the intervention, with a value of $p<0.05$ considered as being statistically significant.
- (Li, et al., 2019) also measured anxiety symptoms, using the Zung Self-rating Anxiety Scale. This scale has the same measurement properties as the SDS: the scale has 20 items and people can be scored between 25 and 100. Each item is scored on a Likert-type scale of 1 to 4, where 1 means the item is present a little of the time, 2 means it is present some of the time, 3 means it is present a good part of the time and 4 means it is present most of the time. The total score is calculated by adding up all the scores of all items and then multiplying by 1.25. A higher score means the anxiety symptoms are more severe. Measurements were taken at baseline, first month, third month, and sixth month of the study. Outcomes were reported for all the time-point measurements for all groups using mean and standard deviations, as well as Cohen's d for effect size. Outcomes were also reported in multilevel analysis in

which they constructed 5 models which accounted for group variables, the interaction effect between group and time, and other sociodemographic variables.

Loss to follow-up in the intervention groups:

Both studies recorded the number of loss of follow-up cases amongst intervention participants:

- In (Zhang, *et al.,* 2021) in the intervention group, 3 participants were lost to follow-up or had poor adherence to the intervention. In the control group, 4 participants were lost to follow-up or did not adhere to the intervention. Reasons for loss to follow-up were not reported for any of the cases.
- In (Li, et al., 2019) in the intervention group, 8 participants were lost to follow-up, dropped out, or died before the end of the study. In the control group, 10 participants dropped out, did not adhere, or died before the end of the study. The reasons for loss to follow-up were not discussed.

Adverse events:

None of the studies reported adverse effects as a result of the intervention.

3.3.3 Excluded studies

We, the two independent reviewers, excluded 10 articles after reviewing full texts. 1 record was not screened since we could not find the full-text version of it (Sun, et al., 2020); I contacted the authors of this study over email, sending a request for access once every month for three months but I did not receive a reply. We excluded 3 records due to ineligible study design (they were not RCTs) (Calligaro, et al., 2021; Kishimoto, 1967; Fossati, 1974). We excluded 2 records due to ineligible diagnostic criteria (did not refer to depression in people with TB but psychological distress or cognitive distortions); (Safa, et al., 2018; Tola, 2016). We excluded 3 records due to being trial entry registries (Alem and Hanlon 2019; Fox 2019; Safa, 2019), of which 2 were not carried out (Fox, 2019; Alem and Hanlon 2019) (for Alem and Hanlon 2019 this was confirmed by the study authors after the first time we contacted them by email) and 1 was linked to a study that was excluded due to ineligible diagnostic criteria (Safa, 2019). Finally, we excluded 1 record due to being an ineligible intervention (Khachadourian, et al., 2020) as it did not meet the criteria for pharmacological or psychological interventions as described in the inclusion criteria in our protocol. (See Figure 3.1).

3.3.4 Synthesis of results: Effects of interventions

I was able to conduct one meta-analysis for the comparison of psychological interventions versus no intervention or usual care. I was able to extract the data on the primary outcome of depressive symptoms for both studies. I assessed the outcomes at the end of the intervention periods.

Primary outcomes: Treatment effectiveness

Both studies were randomised at the cluster level (Li, *et al.,* 2019; Zhang, *et al.,* 2021). However, only one of them accounted for this level of randomization when reporting their results as a multilevel analysis (Li, *et al.,* 2019). The other study did not mention that this level of randomization was included in the analysis, so I assumed that the analysis of the results given in the paper had not accounted for the level of randomization (Zhang, *et al.,* 2021). As described in the "Methods" section, I used the inflated standard error method suggested in the Cochrane Handbook (Higgins, et al., 2019a): I multiplied the standard error of the effect estimate from the analyses (ignoring clustering) by the square root of the design effect.

The two studies varied in terms of the endpoints at which they measured the end of the intervention. In one study, outcomes were measured at baseline, 1 month, 3rd month and 6th month (Li, *et al.,* 2019). In the other study, outcomes were measured at baseline and 1 month (Zhang, *et al.,* 2021). I took the measurements at the end of the intervention as described in the study as we wanted to compare the effect of the full intervention. This means I took the measurements taken at 6^{th} month in (Li, *et al.,* 2019) and the 1^{st} month in (Zhang, *et al.,* 2021) as stated in the protocol.

Both studies reported improvements in depression symptoms in intervention groups. There was a greater reduction in the severity of depression symptoms compared to no-intervention or routine care (SMD -0.29, 95% CI -0.45 to -0.13). The SMD is considered to be a small effect, but the lower limit of the confidence interval might lie close to a moderate effect (Schünemann, et al., 2022). I also observed that the CI around the SMD is large. I reinterpreted the results in terms of the most familiar scale used in the studies, which we decided to be the PHQ-9 as it is one of the suggested scales for assessing depression by the WHO. To reinterpret the results in values of the PHQ-9 scale, I calculated the absolute difference in means by multiplying the SMD by the SD calculated with the inflated SE (which adjusted for the unit of analysis issue in the cRCTs). This yielded a result of -1.12 points in

the PHQ9 scale in the intervention groups in both studies. See Figure 3.2 for the meta-analysis of these results.

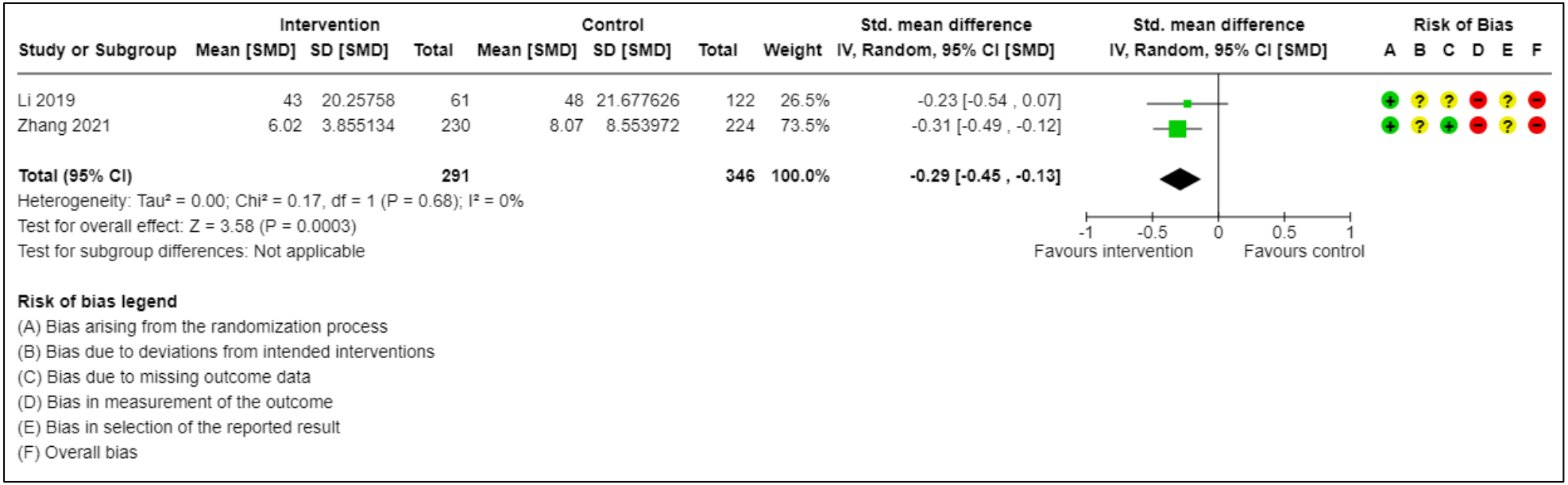

Figure 3.2 Treatment effectiveness on depression symptom severity. Intervention (psychological interventions) vs no-intervention or usual care; using standard error

Secondary outcomes: Health-related quality of life

I was unable to conduct a meta-analysis on the secondary outcomes as this was not measured in all included studies. Only one study assessed health-related quality of life as an outcome so I could not pool results for this outcome. (Zhang, *et al.,* 2021) reported the changes in the health-related quality of life of participants using the Short-Form Health Survey 36 items (SF-36). They reported data on the changes in health-related quality of life of people with TB who received the intervention vs usual care. The scores of the SF-36 scale before and after the intervention for the intervention group were (58.46±12.71) and (74.31±13.22) points. For the control group, the scores before and after intervention were (59.11±13.25) and (60.51±13.76) points, respectively. There was no significant difference in the SF-36 scores in both groups before the intervention (t=0.533, P=0.59). After the intervention, the SF-36 score of the intervention group was higher than that of the control group (t=10.898, P<0.01) and higher than before the intervention (t=13.108, P<0.01). The SF-36 of the control groups showed no significant difference before and after the intervention (t=1.104, P=0.27). With this information, I calculated the SMD and 95%CI using alpha=0.025, assuming a normal distribution. The results were SMD = 1.02, 95% CI (0.83, 1.22). See Figure 3.3.

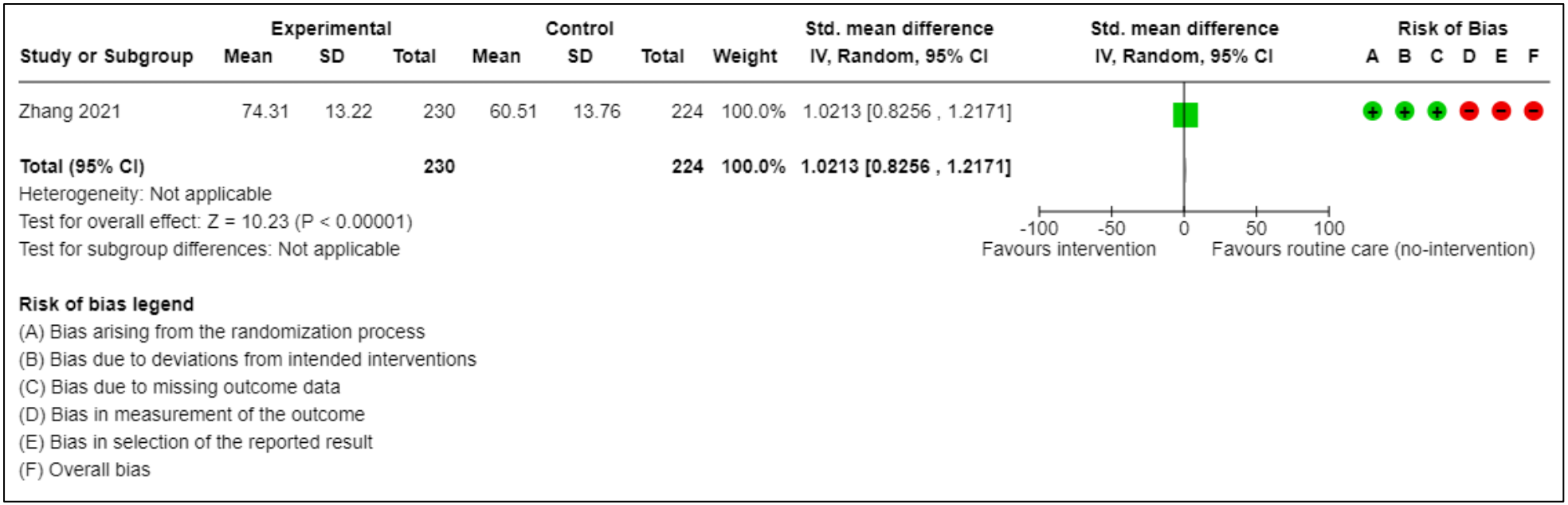

Figure 3.3 Treatment effectiveness on health-related quality of life. Intervention (psychological interventions) vs no-intervention or usual care; using standard mean difference

No studies assessed any of the other outcomes.

I could not conduct the other comparisons we had planned in the protocol (pharmacological interventions versus placebo, no intervention or usual care; and psychological and pharmacological interventions versus placebo, no intervention or usual care) as none of the included studies evaluated the effectiveness of pharmacological or combined interventions. See section 3.4.3 Differences between protocol and review.

3.3.5 Risk of bias in included studies

Me and a second reviewer assessed the risk of bias independently for each of the two outcomes described in the previous section, according to the guidelines specified in the Cochrane Handbook for Systematic Reviews of Interventions for assessing bias in variants on randomised trials (Higgins, et al., 2018c; Page, Higgins, & Sterne, 2020). Figure 3.4 shows a summary of the risk of bias score per domain, for each outcome and each study. The risk of bias per outcome is also displayed in the forest plot for the respective outcome.

Outcome	Treatment effectiveness on depression symptom severity		Treatment effectiveness on health-related quality of life	
Study / **Risk of bias domains:**	Li	Zhang	Li	Zhang
Bias arising from the randomization process			n/a	
Bias due to deviations from intended interventions			n/a	
Bias due to missing outcome data			n/a	
Bias in measurement of the outcome			n/a	
Bias in selection of the reported result			n/a	
Overall bias			n/a	

Legend:

 Low risk of bias

 Some concerns

 High risk of bias

Figure 3.4 Risk of bias assessment for studies included in the review for each outcome.

Below is a description of the rationale for the decisions made for assigning risk of bias scores per each risk of bias category, for each outcome, and for each study.

For outcome "Treatment effectiveness on symptom severity":

- **Bias arising from the randomization process:** For both studies, I considered there to be a low risk of bias for this outcome.
    - (Li, *et al.,* 2019): according to trial registry (although registration was retrospective), "randomization was performed by using a list of random numbers and a sealed envelope method."
    - (Zhang, *et al.,* 2021): The way that clusters were assigned to intervention and control groups was random. This allocation was done before the assignment and recruitment of participants to each cluster. There were not

any baseline imbalances between clusters that were reported by the authors or observed by the reviewer.

- **Bias due to deviations from intended interventions:** For both studies there was an unclear risk of bias for this domain.
    - (Li, *et al.,* 2019): it is unclear if participants were aware they were on a trial, but they were aware they were in a study. “Elderly people with TB and intervention executors, who implemented the intervention, including psychologists, community health workers, and recovered people with TB, were not blinded to the study group.”
    - (Zhang, *et al.,* 2021): There is no information about whether participants knew they were in a study or in a trial. It is unclear whether participants knew they were part of a study and therefore receiving an intervention. However, since the comparison was with routine or usual care, it is possible that they were aware that the care they were receiving was different from that routinely offered and should have signed a participant consent form that provides information on the study. Carers were aware that they were delivering the intervention as they explicitly received training to deliver it and were recorded for consistency and adherence to the intervention protocols. Researchers reported that in the majority of cases, carers delivered the intervention as intended. Individuals were analysed according to the intervention they were assigned to.

- **Bias due to missing outcome data:**
    - (Li, *et al.,* 2019): in one cluster, a significant number of participants were excluded from the analysis (8 out of 69 due to follow-up. In the second cluster, this was not too significant (10 out of 132).
    - (Zhang, *et al.,* 2021): There was little loss to follow-up in both clusters. Data was available for almost all participants in both clusters (230 of 233 in intervention group; 224 of 228 in control group).

- **Bias in measurement of the outcome:**
    - (Li, *et al.,* 2019): Same method for measuring outcomes was used for both clusters and it is a validated tool for measuring the outcome of interest in this study. people with TB, who were the assessors in this outcome, were aware that a study was taking place, but it is unclear if they were aware that this

was a trial. Outcome assessors were people with TB who were not blinded to the intervention they received. It is possible that people' and providers' beliefs and knowledge about the intervention could have influenced the outcome assessment as it was a self-reporting measurement tool.

- (Zhang, *et al.,* 2021): The tools to measure outcomes have been validated and were consistently used at all measurement points during the trial. For all participants, the same baseline and post-intervention measurements were carried out. Outcome assessors were the participants in this study, and it is possible that they were aware they were receiving an intervention. Participants of a study might have had knowledge or beliefs about the intervention that influenced their outcome assessment.

- **Bias in selection of the reported result:**
  - (Li, *et al.,* 2019): The outcomes that were reported in this study are different to those that were reported in the published trial protocol. However, it is mentioned that the people who analysed the data for this outcome were blinded. There is no information of this outcome and its measurement in the published trial protocol (Li, et al., 2018).
  - (Zhang, *et al.,* 2021): The trial was registered retrospectively but there was no analysis plan published in a protocol before this study was carried out even though there is reference in the text to a published research protocol, to my knowledge.

- **Overall bias for this outcome:**
  - (Li, et al., 2019): We considered this study has a high risk of bias for this outcome.
  - (Zhang, et al., 2021): We considered this study has a high risk of bias for this outcome.

For outcome "Treatment effectiveness on health-related quality of life":

- **Bias arising from the randomization process:** In (Zhang, *et al.,* 2021), we assumed that participants were aware they were part of a study when they had to agree to participate in the study and sign consent forms. Participants were aware of the intervention they received during the trial.
- **Bias due to deviations from intended interventions:** In (Zhang, *et al.,* 2021), the participants were the outcome assessors. The same outcome measurement was

used between intervention and control clusters. It is possible participants knew they were receiving an intervention.

- **Bias due to missing outcome data:** In (Zhang, *et al.,* 2021), there were similar attrition levels in both clusters, and these were adequately reported.
- **Bias in measurement of the outcome:** In (Zhang, et al., 2021) outcome assessors were the participants in this study, and it is possible that they were aware they were receiving an intervention. Participants of a study might have had knowledge or beliefs about the intervention that influenced their outcome assessment. We considered this was a high risk of bias for this outcome.
- **Bias in selection of the reported result:** In (Zhang, *et al.,* 2021): the trial was registered retrospectively and there is no pre-specified analysis plan that these results can be compared to. I consider it significant that these results might not have been published if they had not been found relevant by the authors of the study, which is a bias in the selection of reported results towards reporting results which favour intervention.
- **Overall bias for this outcome:** (Zhang, *et al.,* 2021): We consider this study has a high risk of bias for this outcome.

3.3.6 GRADE

I used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to assess the level of confidence I had in the results. I assessed my confidence level for both outcomes included in this review: treatment effectiveness on depression symptom severity, and changes in health-related quality of life. For each outcome, I analysed the factors that can limit the quality of evidence according to the GRADE handbook: limitation in study design or execution, inconsistency of results, indirectness of evidence, imprecision, and publication bias (Schunemann, et al., 2013). I created a Summary of findings table to record the decisions made (Table 3.2). Summary of findings tables are a core part of all Cochrane systematic reviews. These tables are used to provide key information about the magnitudes of observed effects of the interventions examined, and the amount and quality of the available evidence for assessing that outcome (Schünemann, *et al.,* 2020). I created the summary of findings table in line with the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions (Schünemann, *et al.,* 2020). I created it using the GradePRO GDT software (GRADEpro GDT, 2015). Table 3.2 presents data on absolute or relative effects with 95% CI, risk for treatment and for usual care, the number of participants and studies for each outcome, and the quality assessment of the evidence, using the GRADE approach for each outcome.

When certainty on the quality of evidence was downgraded, I explained the reasons for the decision in the footnotes.

Summary of findings:

Cognitive behavioural therapy vs routine care for depression in people with tuberculosis

Patient or population: Depression in people with tuberculosis
Setting: Community-based health centres
Intervention: Cognitive behavioural therapy
Comparison: Routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Routine care	**Risk with Cognitive behavioural therapy**				
Treatment effectiveness (Improvement in depression symptoms) assessed with: Patient Health Questionnaire 9-items and Zung self-rating depression scale follow-up: range 1 months to 6 months	-	SMD **0.29 SD lower** (0.45 lower to 0.13 lower)	-	637 (2 RCTs)	⊕⊕◯◯ Low[a,b]	The evidence suggests that cognitive behavioural therapy results in little to no difference in treatment effectiveness for depression symptoms. We downgraded the certainty of evidence based on serious risk of bias and serious imprecision.[a,b]

Summary of findings:

Cognitive behavioural therapy vs routine care for depression in people with tuberculosis

Patient or population: Depression in people with tuberculosis
Setting: Community-based health centres
Intervention: Cognitive behavioural therapy
Comparison: Routine care

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Routine care	**Risk with Cognitive behavioural therapy**				
Adverse events (for all forms of TB) – not measured	-	-	-	-	-	

Summary of findings:

Cognitive behavioural therapy vs routine care for depression in people with tuberculosis

Patient or population: Depression in people with tuberculosis
Setting: Community-based health centres
Intervention: Cognitive behavioural therapy
Comparison: Routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Routine care	**Risk with Cognitive behavioural therapy**				
Changes in health-related quality of life assessed with: Short-Form 36 item questionnaire Scale from: 0 to 100 (better) follow-up: range 1 months to 2 months	-	SMD **1.023 SD higher** (2.442 higher to 0.395 lower)	-	454 (1 RCT)	⊕◯◯◯ Very low[a,b,c]	The evidence is very uncertain about the effect of cognitive behavioural therapy on changes in health-related quality of life for people with TB. We downgraded the certainty of evidence based on a very serious risk of bias and serious imprecision.[a,b,c]

Summary of findings:

Cognitive behavioural therapy vs routine care for depression in people with tuberculosis

Patient or population: Depression in people with tuberculosis
Setting: Community-based health centres
Intervention: Cognitive behavioural therapy
Comparison: Routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Routine care	**Risk with Cognitive behavioural therapy**				
Effect on TB – not measured	-	-	-	-	-	[d]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **SMD:** standardised mean difference

Summary of findings:

Cognitive behavioural therapy vs routine care for depression in people with tuberculosis

Patient or population: Depression in people with tuberculosis

Setting: Community-based health centres

Intervention: Cognitive behavioural therapy

Comparison: Routine care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Routine care	**Risk with Cognitive behavioural therapy**				

GRADE Working Group grades of evidence

High certainty: *we are very confident that the true effect lies close to that of the estimate of the effect.*

Moderate certainty: *we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.*

Low certainty: *our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.*

Very low certainty: *we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.*

Explanations

[a] As this was a cluster-randomized trial, there was no allocation blinding for participants and personnel. There was no blinding of outcome assessment (as it was self-assessed by participants). Statisticians who assessed the data were blinded. We considered this as a reason to downgrade based on the Risk of bias GRADE domain.

[b] At least in one study, the CI crosses the line of no effect. Thus, we decided there could be some imprecision in the evidence even when the number of participants met the criteria for optimal information size (>300 events or measurements, as described in the handbook). We considered this as a reason to downgrade based on the “Imprecision” domain.

[c] It is unclear if the results published in Zhang *et al.,* for the measurement of quality of life in participants before and after the intervention account for the clustering effect, which is a unit of analysis issue. We considered this as a reason for downgrading the certainty of evidence based on the “Imprecision” domain.

[d] Effect on TB refers to the following outcomes: Adverse events for all forms of TB, self-reported and diagnosed, TB treatment success (cured), TB treatment failure, TB treatment completion, and loss to follow-up. None of these outcomes were measured.

Table 3.2 Summary of findings table (GRADE)

3.4 Discussion

This review aimed to assess the treatment effectiveness of psychological and pharmacological interventions for depression in people with TB.

3.4.1 Summary of main results

I systematically reviewed the literature to assess the effectiveness of psychological and pharmacological interventions for depression treatment in people with TB. The findings of this review are based on two cluster RCTs involving a total of 637 participants. In both studies, the intervention was cognitive behavioural therapy (CBT; including Morita therapy), the population was people with TB, the setting was community-based health centres, the comparison was routine care for TB, and the primary outcome measured was the change in depression symptom severity between baseline and different endpoints (Li, *et al.,* 2019; Zhang, *et al.,* 2021). The details of the included studies are described in Table 3.1. Both studies contributed data to the comparison. Pooled analysis of the studies (N=637) showed a small effect in favour of the intervention for improving depression in people with TB when compared to a pre-intervention or baseline assessment. The quality of evidence for this outcome was graded as low.

As for the secondary outcome, only one study reported the changes in health-related quality of life of participants using the Short-Form Health Survey 36 items (Zhang, *et al.,* 2021). The quality of evidence for this outcome was rated as very low. The 95% CI of this outcome is very wide, and it crosses the line of no effect, meaning there is little knowledge about the effect and this imprecision affects the certainty in the evidence presented here. More information would be needed, such as drawing from other cRCTs measuring this outcome, with a large sample size (>300) before it is possible draw a more certain conclusion from this analysis (Schünemann, et al., 2022).

3.4.2 Strengths and limitations of the review

Overall completeness and applicability of evidence

The evidence base for the use of psychological and pharmacological interventions for the treatment of depression in people with TB is small. Notably, there is a lack of trial designs that research pharmacological interventions for depression and their effects on depression symptoms in people with TB. This comprehensive search identified only two RCTs that met our eligibility criteria and were included in this review. Both included studies were conducted in China, which we consider might influence on the applicability of evidence to populations in

other countries given the prevalence of important comorbidities in the region, such as HIV, and the prevalence of drug-resistant TB (WHO, 2021).

There are additional considerations regarding the methods used in the included studies. The inclusion of one study (Li, *et al.,* 2019) that focused solely on a particular age in people with TB (>65 years of age) might influence the effect size as this particular population may have mental health needs different from those of other age groups (Wilkinson & Izmeth, 2016). Additionally, the mental health needs of people with TB can vary depending on the strain of TB they have and the treatment they receive for it (Dartois & Rubin 2022). As none of the studies included this information for their participants, I think that these results should be interpreted carefully and in accordance with current guidelines for TB treatment for drug-susceptible and for drug-resistant strains (Dartois & Rubin 2022; Sweetland, et al., 2017).

Considering the small number of studies included in the main comparison, the lack of representation from different countries, and the lack of data for the participants' type of TB, I consider the overall completeness and applicability of the evidence found in this review to be poor.

Quality of the evidence

I identified potential concerns related to the lack of allocation concealment, and the lack of blinding of participants and providers, which are two separate domains of bias, as a source of risk of bias. However, I am aware that this is a risk inherent to the randomised design of the studies included in this review (Juul, et al., 2021). Moreover, it is widely considered that psychological interventions such as CBT cannot blind participants and providers from receiving, providing, and assessing the outcome (when the outcome is self-assessed by participants), which can lead to an overestimation of the effect (Savovic, et al., 2015). In both trials, it is mentioned that the people involved in the data analysis were blinded to the groupings.

Furthermore, the effect of psychological interventions may be tied to the competency of the provider. I did not explore this as it is outside the scope of this review, but it is an important point to raise as both studies that were included in this review used psychological interventions delivered by providers trained purposely to deliver the interventions (Li, *et al.,* 2019; Zhang, *et al.,* 2021). The effect of psychological interventions on people with mental health illnesses can be affected by the competency of the provider and the fidelity with which the intervention is delivered (Valenstein-Mah, et al., 2020). This raises issues about whether a similar effect would be observable in populations that receive the intervention by untrained staff, specialist staff, or any other type of provider.

Potential biases in the review process

I minimised selection bias by following the Cochrane guidelines for systematic reviews. These steps included conducting an extensive literature search using a wide range of search terms and databases, two authors independently assessing the titles and abstracts of the search results to evaluate eligibility according to pre-specified criteria published in the protocol. However, I acknowledge that our decision to limit the eligibility criteria to studies reporting the outcomes of interest for our study may have resulted in omitting relevant studies. I do not suspect that inadequate searches may have biased the results, but it is difficult to rule out if there are any additional studies relevant to our review which may have impacted on our conclusions, and which were published after the searches were carried out. I could not examine funnel plots given the small number of studies included in the analysis.

Agreements and disagreements with other studies or reviews

This is the first full systematic review of interventions used to treat depression in people with TB. The results of this review and meta-analysis reflect the paucity of evidence there is on the effectiveness of interventions for depression in people with TB. Other systematic reviews have explored the use of interventions to treat common mental disorders in people with TB but have only produced a narrative synthesis of the evidence (Farooq, Tunmore, and Comber, 2021; Van Rensburg, et al., 2020).

Other reviews have focused on assessing the effectiveness of different types of pharmacological and/or psychological therapies for adults with depression (Cuijpers, et al., 2020). Recently, it was established that the effect of CBT and other psychotherapies compared to waiting lists was 0.79; 95% CI: 0.70-0.89, for a sample size of 52,702 people (409 trials) with depression of different ages (40.1 ± 15.0; mean, SD), countries (mostly US, Western Europe, and UK), and receiving different number of sessions in diverse clinical or community settings (Cuijpers, et al., 2023a).This is very robust evidence showing that psychological therapies have a positive impact on people with depression, across different settings. The positive effects of psychotherapies on depression can also be observed in people with comorbid mental health illnesses, such as anxiety, insomnia, and substance use (Cuijpers, et al., 2023b). In people with chronic conditions such as cancer, HIV, renal disease, cardiovascular disease, and type 2 diabetes, a moderate effect of 0.61 (95% CI: 0.49, 0.73) was observed in people receiving CBT compared to care as usual or control groups (Scott, et al., 2023).

Our review is the first to focus on depression and the first to include only RCTs. Overall, the findings in this review reflect the potential benefits of using psychological interventions to

treat depression symptoms in people with TB found in other reviews (Farooq, Tunmore, and Comber, 2021). Future research is needed to explore further the effects of different types of interventions for depression symptoms in people with different types of TB.

3.4.3 Differences between protocol and review

Assessment of reporting biases

In the protocol I wrote "*Use of funnel plot to assess bias in reporting of effects when 10 or more studies report on the same outcome of interest*". In this study it was not possible, as only two studies included in meta-analysis.

Data synthesis

Subgroup analysis

None of the sub-group analyses I planned in the protocol were possible for the following reasons:

- Type of TB: Not possible because none of the included studies disclose the type of TB of the people included in the analysis.
- Age and gender: Only narratively. A quantitative analysis was not possible because studies were not similar enough in terms of age distribution (one study was exclusively aimed at people >65 and the mean age in the other study was 41). In terms of gender, none of the studies disaggregated treatment effect measurements by gender.
- Intervention duration: Not possible as only two studies were included in this review.
- Length of follow-up: Not possible because none of the interventions reported on follow-up of the intervention outcomes after the intervention ended.
- Risk of bias: Not possible because both studies scored high on the risk of bias assessment.
- Presence of other comorbidities: Possible. Data on anxiety as a comorbidity was reported in both studies. However, due to the presentation of data in the published studies, we could not disaggregate the comorbidity data for its analysis.
- Severity of depression: Not possible because none of the studies disaggregated data by severity of depression of participants, nor was this data available at baseline for one study.

Sensitivity analysis:

None of the sensitivity analysis I planned in the protocol were possible for the following reasons:

- “Effect of trial size”: Not possible as none of the studies had a sample size smaller than 50 participants.
- “Effect of choosing the most prevalent measurement scale*”:* Not possible as the two eligible studies used a different scale to measure treatment effect.

3.5 Conclusions

The findings of this review are based on two cRCTs that assessed the effectiveness of psychological interventions for depression in people with TB. The findings from the meta-analysis suggest a small effect and the grading of our confidence in the quality of the evidence was low. Thus, we consider that CBT as a psychological intervention for depression in people with TB may result in a moderate beneficial effect in the severity of depression symptoms experienced by people with TB during treatment. This conclusion is based on the efficacy of CBT, a psychological therapy, as a therapeutic intervention for 52,702 people across different ages, intervention groups, and settings (Cuijpers, et al.,2023a; Cuijpers, et al., 2023b; Scott, et al., 2023).However, my findings also show that there is a need for high-quality randomised trials conducted in a variety of contexts that assess the effectiveness of interventions for depression in people with TB given the unique characteristics of this population in terms of TB treatment, anti-TB drugs side-effects, and other risk factors for ill mental health.

3.5.1 Implications for practice

The literature indicates that depression is a common comorbidity in people with TB. The role of depression in other comorbidities can worsen symptoms and prognosis. It is important to prevent and treat depression in people with tuberculosis. This review indicates that psychological treatment of depression for people with TB can improve the severity of their depression symptoms. It is unknown, however, what impact it will have on TB-related outcomes such as self-reported and diagnosed adverse events, TB treatment failure, cure, completion, loss to follow-up, relapse, or death.

3.5.2 Implications for research

Although the included studies had a high risk of bias due to inadequate concealment of providers and participants. I acknowledge that allocation concealment can be hard to avoid in the case of psychological interventions, but it can be possible to attain it - I also acknowledge that blinding, in the case of psychological interventions, is not always feasible.

However, there are other considerations that researchers in this area should consider for future research:

- Future studies should report the type of TB that participants in their trials experience and, where possible, disaggregate results by the type of TB in participants. When possible, studies should also report the stage of TB treatment the participants are in (initial phase, follow-up, reincidence). Future studies could also provide more detailed information on the severity of depression at baseline of included participants and disaggregate results according to symptom severity.
- In the future, studies could elaborate further on the length, dose, and frequency of the (sessions of) psychological interventions delivered. Future studies could also explore the role of other types of treatment for depression, such as pharmacological interventions, or pharmacological combined with psychological interventions.
- Future studies assessing the treatment effectiveness of depression in people with TB should report the TB treatment outcomes for the people enrolled in the trial, as well as provide more detail regarding the loss to follow-up and mortality that occur during the study. Future studies should also include the measurement of health-related quality of life in participants.
- Finally, future studies should focus on the perspectives of health systems and providers to explore the feasibility and sustainability of the delivery of interventions for depression in people with TB.

Chapter 4 - Approaches to deliver depression care and understanding barriers and facilitators to implementation in people with TB in LMICs: a systematic review.

Chapter Summary

In Chapter 2, I described the rationale for researching the approaches used to treat depression in people with TB. In Chapter 3, I described a systematic review that evaluated current peer-reviewed literature on the effectiveness of treatment for depression in people with TB. In this Chapter, I describe a systematic review that explored the barriers and facilitators in delivering depression care in people with TB in low- and middle-income countries (LMICs).

4.1 Introduction

There is strong support within global guidelines for person-centred approaches to TB care (TB CARE I, 2014; WHO, 2021; Global Fund, 2019), which include addressing the psychosocial aspects of TB. Providing depression care in TB services would be an opportunity to deliver a more person-centred approach to TB care and address the psychosocial and mental health needs of people with TB.

However, depression is not routinely diagnosed or treated as part of TB services in low- and middle-income countries (LMICs). Despite global policy support for person-centred approaches, there is little guidance on how to implement them into current practice. Understanding how to improve the management of comorbid depression as part of routine TB services is important, particularly for LMICs where the provision of mental health services is already significantly constrained (Rathod, *et al.,* 2017). There have been some attempts in some LMICs to provide depression care for people with TB, but these have not been systematically documented or analysed.

4.1.1 Aims and objectives of this review

In this review I aimed to explore the approaches that had been used in low- and middle-income countries (LMICs) to deliver depression care as part of TB services, and to understand the barriers and facilitators in their implementation.

4.2 Methods

4.2.1 Protocol and registration

I registered the protocol of this review with PROSPERO under registration number: CRD42020201095 (Nava-Ruelas, *et al.,* 2020).

4.2.2 Eligibility criteria

Inclusion criteria are described in Table 4.1. I included studies conducted in LMICs, according to the World Bank classification at the time of the searches, in primary, secondary, or tertiary care, with the following characteristics:

Criteria	Description
Population	I included studies addressing anxiety and depression (anxiety is a common comorbidity for depressive disorders and anxiety symptoms are commonly part of the presentation in depressive disorders) in people with TB, or attending TB services, in LMICs. Studies aimed at people attending TB services in LMIC with pulmonary (latent, drug-susceptible, or drug-resistant) TB and symptoms (or a diagnosis) of depressive disorder were included. For the purpose of this review, TB was defined as symptoms or signs suggestive of TB or confirmed laboratory or clinical diagnosis of TB.
Intervention	I included studies describing approaches or arrangements for delivering services for depression as part of, alongside, or coordinated or integrated with services, public and/or private, for pulmonary TB that have been implemented in LMICs. For the purpose of this review, integrated approaches were defined as: A process that brings together one or more of funding, administrative, organisational, service delivery, and clinical sectors to deliver benefits to people (Kodner & Spreeuwenberg, 2002) or any management or operational changes implemented in health systems that bring together or coordinate inputs, delivery, management or organisation of services and functions, with the goal of improving quality, access, coverage, acceptability, or cost-effectiveness of care (Chuah, *et al.,* 2017).
Comparator	I did not exclude any studies based on the type of comparator, or the absence of one.

Criteria	Description
Outcome	I did not exclude any studies based on the type of outcome they measured.
Study design	I included any type of study that described or evaluated an attempt to, or experience of, implementing an approach to deliver depression care as part of existing TB services in LMICs. Studies consisting of primary research, secondary data analysis, or reviews were eligible for inclusion.

Table 4.1 Inclusion criteria

4.2.3 Search strategy

I designed and carried out the searches with the advice from the librarian of the Health Sciences Department at the University of York from 05th June 2020 – 3rd July 2020. I searched ten peer-reviewed and grey literature electronic databases from inception:

- Medline
- PsycINFO
- EMBASE
- Scopus
- PubMed
- Web of Science
- Cochrane Library
- Health Management Information Consortium
- Scientific Electronic Library Online (SciELO)
- Latin American and Caribbean Health Sciences Literature (LILACS)

I also searched websites of relevant organisations (World Bank, Global Fund to fight AIDS, Tuberculosis and Malaria, and World Health Organisation) using the Google Advanced Search feature. I considered these organisations important as they are major stakeholders in the delivery and funding of TB services in LMICs (Bowser, *et al.,* 2014). I also hand-searched the references list of included studies to identify other relevant studies. An example of the search strategy used across databases is included in Appendix 2.

4.2.4 Data extraction

I collaborated with a post-doctoral researcher in the Health Sciences Department at the University of York, and we acted as the two independent reviewers for this study. Both of us participated in the screening and data extraction process. We used Rayyan software for the title and abstract screening phases (Ouzzani, *et al.,* 2016). We resolved disagreements through consensus and discussion before proceeding to the next stage. We both screened

the full texts of eligible studies independently. For the data extraction, I extracted the data of included studies, and the second reviewer cross-checked the data extracted against the original study to ensure consistency and reliability for two studies.

Quantitative and qualitative data was extracted from the results and discussion sections of the included studies (see Appendix 3). I extracted the description of the study design, the type of intervention, and the implementation process from the background and methods sections of included studies. From qualitative studies, or studies with qualitative components, I extracted the narrative descriptions of the intervention, such as number and type of study participants, therapeutic strategies, thematic content of sessions, narrative descriptions of participants' responses to the interventions, interview responses, and other excerpts verbatim from the article. From quantitative studies, or studies with quantitative components, I extracted narrative descriptions of the intervention and participants' experiences (if available), numeric data on the type and number of participants, number of participants who received (or not) the intervention, number of participants who received training (if applicable), number of participants who adhered (or not) to the intervention, depression scores at baseline, depressions scores at end of intervention, number of deaths, descriptive statistics about the characteristics of participants, descriptive statistics about process outcomes (e.g., number and type of intervention delivered, enrolment rate), and descriptive statistics about clinical outcomes (e.g. depression scores, TB treatment outcomes, lost to follow-up rates). From mixed methods studies, I extracted both quantitative and qualitative data. A detailed description of the qualitative and quantitative data I extracted from each study is available in Appendix 3.

To describe the interventions implemented, I used the description as it was stated in the included studies (see Table 4.2; further descriptive information of the interventions and their implementation is described in Table 4.4). After this, I classified them according to the main categories of interventions used for depression, according to the NICE guidelines (NICE, 2022), and based on the descriptions provided in the studies. I created four intervention categories based on the descriptions provided (*i)* psychological-only, (*ii*) combined, (*iii*) combined, with socioeconomic support, and (*iv*) screening-only. I defined psychological-only interventions as any type of group or individual therapy used to treat mental health conditions, such as depression, anxiety, or psychosis (e.g., behavioural therapy, interpersonal therapy, cognitive behavioural therapy, psychodynamic therapies, family therapy). I defined combined interventions as psychological and pharmacological interventions delivered simultaneously to the patient. I defined combined interventions with socioeconomic support as combined interventions provided alongside any form of support that aimed to address socioeconomic needs in people with TB. I defined screening-only

interventions as screening for mental health conditions, followed by referral to mental health services outside TB services, if needed.

4.2.5 Data synthesis

I coded quantitative and qualitative data from all studies under the Consolidated Framework for Implementation Research (CFIR). This framework was chosen for analysis given its appropriateness to explore the facilitators and barriers for implementing diverse types of interventions (Damschroder, Reardon, & Lowery, 2020). This framework encompasses five main domains (**Intervention Characteristics, Inner Setting, Outer Setting, Characteristics of Individuals involved,** and **Process**), divided into 26 sub-domains.

After extracting data from the eligible studies, I converted quantitative data, (e.g., frequency tables, forest plots, ratios, number of participants who received (or not) the intervention) to qualitative data by creating narrative descriptions of quantitative data and results. This process of qualitizing data is used in mixed methods literature reviews to synthesize diverse types of evidence (Heyvaert, Hannes, & Onghena, 2017; Pope, Mays, & Popay, 2007). I coded the narrative descriptions of quantitative data along with qualitative data. I used an analytical approach that was based on the framework method (Gale, *et al.,* 2013): I treated all data as primary qualitative data and coded this information in each study as barriers or facilitators. To create framework matrices, I used the CFIR domains and their sub-domains as *a priori* coding framework, with the domains and sub-domains organised in columns while the different intervention categories were organised in rows. The data in each cell were verbatim extracts of qualitative data or narrative descriptions of quantitative results from the included studies. For the purposes of this review, I defined the **Inner setting** as the TB national services and/or where healthcare delivery for TB was routinely provided. I defined the **Outer Setting** as other governmental or private healthcare services provided within the country, or any other national and international institutions collaborating with TB national services.

The CFIR rating rules describe that the coding process should consider the positive or negative influence that coded data have on implementation, and how weak or strong that influence is on implementation (Damschroder, Reardon, & Lowery, 2020; CFIR, 2020). To determine valence, a rating of '*X,' '0', '+'*, or *'-'* is assigned to the coded data. These symbols mean that the coded data had a mixed (positive and negative), null, positive, or negative influence on implementation, respectively. To determine strength, a rating of '*1*' or '*2*' is assigned to the coded data. A notation of '*1'* means that the coded data had weak influence on implementation while '*2'* means its influence was stronger. To determine the valence of the influence, I considered how many times the narrative data was mentioned in the study,

the adjectives used to describe the influence of a sub-domain (e.g. ‘very strong’, ‘very important’, ‘not strong’, ‘not important’), and whether the influence it had on implementation was negative, positive or mixed. I adapted the CFIR domains and sub-domains definitions to the research objectives of the study. I used the definitions provided in the handbook and the website and then re-interpreted them according to their relevance to TB services and mental health interventions (see Table 4.5).

4.2.6 Quality assessment

I used the Mixed Methods Appraisal Tool (MMAT) to appraise quality of eligible studies (Hong, *et al.,* 2018). I used this tool anticipating that included studies could vary methodologically and could be qualitative, quantitative or mixed-methods studies. The advantage of the MMAT tool is that it provides a framework to assess that qualitative, quantitative, and mixed-methods studies following a minimum set of quality criteria for methodological design (Heyvaert, Hannes, & Onghena, 2017). This tool was developed in response to the inclusion of different types of evidence into systematic reviews for health services research (Pluye, *et al.,* 2009). This facilitates their integration into systematic reviews as it allows the comparison of overall quality between different methodological study designs according to the quality criteria they have met, although in this review no studies were excluded based on their quality criteria.

4.3 Results

4.3.1 Search results

Figure 4.1 describes the selection process for the retrieved records using PRISMA standards (Page, et al., 2021). The total number of records I retrieved from the electronic database and website searches was 10,982. After deduplication (Bramer, *et al.,* 2016), I worked with a second reviewer to independently screen the titles and abstracts of 8,858 records.

We included 39 articles in the full text screening phase. At this stage, eleven articles were excluded because they were based in high-income countries, mostly the US. One study was excluded because it did not include people with pulmonary TB. Two studies were excluded because they were prevalence studies. Five studies were excluded because they were discussion papers or reports. Eight studies were excluded because they did not describe interventions to treat depression – they focused on adherence or psychosis without depression as a comorbidity. Two articles were excluded because it was not possible for me to establish contact with the authors or national libraries in Brazil and Bolivia to access the

full texts. I described the full list of references for excluded studies and their reasons for exclusion in Appendix 4.

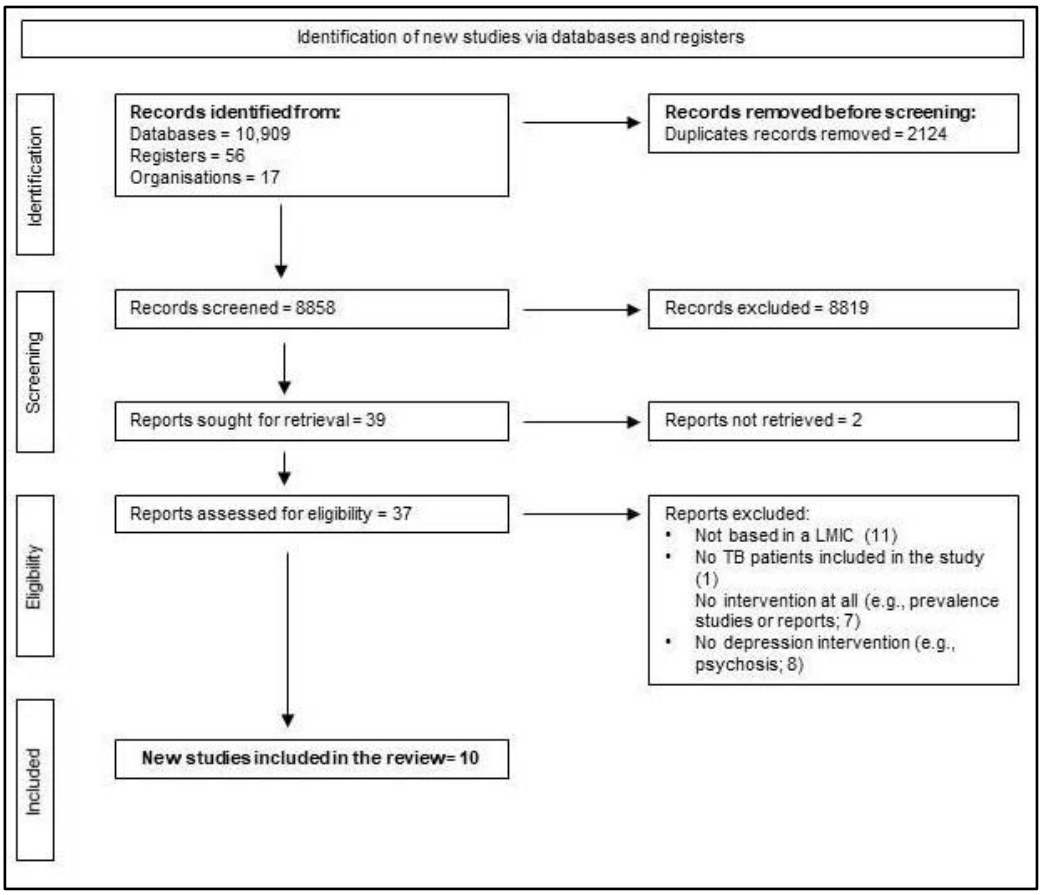

Figure 4.1 PRISMA guidelines for systematic reviews, NIHR review (Page, et al., 2021).

4.3.2 Included studies

Ten articles met the inclusion criteria and were included in the analysis. They varied in terms of study design. One was a qualitative study (Acha, *et al.,* 2007), three were retrospective cohort studies (Contreras, *et al.,* 2017; Das, *et al.,* 2014; Vega, *et al.,* 2004), one was a controlled-cohort study (Kaukab, *et al.,* 2015), two were cluster randomised trials (Khachadourian, *et al.,* 2020; Li, *et al.,* 2018), and three were mixed-methods (Diez-Canseco, *et al.,* 2018; Lovero, *et al.,* 2019; Walker, *et al.,* 2018b).

Four studies described a psychological intervention (Acha, *et al.,* 2007; Khachadourian, *et al.,* 2020; Li, *et al.,* 2018; Walker, *et al.,* 2018b). Three studies described interventions that combined psychological and pharmacological approaches (combined) (Das, *et al.,* 2014; Vega, *et al.,* 2004; Lovero, *et al.,* 2019). Two studies described a pharmacological and psychological intervention that also included socioeconomic support (combined, with socioeconomic support) (Contreras, *et al.,* 2017; Kaukab, *et al.,* 2015). One intervention consisted of screening-only followed by referral to mental health services, when needed (Diez-Canseco, *et al.,* 2018). I describe more details of included studies in Table 4.2.

Study	Year of study	Country	Intervention category	Type and no. of participants		Study design	Outcomes measured in the study			
							TB-related outcomes	Mental health outcomes	Process outcomes	Other outcomes
(Acha, *et al.,* 2007)	1999-2004	Peru	Psychological-only	Multidrug-resistant TB	285	Qualitative	TB treatment success (treatment completion and cure).	None reported.	Adherence to TB treatment.	Participants' experiences during implementation, all-cause mortality, quality of life for people with TB.
(Contreras, *et al.,* 2017)	2015-2016	Peru	Combined, with socioeconomic support	Unspecified type of TB	192	Quantitative (cohort study)	None reported.	None reported.	Number of depression screenings, mental health treatment attendance, completed socioeconomic support	None reported.

Study	Year of study	Country	Intervention category	Type and no. of participants		Study design	Outcomes measured in the study			
							TB-related outcomes	**Mental health outcomes**	**Process outcomes**	**Other outcomes**
									evaluations for people with TB.	
(Das, *et al.,* 2014)	2012-2014	India	Combined	Multidrug-resistant TB comorbid with HIV	45	Quantitative (cohort study)	None reported.	Changes in depression symptoms severity.	Number of eligible people screened for depression; number of referrals (to hospital care for TB).	None reported.
(Diez-Canseco, *et al.,* 2018)	2015	Peru	Screening-only	Unspecified type of TB	85	Mixed-methods	None reported.	None reported.	Number of depression screenings, number of referrals to mental health specialist services, appointment	Participants' experiences pre-, during, and post-implementation.

Study	Year of study	Country	Intervention category	Type and no. of participants		Study design	Outcomes measured in the study			
							TB-related outcomes	Mental health outcomes	Process outcomes	Other outcomes
									attendance after referral.	
(Kaukab, *et al.,* 2015)	2014	Pakistan	Combined, with socioeconomic support	Multidrug-resistant TB	70	Quantitative (controlled-cohort study)	None reported.	Changes in depression symptom severity.	None reported.	None reported.
(Khachadourian, *et al.,* 2020)*	2014	Armenia	Psychological-only	Drug-susceptible TB	385	Quantitative (cluster randomized trial)	TB treatment success, loss to follow-up, treatment failure.	Changes in depression symptom severity.	None reported.	Changes in stigma score, changes in quality of life, all-cause mortality, changes in perceived social support.
(Li, *et al.,* 2018)	2015-2016	China	Psychological-only	Unspecified type of TB	183	Quantitative (cluster	None reported.	Changes in depression	None reported.	None reported.

Study	Year of study	Country	Intervention category	Type and no. of participants		Study design	Outcomes measured in the study			
							TB-related outcomes	Mental health outcomes	Process outcomes	Other outcomes
						randomized trial)		symptom severity.		
(Lovero, *et al.,* 2019)	2016-2017	South Africa	Combined	Unspecified type of TB	N/A	Mixed-methods	None reported.	None reported.	Healthcare workers knowledge and adherence to mental health diagnosis, treatment, and referral guidelines for people with TB.	Non-patient participants' experiences of the mental health intervention.
(Vega, *et al.,* 2004)	1996-1999	Peru	Combined	Multidrug-resistant TB	75	Quantitative (cohort study)	None reported.	Changes in depression symptom severity.	None reported.	None reported.
(Walker, *et al.,* 2018b)	2015	Nepal	Psychological-only	Multidrug-resistant TB	135	Mixed-methods	None reported.	Changes in depression	Fidelity, feasibility,	Participants' experiences during

Study	Year of study	Country	Intervention category	Type and no. of participants		Study design	Outcomes measured in the study			
							TB-related outcomes	Mental health outcomes	Process outcomes	Other outcomes
								symptom severity.	acceptability of the intervention.	implementation.
Legend: *Refers to data used in the per-protocol analysis.										

Table 4.2 Characteristics of included studies

4.3.3 Quality assessment

In Table 4.3 I describe the results of the included studies' quality assessment using MMAT tool. I assessed the included studies against the appropriate methodological quality criteria according to their study design. Given the research objectives of this review, I did not exclude any of the studies based on methodological quality. The purpose of quality assessment was to explore whether the findings from the included studies were of sufficient methodological quality. All studies had appropriate study designs for their stated research questions, except for one (Kaukab *et al.,* 2015). In this study, I considered the study design (quantitative non-randomized) to be inappropriate for the research questions that the authors described in the study, which were to examine the effectiveness of a combined intervention, with socioeconomic support, delivered by pharmacists (Kaukab, *et al.,* 2015).

Study designs	**Methodological quality criteria**	**Studies:**	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**	**(10)**
Screening questions (for all types)	Are there clear research questions?		N	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Do the collected data allow to address the research questions?		Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Qualitative	Is the qualitative approach appropriate to answer the research question?		Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Are the qualitative data collection methods adequate to address the research question?		Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Are the findings adequately derived from the data?		Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Is the interpretation of results sufficiently substantiated by data?		Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Is there coherence between qualitative data sources, collection, analysis, and interpretation?		Y	NA	NA	NA	NA	NA	NA	NA	NA	NA
Quantitative randomized controlled trials	Is randomization appropriately performed?		NA	NA	NA	NA	NA	Y	Y	NA	NA	NA
	Are the groups comparable at baseline?		NA	NA	NA	NA	NA	Y	Y	NA	NA	NA
	Are there complete outcome data?		NA	NA	NA	NA	NA	Y	N	NA	NA	NA
	Are outcome assessors blinded to the intervention provided?		NA	NA	NA	NA	NA	Y	N	NA	NA	NA
	Did the participants adhere to the assigned intervention?		NA	NA	NA	NA	NA	Y	Y	NA	NA	NA
Quantitative non-randomized	Are the participants representative of the target population?		NA	N	N	NA	N	NA	NA	NA	Y	NA
	Are measurements appropriate regarding both the outcome and intervention (or exposure)?		NA	Y	Y	NA	Y	NA	NA	NA	Y	NA
	Are there complete outcome data?		NA	Y	N	NA	Y	NA	NA	NA	Y	NA
	Are the confounders accounted for in the design and analysis?		NA	N	N	NA	N	NA	NA	NA	Y	NA

Study designs	Methodological quality criteria	Studies:	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
	During the study period, is the intervention administered (or exposure occurred) as intended?		NA	Y	N	NA	Y	NA	NA	NA	Y	NA
Quantitative descriptive	Is the sampling strategy relevant to address the research question?		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Is the sample representative of the target population?		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Are the measurements appropriate?		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Is the risk of nonresponse bias low		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Is the statistical analysis appropriate to answer the research question?		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mixed methods	Is there an adequate rational for using a mixed methods design to address the research question?		NA	NA	NA	Y	NA	NA	NA	Y	NA	Y
	Are the different components of the study effectively integrated to answer the research question?		NA	NA	NA	Y	NA	NA	NA	Y	NA	Y
	Are the outputs of the integration of qualitative and quantitative components adequately interpreted?		NA	NA	NA	Y	NA	NA	NA	Y	NA	Y
	Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?		NA	NA	NA	Y	NA	NA	NA	Y	NA	Y
	Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?		NA	NA	NA	Y	NA	NA	NA	Y	NA	Y
	Total quality criteria met		**6/7**	**5/7**	**3/7**	**7/7**	**4/7**	**7/7**	**5/7**	**7/7**	**7/7**	**7/7**
Legend:												

Study designs	**Methodological quality criteria**	**Studies:**	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**(9)**	**(10)**
The cells shaded represent the criteria that is applicable to each included study according to their study design.												
Y = Yes; N = No; NI = No information; NA = Not applicable												
(1) (Acha, *et al.,* 2007)												
(2) (Contreras, *et al.,* 2017)												
(3) (Das, *et al.,* 2014)												
(4) (Diez-Canseco, *et al.,* 2018)												
(5) (Kaukab, *et al.,* 2015)												
(6) (Khachadourian, *et al.,* 2020)												
(7) (Li, *et al.,* 2018)												
(8) (Lovero, *et al.,* 2019)												
(9) (Vega, *et al.,* 2004)												
(10) (Walker, *et al.,* 2018b)												

Table 4.3 Methodological quality assessment for included studies.

4.3.4 Description of approaches to deliver depression care as part of TB services

The ten studies included in this analysis describe four main types of interventions that aim to provide depression diagnosis and/or treatment, or referral to mental health services, to people with TB in LMICs at the point of care for TB services. The four major approaches used to deliver depression care for people with TB in LMICs were psychological interventions, combined (pharmacological and psychological) interventions, combined interventions with socioeconomic support, and screening-only interventions. In Table 4.4 I provide a detailed description of the interventions, components, and resources required for implementation.

The most commonly implemented intervention was psychological. Nine out of ten studies included in this review described the implementation of psychological interventions, or interventions with a psychological component, alone or in combination with other approaches; only one study did not describe the implementation of a psychological intervention (Diez-Canseco, *et al.,* 2018). Psychological interventions were described as counselling or psychotherapy. The most common intervention for depression was described as counselling (Contreras, *et al.,* 2017; Das, *et al.,* 2014; Vega, *et al.,* 2004; Kaukab, *et al.,* 2015; Khachadourian, *et al.,* 2020; Lovero, *et al.,* 2019; Walker, *et al.,* 2018b). Counselling was delivered in interventions that implemented psychological interventions only, combined, or combined with socioeconomic support. Counselling was defined as motivational and emotional counselling (Das, *et al.,* 2014), patient counselling (Khachadourian, *et al.,* 2020), psychological counselling (Walker, *et al.,* 2018b), or TB counselling (Khachadourian, *et al.,* 2020). Most counselling sessions were individual, except when given to also to family members (Khachadourian, *et al.,* 2020) and/or patient groups (Walker, *et al.,* 2018b). The content of counselling sessions was not described in most interventions. Only one study described the content of the counselling sessions as based on behavioural activation (Walker, *et al.,* 2018b).

None of the interventions used pharmacological treatment alone; all pharmacological interventions were part of a combined strategy, incorporating psychological and socioeconomic support components.

Two interventions included socioeconomic support components combined with psychological and pharmacological interventions (Contreras, *et al.,* 2017; Kaukab, *et al.,* 2015). Socioeconomic support consisted of transport subsidies, food, fees for medical tests, school fees for family members, and covered diagnostic tests' fees for other comorbidities. Both studies justified the inclusion of socioeconomic support given the socioeconomic needs of

people with TB. Both studies mentioned that the socioeconomic support was provided by non-governmental organisations (Contreras, *et al.,* 2017; Kaukab, *et al.,* 2015).

All the included interventions were described inconsistently. Information on treatments' length, dose, and endpoints was often missing from published data in all included studies. Studies that reported on psychological interventions, combined interventions, and combined interventions with socioeconomic support did not report on treatment length or number of psychological sessions received by participants. The frequency of psychological treatment sessions was mentioned in four studies (Acha, *et al.,* 2007; Kaukab, *et al.,* 2015; Khachadourian, *et al.,* 2020; Li, *et al.,* 2018). Of the three combined interventions, one study provided detail about the combination of pharmacological therapy with psychotherapy given to people, which were selective serotonin reuptake inhibitors, tricyclic antidepressants, or benzodiazepines (Vega, *et al.,* 2004); dosage was not reported.

I observed variability in the instruments used to measure and diagnose depression; some studies described the use of more than one tool (Contreras, *et al.,* 2017; Walker, *et al.,* 2018b). All studies reported measurements of depression scores at baseline. Baseline referred to the beginning of the intervention for depression in some studies, while in others it referred to the beginning of TB treatment. I found the same patterns in endpoint measurements. Endpoint measurements could refer to the end of the depression intervention or the end of the TB treatment. The follow- up measurements of depression scores were taken at different points in all interventions; one study had no follow up measurement (Diez-Canseco, *et al.,* 2018). I extracted this quantitative data as it was reported in the studies (see Appendix 3).

All interventions were implemented as part of routine public TB services and were often implemented in the same location and time of TB service delivery, except in two interventions where people received mental health services elsewhere (Diez-Canseco, *et al.,* 2018; Lovero, *et al.,* 2019). Where applicable, interventions used routine TB care as a control or comparator (Kaukab, *et al.,* 2015; Khachadourian, *et al.,* 2020; Li, *et al.,* 2018). All interventions relied on existing TB care pathways to incorporate screening and treatment for depression. All interventions were provided free of charge for participants at the point of service delivery.

All interventions relied on multidisciplinary teams to deliver the depression intervention. Teams comprised TB healthcare workers, primary healthcare workers with training in mental health, or mental health specialists (i.e., psychologists or psychiatrists); see Table 4.4. In studies that described the number and type of providers involved, there was a higher number of community or lay healthcare workers in comparison to the mental health

specialists within the intervention team (Acha, *et al.,* 2007; Contreras, *et al.,* 2017; Das, *et al.,* 2014; Lovero, *et al.,* 2019; Walker, *et al.,* 2018b). When community or lay healthcare workers were involved in the intervention delivery, this was due to their role in the existing TB service delivery structure, as they were often responsible for diagnosis and follow-ups for people with TB, and were often service users' first and only contact with TB services.

Most studies described how they required additional human or physical resources to those routinely used or available in existing TB services. For example, most interventions described the requirement of additional human resources to deliver the intervention; the exceptions to this were combined (Das, *et al.,* 2014; Vega, *et al.,* 2004; Lovero, *et al.,* 2019). and screening-only interventions (Diez-Canseco, *et al.,* 2018) where they used routinely available human resources. Studies describing psychological interventions also showed that there was a need for mental health specialists (psychologists, psychiatrists, or both), social workers, or additional community healthcare workers working alongside routinely available TB healthcare workers to deliver the intervention (Acha, *et al.,* 2007; Khachadourian, *et al.,* 2020; Li, *et al.,* 2018; Walker, *et al.,* 2018b).

All interventions required community or lay healthcare workers to be trained to screen for depression and deliver the described intervention. Training components were described unevenly in all studies. In some studies, it was not specified whether the training that the healthcare workers obtained was delivered as part of the intervention or before its implementation (Contreras, *et al.,* 2017; Das, *et al.,* 2014; Vega, *et al.,* 2004; Khachadourian, *et al.,* 2020). In some studies training was only provided for the use of diagnostic tools (Li, *et al.,* 2018). In two studies, training content or length was not described at all (Acha, *et al.,* 2007; Kaukab, *et al.,* 2015). In the studies that described training components, these usually covered the use of diagnostic tools and the provision of mental healthcare and were targeted to TB healthcare workers (Vega, *et al.,* 2004; Lovero, *et al.,* 2019; Walker, *et al.,* 2018b). One study mentioned training the TB healthcare workers for the total period of six days (Walker, *et al.,* 2018b).

All interventions required the use of additional physical spaces to those routinely available in TB services on which to deliver the diagnosis, treatment, or follow-up sessions of the intervention. Other requirements were specific to the types of intervention described, such as the use of IT infrastructure or mobile data plans to facilitate communication between people and healthcare workers, or between healthcare workers and the implementation team (Khachadourian, *et al.,* 2020; Diez-Canseco, *et al.,* 2018). In the case of interventions that delivered antidepressants as part of treatment, these were offered to people at no cost (Das,

et al., 2014; Vega, *et al.,* 2004). Only one study provided in-kind incentives for community healthcare workers to participate in the intervention delivery (Diez-Canseco, *et al.,* 2018).

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
Definition		Defined as any type of group or individual therapy used to treat mental health conditions such as depression, anxiety, or psychosis. Examples of psychological interventions for depression are behavioural therapy (e.g., behavioural activation), interpersonal therapy, cognitive behavioural therapy (including third-wave cognitive behavioural therapies, such as behavioural activation), psychodynamic therapies (e.g., group therapy or psychoanalytic therapy), and other types of psychological therapies (e.g., family therapy).	Defined as psychological and pharmacological interventions delivered simultaneously (e.g., combined treatment).	Defined as psychological and pharmacological treatment with provision of socioeconomic support for people with TB.	Defined as screening for mental health conditions, followed by referral to mental health services outside TB services, if needed.
Studies included in this review that described this type of intervention		*Acha, et al. (2007).* *Khachadourian, et al. (2020).* *Li, et al. (2018).* *Walker, et al. (2018b).*	*Das, et al. (2014).* *Lovero, et al. (2019).* *Vega, et al. (2004).*	*Contreras, et al. (2017).* *Kaukab, et al. (2015).*	*Diez-Canseco, et al. (2018).*
	Content	Defined in the included studies as screening for depression, followed by psychological	Screening for depression,	Screening for depression,	Screening followed by

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
Intervention description		interventions for depression such as counselling (Khachadourian, *et al.,* 2020), psychotherapy (Li, *et al.,* 2018), or behavioural activation (Walker *et al.,* 2018b). <u>Other:</u> Educational session (Khachadourian, *et al.,* 2020); daily SMS and phone calls to people and supporters (Khachadourian, *et al.,* 2020); peer support and psychoeducational workshops (Li, *et al.,* 2018); bonding activities such as excursions and celebrations (Acha, *et al.,* 2007).	followed by psychological and pharmacological treatment for depression when needed. <u>Psychological component:</u> individual counselling (Das, *et al.,* 2014), individual psychotherapy (Vega, *et al.,* 2004), or unspecified (Lovero *et al.,* 2019).	followed by psychological and pharmacological treatment, with socioeconomic support when needed, for all interventions. <u>Psychological component:</u> counselling, for all interventions. <u>Pharmacological component:</u> unspecified, for all interventions.	referral to mental health services, if needed. The type of treatment that was received is unspecified.

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
			<u>Pharmacological component</u>: Antidepressants and anxiolytics in one intervention (Vega *et al.,* 2004); unspecified for two interventions (Das *et al.,* 2014; Lovero, *et al.,* 2019).	<u>Other:</u> socioeconomic support, for all interventions.	
	Dose, frequency, number of sessions and length	Bi-weekly group sessions (Acha, *et al.,* 2007); 1 group session and daily individual reminders (Khachadourian, *et al.,* 2020); individual bi-weekly, 30 min sessions, home visits (Li, *et al.,* 2018); 30-45 min individual or group sessions, with frequency unspecified (Walker, *et al.,* 2018b).	No data for all interventions.	Unspecified (Contreras, et al; 2017) or individual, monthly (Kaukab et al, 2015).	Unspecified.

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
	Screening tool	Unspecified (Acha *et al.,* 2007), CES-D (Khachadourian *et al.,* 2020), Zung Self-rating depression scale (Li, et al, 2018); or HCSL, PHQ-9, and PHQ-2 (Walker, *et al.,* 2018b).	PHQ-9 (Das et al; 2014), PC101 (Lovero *et al.,* 2019); or DSM-IV (Vega, *et al.,* 2004).	SRQ-18 (Contreras, et al; 2017), PHQ-9 (Contreras et al; 2017), or BDI (Kaukab et al; 2015).	Unspecified.
	Points of screening	At baseline for all interventions. At follow-up of TB appointments (monthly, or tri-monthly) for three interventions (Li, *et al.,* 2018; Khachadourian *et al.,* 2020; Walker, *et al.,* 2018b).	At baseline for all interventions; and at 3 months for one intervention (Das et al; 2014).	At beginning of intervention for one intervention (Kaukab, *et al.,* 2005); at first visit to TB health centre for one intervention (Contreras, *et al.,* 2017); and at end of treatment for one intervention	At baseline.

Intervention type	Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
			(Kaukab, *et al.,* 2015).	
Individuals or groups delivering the intervention	Multidisciplinary teams for three interventions (e.g., community health workers, trained therapists, community administrators, psychologists, nurses) (Khachadourian, *et al.,* 2020; Li, *et al.,* 2018); community healthcare workers for one intervention (Walker, *et al.,* 2018b).	Multidisciplinary teams, for all interventions (e.g., nurses, mental health primary healthcare workers, psychologists, or psychiatrist).	Multidisciplinary team (Contrera, *et al.,* 2017); or pharmacists (Kaukab *et al.,* 2015).	Primary healthcare workers.
Setting of intervention delivery	At outside facilities and/or at TB treatment centre for two interventions. At TB treatment centre and at home for one intervention (Khachadourian, *et al.,* 2020). Not specified for one intervention, at home (Li, *et al.,* 2018).	At TB treatment centre, for all interventions; and at participants' homes for one intervention (Vega, *et al.,* 2004).	At TB treatment site for all interventions.	Screening at TB treatment site. Unspecified for treatment.

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
Training for delivery		Yes, for diagnosis screening and for delivering the intervention, for all interventions.	Yes, for screening, in two interventions (Das, *et al.,* 2014; Lovero, *et al.,* 2019).	Unspecified, for all interventions.	Yes, training for screening.
Physical resources	Defined as those necessary to deliver the intervention (i.e., facilities) or additional to those routinely used (i.e., training materials,	Subsidies for transport, physical space to deliver the sessions, training sessions, financing group activities outside intervention sessions (Acha, *et al.,* 2007). Mobile data to communicate with people (Khachadourian, *et al.,* 2020). For conducting home visits, training materials (Li, *et al.,* 2018). Educational materials, training materials, physical space to deliver the sessions (Walker, *et al.,* 2018b).	Anti-depressants for one intervention (Vega, *et al.,* 2004); unspecified for other interventions (Das, *et al.,* 2014; Lovero *et al.,* 2019).	In kind support (i.e., food vouchers, transport, coverage of other medical fees, healthcare supplies, rent and utilities), for all interventions.	Yes, educational vouchers for HCWs, IT equipment, mobile data plan. Yes, educational material used by pharmacists, free antidepressants, food basket, transport,

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
	educational materials, equipment).				coverage of other medical fees.
Human resources	Defined as additional human resources needed to deliver the intervention and that are not routinely available in existing TB services (i.e., psychologists, psychiatrists, translators,	Psychiatrists and/or psychologists for three interventions (Acha, *et al.,* 2007; Khachadourian, *et al.,* 2020; Li, *et al.,* 2018). Mental health nurse for one intervention (Khachadourian, *et al.,* 2020). Community healthcare workers for one intervention (Walker *et al.,* 2018b).	None other than routinely used, for all interventions.	Additional psychologists, nurses, and social workers in one intervention (Contreras *et al.,* 2017). Unknown for the other intervention (Kaukab, *et al.,* 2015).	None other than those routinely available.

Intervention type		Psychological-only	Psychological and pharmacological (combined)	Psychological and pharmacological, with socioeconomic support	Screening-only
	and other personnel not routinely available in existing TB services).				

Table 4.4 Approaches to deliver depression care as part of routine TB services.

4.3.5 Barriers and facilitators for implementing depression care as part of routine TB services

There was a lot of variability in terms of what represented barriers or facilitators for implementation across intervention types and CFIR domains. In Table 4.5, I describe an overview of the barriers and facilitators for the implementation of each type of interventions described in the included studies according to the CFIR framework, including information on the sub-domains where there was no data available. Table 4.5 also includes the definition of the CFIR sub-domains I used for the purposes of this review.

Barriers across all intervention types

The sub-domain **Cost of intervention and/or implementation** is contained within the **Intervention Characteristics domain** in the CFIR framework. Most studies discussed the spill-over effects of this barrier on the context of implementation. This was a major barrier for implementation for all intervention types. There were different types of costs referenced in the studies, associated with additional human resources, lack of physical spaces, and lack of funding for the mental health intervention:

- All intervention required the use of additional physical and/or human resources to those routinely available and required additional resources for training activities. Examples of additional human resources were the recruitment of specialist mental health workers (i.e., psychiatrists or psychologists) and additional community health workers (Acha, *et al.,* 2007; Walker, *et al.,* 2018b).
- The lack of physical spaces to deliver the intervention for depression was also a recurring barrier in most studies. Only the screening-only intervention did not mention lack of physical space as a barrier since people were referred to spaces outside the TB clinic to receive mental healthcare (Diez-Canseco, *et al.,* 2018).
- One study describing a combined intervention mentions the lack of funding as a worsening factor that negatively impacts on implementing mental health interventions in routine primary care services: *"…the problem is human resources, material resources, and funding all combined…* " (Lovero, *et al.,* 2019:p.7).

Other barriers across interventions

Complexity is part of the Intervention Characteristics domain. This was a barrier for psychological and combined interventions, but it had a mixed impact in interventions combined with socioeconomic support and screening-only. For a detailed description of the role of this sub-domain as a barrier, see Appendix 5.

Culture was referred to as a barrier when organisational or people' culture clashed with the goals of the intervention. **Culture** was a barrier for all types of interventions, except for combined interventions with socioeconomic support where there was no data available. For a detailed description of the role of this sub-domain as a barrier, see Appendix 5.

Facilitators across all intervention types

The sub-domain **Relative advantage** was a facilitator across all intervention types. Participants perceived it was advantageous to implement the depression interventions since they improved the TB care provided at the time of implementation. All studies reported statements referring to participants' belief in the advantage and benefit of delivering mental healthcare to people with TB as opposed to routine care or no mental health intervention at all. In most studies, it was recognised that people with TB have complex care needs that cannot be addressed by focusing on providing TB treatment alone. One study explicitly stated that the intervention improved and complemented the current services provided for people with TB and improved their access to integrated care. "[The intervention] *offered additional evaluations to supplement those covered by the TB services at the health facilities…* [the intervention's] *strategy of having a field team who function as case managers and patient advocates is one method for offering coordinated care in a system where care is not integrated at the provider level*" (Contreras, *et al.,* 2017:p.509). The favourable opinion about the Relative Advantage of the intervention was shared by people, TB healthcare workers, and policymakers. "Some [people] also stated that the intervention should be available in all MDR-TB centres" (Walker, *et al.,* 2018b:p.9). Healthcare workers felt the intervention helped them to provide better care to their people. "*They [the healthcare workers] believed the training made them more aware of the importance of caring for people's mental health, provided them with knowledge and skills in mental health—an understudied topic in their professional education—taught them how to use a screening tool to assess their people' mental health, and offered them necessary skills to help their people*" (Diez-Canseco, *et al.,* 2018:p.14). TB programme leaders at district level mentioned that mental health delivery programmes had achieved some improvements on routinely provided TB care (Lovero, *et al.,* 2019).

The sub-domain **Compatibility of the intervention,** part of the Inner Setting domain, was a facilitator for implementation across all intervention types. Studies reported positive statements about the compatibility of the intervention's components (i.e., screening, treatment) with the values of the TB services and current practices. In two studies that described a psychological and a screening-only intervention, the intervention's components were designed with the input from healthcare workers delivering them and adapted according to their feedback as the implementation progressed (Diez-Canseco, *et al.,* 2018; Walker, *et al.,* 2018b). The studies describing combined interventions for depression also reported how the screening and treatment components were compatible with their existing TB programmes and were included in their operational manuals or supported by national TB policies (Contreras, *et al.,* 2017; Das, *et al.,* 2014; Vega, *et al.,* 2004; Lovero, *et al.,* 2019).

The **Innovation Participants** (i.e., the people who received the intervention which were people with TB and, in some psychological interventions, also their families) were facilitators for implementation. In all interventions, there were comprehensive measures taken to involve the people with TB and their families in the implementation and delivery processes. In some interventions, this included providing home visits to people with TB (Acha, *et al.,* 2007; Contreras, *et al.,* 2017; Vega, *et al.,* 2004; Li, *et al.,* 2018). In some interventions, family members and friends were included in the psychological component of the intervention (Acha, *et al.,* 2007; Khachadourian, *et al.,* 2020; Li, *et al.,* 2018; Walker, *et al.,* 2018b). In one intervention, people were given an option of where to receive care, depending on their situation at home (Contreras, *et al.,* 2017; Lovero, *et al.,* 2019). In all interventions, the active and positive participation of the people with TB, their families, or their communities was a facilitator for the implementation of the intervention for depression, regardless of the type of intervention.

Other facilitators across intervention types

There were other facilitators across most, but not all, intervention types.

Evidence strength and quality was defined as the belief, sustained by evidence, that the intervention would have the desired outcome. This was a facilitator in psychological, combined, and combined with socioeconomic support interventions. For a detailed description of the role of this sub-domain, see Appendix 5.

Cosmopolitanism, part of the Outer Setting domain, seemed to be a facilitator for all types of interventions, except for screening-only where there was no data to assess this. Cosmopolitanism, defined as the linkages between TB services and other public or private services. For a detailed description of the role of this sub-domain, see Appendix 5.

External policy and incentives, part of the Outer setting domain, seemed to be facilitators for all types of interventions, except for screening-only for which there was no data to assess this. For a detailed description of the role of this sub-domain, see Appendix 5.

Access to Knowledge and Information, part of the Inner Setting domain, acted as a facilitator for all types of interventions, except for combined interventions with socioeconomic support, where there was no data available to assess this. More details of the role of this sub-domain are included in Appendix 5.

Individual stage of change, part of the Characteristics of Individuals domain, seemed to be a facilitator for all types of interventions, except for combined interventions with socioeconomic support, where there was no data to assess this. This sub-domain refers to the stages that healthcare workers go through towards the sustained and skilled delivery of the intervention, in terms of change in their confidence and knowledge to implement the intervention. See Appendix 5 for a detailed description of the role of this sub-domain.

The influence of **External change agents** as facilitators of implementation was present in all interventions, except for the screening-only intervention where there was no data available to assess this. External change agents were defined as individuals affiliated to other organisations that are not governmental or public TB services. See Appendix 5 for a detailed description of the role of this sub-domain.

Discrepancies in barriers and facilitators across intervention types

There were some discrepancies in the roles that some sub-domains had across interventions. This section describes the sub-domains that were facilitators for implementation in some interventions whilst acting as barriers for implementation in other interventions, based on the data available in the included studies.

Adaptability, a sub-domain part of the Intervention Characteristics domain, had a different role in the implementation of different intervention types. It acted as a facilitator in the implementation of psychological-only and combined interventions with socioeconomic support; it was a barrier to the implementation of the screening-only intervention; and it had a mixed impact in the implementation of combined interventions (without socioeconomic support). As a facilitator, the sub-domain of Availability included statements from the included studies that referred to how screening and treatment components were adapted to meet the local cultural needs. In one psychological intervention, this involved the change of screening tool from less compatible (PHQ-9) to one more compatible (PHQ-2) with healthcare workers routine activities (Walker, *et al.,* 2018b). In other psychological interventions, this involved

the use of culturally adapted treatments for depression according to people' needs (Li, *et al.,* 2018). However, in the implementation of combined interventions, one of the studies described how the adaptability of the intervention led to its uneven implementation in different primary care settings (Lovero, *et al.,* 2019). The characteristics of the screening-only intervention meant that it was not possible to fully adapt the intervention to local practices and workflows, even if it had been designed to be compatible before the implementation process (Diez-Canseco, *et al.,* 2018).

The sub-domain **Needs of those served by the organisation** (i.e., needs of people with TB), part of the Outer Setting domain, was a facilitator in psychological, combined, and combined with interventions with socioeconomic support. However, it was a barrier in the screening only intervention. For a detailed description of the role of this sub-domain as a barrier and facilitator, see Appendix 5.

The role of **Available resources**, a sub-domain part of the Inner Setting domain, was a facilitator for implementation in combined interventions with socioeconomic support. However, this sub-domain acted as a barrier for implementation in psychological and combined interventions. Additionally, this sub-domain was one of the few ones to have a mixed impact, as a barrier and facilitator, in the implementation of screening-only interventions. For a detailed description of the role of this sub-domain as a barrier and facilitator, see Appendix 5.

Self-efficacy, part of the Characteristics of Individuals domain, was a facilitator for the implementation of psychological-only and screening-only interventions, but it was a barrier for implementation for combined interventions. For a detailed description of the role of this sub-domain as a barrier and facilitator, see Appendix 5.

In psychological, combined, and screening-only interventions the role of **Key stakeholders** was as a facilitator for implementation. However, the same sub-domain had a mixed impact in the implementation of combined interventions with socioeconomic support. Key stakeholders were defined as healthcare workers part of TB services and involved in TB service delivery. Key stakeholders were multidisciplinary: the teams involved in the implementation of screening and treatment of interventions were social workers, counsellors and psychologists or psychiatrists, nurses with training mental health, community healthcare workers, or TB healthcare workers. In interventions that involved mental health specialists such as psychologists or psychiatrists, these would often be involved in the training and supervision of community health workers or data collectors implementing the screening and treatment (Acha, *et al.,* 2007; Das, *et al.,* 2014; Diez-Canseco, *et al.,* 2018). In these interventions, the role of specialists was also to provide on-going support and sometimes

feedback to community health workers providing the intervention. However, in one combined intervention with socioeconomic support, the role of psychologists or mental health specialists was unclear in terms of their role providing support or training to healthcare workers delivering the intervention (Kaukab, *et al.,* 2015). In this intervention the role of TB healthcare workers was also unclear as it was noted that pharmacists delivered the intervention, and it was unclear what the affiliation of the pharmacists was at the time of implementation.

Executing, part of the Process domain, was a facilitator for the implementation of the screening-only intervention and a barrier for implementation for psychological and combined interventions. In the screening-only intervention, its technological characteristics (i.e., being app-based) allowed for the consistent implementation of the intervention, and the intervention implementing process was designed so that researchers could provide support to healthcare workers quickly if they noticed the intervention was not being implemented adequately (Diez-Canseco, *et al.,* 2018). However, in the implementation of psychological interventions, the studies described issues with the adequate execution of the intervention. These were attributed in part to the insufficient resources or to the unsustainability of the interventions when healthcare workers aimed to include it in their day-to-day practice. "*Although it only took 5–10 minutes to go through, this seemed to become a barrier to them using the flipbook. They stated that they gave the same messages but more briefly*" (Walker, *et al.,* 2018b:p.9). In combined interventions, two studies described issues with uneven implementation. They described deficiencies associated with the adequate, sustained, and consistent implementation of the intervention across settings (Lovero, *et al.,* 2019). One study mentioned that the mental health intervention components (i.e., routine screening, the use of the designated screening tool, referral, and treatment) were unevenly implemented according to healthcare workers self-reported performance (Das, *et al.,* 2014).

<u>Sub-domains with no data</u>

There were some sub-domains that had no data available across all intervention types. Most of the data coded in the studies was attributed to the sub-domains included in the larger **Intervention Characteristics** and **Characteristics of Individuals** domains. However, there were evident gaps in information in other domains. The most evident gap in evidence was in the **Inner Setting** domain. In this sub-domain, few studies described data that could be used to draw patterns about the influence of this domain and its sub-domains as barriers of facilitators. The lack of data was evident also in the **Process** domain of the framework, where there was little information available on the role of Planning and Engaging different actors in the implementation of the intervention. See Table 4.5 for more details.

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
Intervention characteristics	Intervention source	Defined as the perception of healthcare workers or people with TB about whether the depression intervention is developed by local or national TB services or not.	ND	ND	ND	ND
	Evidence strength and quality	Defined as the authors,' healthcare workers,' or other participants' perceptions on the evidence supporting the belief that the depression intervention will have the desired outcomes described in the study.	2	2	2	**0**
	Relative advantage	Defined as the healthcare workers' and/or people with TB's perception about the advantage of delivering the depression intervention over the status quo or not delivering the intervention.	2	1	2	2
	Adaptability	Defined as the degree to which a depression intervention was or can be adapted to meet local needs.	1	X	1	-1
	Trialability	Defined as the ability or possibility to test the depression intervention on a small scale in existing TB services. Previous experiences of piloting the depression intervention or one of its components was also considered in this sub-domain.	X	ND	ND	2
	Complexity	Defined as healthcare workers' and/or people with TB's perception about the difficulty to implement or deliver the	-2	-1	X	X

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
		depression intervention, which could also be reflected in the intricacy and number of steps required to deliver the depression intervention.				
	Design quality and package	Defined as the perceptions of the intervention participants about the presentation and quality of the materials needed for delivering the depression intervention.	2	ND	ND	2
	Cost of intervention and or implementation	Defined as the costs of the depression intervention and costs associated to its implementation, including opportunity costs.	-2	-2	-1	-1
Outer setting	Needs of those served by the organisation	Defined as the extent to which the needs of people with TB are identified or met by the depression intervention.	2	1	1	-1
	Cosmopolitanism	Defined as the degree to which TB services are linked with other organisations and its influence on the implementation of the depression intervention.	2	2	2	ND

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
	Peer pressure	Defined as the perceived competitive pressure to implement the depression intervention in TB services.	ND	ND	ND	ND
	External policy and incentives	Defined as the local, regional, or national public policies that support the implementation and delivery of depression care in TB services or for people with TB. Also defined as non-governmental organisations' mandates and guidelines that support the implementation and delivery of the intervention.	1	2	2	ND
Inner setting	Structural characteristics of an organisation	Defined as the architecture, size, and other organisational characteristics of TB services.	ND	X	1	ND
	Networks and communications	Defined as the quality of formal and informal social networks and communications within TB services.	ND	-2	1	ND
	Culture	Defined as the norms, values, and basic assumptions of people, communities, and the healthcare workers employed by TB services or the organisation delivering the depression intervention.	-1	-2	ND	-1

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
	Implementation climate:	Defined as the general receptivity to change within TB services and shown by healthcare workers or other participants, and which cannot be coded to any of the sub-domains below:	-	-	-	-
	a) Tension for change	Defined as the authors,' healthcare workers,'', or other participants' perceptions about the need for change of the current service provided to people with TB or its need for change.	2	ND	ND	ND
	b) Compatibility	Defined as the authors,' healthcare workers,'', or other participants' perceptions about the compatibility or fit of the depression intervention with their current practices, values, and/or systems.	1	1	1	1
	c) Relative priority	Defined as the authors,' healthcare workers,'', or other participants' perceptions about the importance of the implementation and delivery of depression care in existing TB services.	ND	-2	ND	ND
	d) Organisational incentives and rewards	Defined as the incentives and rewards provided by study leads, TB services or other organisations involved in the implementation of the intervention that have as a goal to increase or improve the uptake of the depression intervention.	ND	ND	ND	ND

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
	e) Goals and feedback	Defined as the communication of goals and feedback to healthcare workers delivering the depression intervention.	ND	-1	ND	2
	f) Learning climate	Defined as the presence or absence of a learning climate in TB services. A learning climate is defined as a climate in which leaders express their own fallibility and need for team members' assistance and input; team members feel that they are essential, valued, and knowledgeable partners in the change process; individuals feel psychologically safe to try new methods; and there is sufficient time and space for reflective thinking and evaluation (CFIR, 2020).	ND	ND	ND	ND
	Readiness for implementation:	Defined as the tangible indicators of TB services' commitment to the implementation of depression in its routine services, and which cannot be coded in the sub-domains below:	-	-	-	-
	a) Leadership engagement	Defined as the involvement of TB services or other relevant organisational leaders in the implementation and delivery of the depression intervention.	ND	1	ND	ND

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
	b) Available resources	Defined as the availability of resources (i.e., physical, human, financial) dedicated to the implementation and delivery of the depression intervention.	-2	-2	1	X
	c) Access to knowledge and information	Defined as the provision or knowledge and information to healthcare (e.g., training) and people with TB (e.g., educational materials or sessions) about the depression intervention and/or TB.	2	2	ND	2
Characteristics of individuals	Knowledge and beliefs about the intervention	Defined as the authors,' healthcare workers,'', or other participants' (i.e., people) attitudes and beliefs about the depression intervention.	1	X	ND	2
	Self-efficacy	Defined as the healthcare worker's belief in their capacity to implement and deliver the depression intervention.	2	-2	ND	2
	Individual stage of change	Defined as the individual stages through which healthcare workers as they move towards the sustained and skilled delivery of the depression intervention.	1	2	ND	2
	Individual identification	Defined as healthcare workers and people with TB perceptions of TB services and their commitment to them.	ND	ND	ND	ND

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
	with organisation					
	Other individual characteristics	Defined as healthcare workers' personality traits such as tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style (CFIR, 2020).	2	ND	ND	ND
Process	Planning	Defined as the development of plans and strategies for the implementation and delivery of depression care before its implementation.	X	ND	ND	2
	Engaging:	Defined as the strategies and outcomes of activities to engage different individuals in the implementation and use of the depression intervention, and which cannot be coded in the sub-domains below:	-	-	-	-
	a) Opinion leaders	Defined as individuals or groups of individuals (e.g., family, community members) that have a formal or informal influence on the attitudes or beliefs of others towards the intervention and its implementation.	2	ND	ND	2
	b) Formally appointed	Defined as healthcare workers or Individuals from within TB services who have been formally appointed as implementers,	ND	0	ND	ND

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
	internal implementation leaders	coordinators, project manager, team leader, or other similar roles.				
	c) Champions	Defined as individuals who help overcome indifference or resistance to the depression intervention within TB services or by other participants.	2	ND	ND	ND
	d) External change agents	Defined as individuals affiliated with other organisations outside TB services that facilitate the implementation of the intervention.	1	1	1	ND
	e) Key stakeholders	Defined as the healthcare workers within TB services or organisations involved in delivering the intervention.	2	2	X	2
	f) Innovation participants	Defined as people with TB, their families, and/or caregivers.	2	1	1	2
	Executing	Defined as the implementation of the depression intervention according to what was planned (i.e., fidelity).	-1	-2	ND	2
	Reflecting and evaluating	Defined as the feedback about the process of implementation and/or the intervention from healthcare workers and people with TB towards study leads or implementation leaders.	2	0	ND	2
Legend:						

Domain	Sub-domain	Definition of the CFIR sub-domains for the purposes of this review and in line with the CFIR handbook*	Psychological-only	Combined	Combined, with socioeconomic	Screening-only
Barriers: Shaded in red; with a notation of-1 or -2 **Facilitators:** Shaded in green; with a notation of 1 or 2 **Barrier and facilitator (mixed impact):** Shaded in yellow, marked with 'X' **Unclear if barrier or facilitator:** Shaded in grey; marked with a '0' **No data:** Not shaded; marked with ND						

Table 4.5 Barriers and facilitators for implementation according to intervention type

*I adapted the original definitions of the CFIR framework sub-domains to fit the purposes of our study (CFIR, 2020). The shading in the third column represents individual the sub-domains that are included in the wider sub-domains of Implementation Climate, Readiness for Implementation, and Engaging.

4.4 Discussion

In this systematic review, I aimed to explore the approaches that have been used to deliver depression care as part of TB services in LMICs. I also aimed to describe the barriers and facilitators for their implementation using the CFIR framework as an analytical framework. While the goal of this review was not to assess effectiveness, two studies that used cluster randomised controlled trial design reported improved TB and/or mental health outcomes compared to baseline assessments. This is consistent with findings about the efficacy of delivering pharmacological and non-pharmacological interventions for common mental disorders in people with TB (Farooq, Tunmore, and Comber, *et al.,* 2021). This potential effectiveness makes it important to identify how to best deliver mental health interventions for people with TB and implement them within routine TB services.

Most studies met the criteria for quality of reporting according to their study design. However, the studies described the implemented interventions inconsistently, and some of them did not report dose, length of treatment, or follow-up information about the interventions, which are factors that can mediate the efficacy of the interventions. This is consistent with other reviews carried out to evaluate the effectiveness of pharmacological and non-pharmacological interventions for common mental disorders in people with TB where meta-analyses were not possible due to the sparse data reported in studies and the methodological variation in study designs (Farooq, Tunmore, and Comber, *et al.,* 2021).

4.4.1 Approaches to deliver depression care as part of TB services

I identified different approaches to deliver depression care for people with TB in LMICs. The most common approach was the implementation of psychological components alone or in combination with pharmacological components, and with socioeconomic support. This is consistent with the findings of other systematic reviews for interventions that integrate mental health into primary care in LMICs (Cubillos, *et al.,* 2021). Psychological and pharmacological interventions for depression have the potential to be delivered in resource-constrained settings by providing training to non-specialist mental healthcare providers and using task-shifting approaches, achieving highly effective results when delivered by non-specialists alone or supervised by mental health specialists (Barbui, *et al.,* 2020). However, the implementation process will inevitably require additional physical and training-related resources (Barbui, *et al.,* 2020).

4.4.2 Barriers and facilitators for implementation

I learned that the availability and reliability of information on implementation efforts depends more on the study design (e.g., feasibility and acceptability) rather than on the intervention type being implemented (e.g., psychological, combined). The majority of the studies were not focused on implementation which meant that a lot of cells within the framework matrix were empty (i.e., marked as 'No data') for most intervention types and studies, except for the two studies with implementation-focused study designs (Diez-Canseco, *et al.,* 2018; Walker, *et al.,* 2018b). This is consistent with other implementation reviews that focus on depression interventions in LMICs (Wagenaar, *et al.,* 2020; Means, *et al.,* 2020). Thus, I would recommend that future studies should be based on implementation-based questions and research objectives such as exploring feasibility, acceptability, and sustainability of the intervention. Also, future research should focus on assessing the interventions' effectiveness and their implementation in resource-constrained settings, which focuses on later implementation stages outcomes such as cost, penetration, and sustainability (Means, *et al.,* 2020).

I found that the provision of mental health training to lay or community healthcare workers was an important facilitator for implementation. This finding is in line with the results of other systematic reviews: it is essential to provide training to lay healthcare workers or community healthcare workers to provide mental healthcare (Connolly, *et al.,* 2021). The type of training and the number of sessions required will vary according to the healthcare workers' baseline characteristics and their previous knowledge of mental health and mental health interventions. There is some preliminary research on the activities within training that are necessary to implement sustained change, such as formal appointment of supervisors and self-reflection or evaluation of fidelity to the intervention, to name a few (Murray, *et al.,* 2011). Training content should cover basic information about mental health conditions, interventions, terminology, diagnostic, and referral criteria. Also, the provision of mental health and TB knowledge to people, families, and communities facilitates implementation. Other studies have similar findings: when mental health interventions facilitate interaction between providers, beneficiaries, and their families, in culturally appropriate ways, it facilitates the implementation process and creates a positive experience for those involved (Qureshi, *et al.,* 2021). When healthcare workers felt they lacked the skills to address mental health in their people, they regarded this as a barrier to

integrate mental health assessments or related activities in their practice (Wakida, *et al.,* 2018).

My findings in this review described how all interventions and their implementation processes incurred in costs, mainly related to the use of human resources, training, and physical spaces. This finding is consistent with the results of a systematic review that analysed the effectiveness and cost-effectiveness of integrating mental healthcare in LMICs, where the findings of the study discuss that all interventions arms increased effectiveness of depression treatment and costs (Cubillos, *et al.,* 2021). The cost of the intervention and its implementation can be attributed to the legacy of insufficient funds allocated to mental healthcare (Rathod, *et al.,* 2017). "*Given the low levels of spending on mental healthcare…the finding that increasing the availability of mental health services increases direct costs should not surprise*" (Cubillos, *et al.,* 2021:p.48). Based on evidence from 42 studies, the integration of mental health services for depression in primary care can result in an immediate increase in health costs at the service level, mainly due to increased use of human resources and cost of treatment, but are cost-effective from a healthcare perspective or reduce costs from a societal perspective (Cubillos, *et al.,* 2021).

To date, there is not a systematic review that analyses the costs of implementation of depression interventions in LMICs, which makes it hard to assess what resources are needed for implementation. In all the included studies it was mentioned that there were not enough resources available for TB services which will impact the feasibility of the implementation of mental health interventions in routine TB services. This tension overlaps with the availability of human resources for the delivery of mental health services. It is often not enough to train existing healthcare workers to deliver mental healthcare in a context of poorly resourced workforce (Qureshi, *et al.,* 2021). Further resources should be created and earmarked to facilitate the training of healthcare professionals on mental healthcare, add dedicated healthcare workers to provide mental healthcare, add specific mental healthcare tasks to existing care pathways, or use a care coordinator (Cubillos, *et al.,* 2021). The findings of this review suggest that the addition of workload related to mental health to existing healthcare workers is likely to be unfeasible and unsustainable within existing TB programmes. TB services in LMICs are well established and have dedicated resources apart from wider health systems structures (Lei, *et al.,* 2015). Thus, in this context, it would be more effective to earmark existing resources to train TB healthcare

workers on mental healthcare delivery or use care coordinators to integrate mental healthcare into people with TB's care. Mental health interventions in LMICs can be more effectively implemented if they adhere to existing care pathways and service delivery networks (Qureshi, *et al.,* 2021).

The provision of training alone is not sufficient if this is not accompanied with earmarked resources that create a space to deliver these interventions in existing service delivery structures, including considerations to increase the number of providers. TB services, as part of their aim to provide person-centred care (Global Fund, 2019), could frame that as a window of opportunity to create said space and use existing resources to deliver mental health interventions for people with TB as part of their routine care.

Greater understanding and information on the organisational Characteristics of TB services such as the internal **Incentives and rewards,** the role of **Peer Pressure,** the **Learning Climate,** or the **Individual Identification with the Organisation** can help to inform how to integrate care for mental health into TB services so that they can be feasibly and sustainably delivered. Understanding organisational characteristics can help to plan adequate interventions and implementation strategies. For example, interventions for depression that include financial incentives can help to alleviate the economic vulnerability of people with TB in LMICs (Richterman, *et al.,* 2018; Boccia, *et al.,* 2011). This is important to explore because the way that TB care is financed and provided in LMICs, which includes a range of organisations and collaborations (Bowser, *et al.,* 2014). Published peer reviewed systematic reviews hint that health system characteristics such as funding structures and available human resources can become important barriers for implementation if they are not addressed before implementation stages, or if there are not discrete resources allocated to the integration of mental healthcare in existing health services (Wakida, *et al.,* 2018).

4.4.3 Limitations

I found that the CFIR framework may not be able to capture the full complexity of TB services and their impact on mental healthcare delivery in LMICs. Although this framework was useful in identifying barriers and facilitators, there were characteristics from local health systems that I could not code to the existing sub-domains in the framework. For example, national and international donors for TB and mental health programmes can influence the interventions that are implemented, based on their preferences and agendas

(Qureshi, *et al.,* 2021). Adaptations that make the CFIR framework more relevant to LMICs contexts are possible and should be explored as they can help assess barriers and facilitators that are prevalent in resource-constrained settings (Means, *et al.,* 2020). In line with the findings from other reviews (Wagenaar, *et al.,* 2020; Means, *et al.,* 2020), the next research priorities should move away from trying to test the effectiveness of interventions and rather focus on the implementation strategies and outcomes that can lead to successful implementation efforts of depression interventions in LMICs.

4.4.4 Differences between protocol and review

Outcomes of interest described in the protocol were defined as “those described in eligible studies, which could be process or clinical outcomes, for example: process outcomes (e.g., number of diagnostic tests performed, number of people with access to the intervention to treat depression) or clinical outcomes (e.g., people with negative sputum smear test, mortality, people with reduced depression severity)”. In practice, I did not extract any of this data as it was not consistently reported across studies, and it was not required for the main analysis of barriers and facilitators.

Due to the objectives of this study, the information I analysed corresponds only to that reported in the published studies and is therefore subjected to reporting bias in the individual studies. Although I carried out a quality assessment according to each study type, this did not influence the weight of how findings were represented in this review as this study was concerned with providing a narrative synthesis of the approaches to depression care in TB services. Thus, this study should not be misinterpreted as evaluating the effectiveness of the interventions included in the analysis. Nonetheless, I am confident that I was able to identify and describe the various diverse approaches that have been implemented in providing depression care in TB services in LMIC.

4.5 Conclusion

In this review I aimed to identify the approaches used in LMICs to provide depression care for people with TB. I also aimed to explore the barriers and facilitators for their implementation.

4.5.1 Future research

I designed the protocol and carried out this review before the COVID-19 pandemic. Thus, this review includes studies that were published or carried out before the pandemic. I

consider that the results presented here are likely to not be reflective of the current status of mental health and TB services in the countries of the studies included in this review. A feasible way to improve this review would be to include an analysis of how the TB and mental health services of the countries represented have been affected by the pandemic.

I identified psychological interventions as the most common approach used to deliver depression care for people with TB in LMICs. The findings from this review suggest that implementation of interventions for depression is facilitated by the belief that the intervention is advantageous to the status quo (i.e., no provision of mental healthcare) (**Relative Advantage**), the **Compatibility** of the intervention with existing workflows, and the positive attitude that people, families, and communities display towards the intervention (**Innovation participants**). All the interventions faced barriers for implementation related to the **Costs** of the intervention and/or implementation, which were expressed in terms of costs associated with insufficient human resources, lack of physical resources, and lack of financial resources altogether for the provision of mental healthcare to people with TB. The choice of the best intervention to implement will depend on available resources and the attitude of stakeholders to the intervention. From the evidence reported in the included evidence in this study, it appears that psychological interventions with some form of community engagement are the most compatible with local attitudes towards mental health interventions and can be delivered with existing or little additional resources, if training is provided. These are important factors that will facilitate the implementation of these types of interventions.

4.5.2 Lessons learned

The availability and reliability of the information on implementation efforts depend more on the study design (e.g. feasibility and acceptability) rather than on the intervention type being implemented (e.g. psychological, combined). Because the nature of the majority of the studies was not focused on implementation, that meant that a lot of cells within the framework matrix were empty (no data) for most intervention types and studies, except for two which had implementation-focused study designs (Diez-Canseco, *et al.,* 2018; Walker, *et al.,* 2017). This is consistent with other implementation reviews that focus on depression interventions in LMICs (Wagenaar, *et al.,* 2020; Means, *et al.,* 2020). Future studies should be based on implementation-based questions such as the feasibility, acceptability, and sustainability of the intervention. Future research should focus on assessing the interventions' implementation in resource-constrained settings, focusing on the later

implementation stages' outcomes, such as cost, penetration, and sustainability (Wagenaar, *et al.,* 2020). It has been established in the previous chapter and in peer-reviewed articles that providing mental healthcare to people with TB is beneficial to them, particularly given the intersectionality of poverty, mental illness, physical illness, and stigma that affects this population. Thus, by focusing on implementation research, steadier progress can be made to actually deliver sustainable mental healthcare to people with TB.

Chapter 5 – Barriers and facilitators for implementing depression care into TB services in LMICs: A qualitative case study of TB services in Karachi, Pakistan.

Chapter summary

As discussed in previous chapters, addressing depression in individuals with tuberculosis can significantly improve their mental health and health-related quality of life (Chapter 3). Various national tuberculosis services have made efforts to integrate mental healthcare into routine TB services, using diverse approaches and encountering distinct barriers and facilitators during implementation (Chapter 4). This chapter describes the qualitative case study I employed to explore further the barriers and facilitators for the implementation of an intervention for depression in people with TB in Pakistan.

The first section of this chapter describes the purpose of the study, and the research questions it aimed to answer. The second section contains background information about the prevalence of TB and mental health illness in Pakistan and health services in the country. It also describes the setting for the case study - the intervention implemented, and the implementing organisation. The third section describes the methodology used to address the research questions. The fourth section describes the results of my research and the approaches to addressing the research objectives. The fifth and last section covers the discussion of the research results, the strengths and limitations of case study methodology, and the limitations of this study.

5.1 Purpose of this study and research questions

In 2021, I identified a mental health intervention for depression in people with drug-susceptible TB implemented between 2017 - 2018 in Karachi, Pakistan (Pasha *et al.,* 2021). At the time, this was the first study I could find that described the evaluation of an intervention for depression in people with TB and explored the integration of mental health services into existing TB services, private and public. The study also described the allocation of participants to primary and tertiary care units and reported the outcomes of the intervention for depression in these categories. I considered this was a good

opportunity to explore further the barriers and facilitators to implementation of mental health interventions for depression in real settings and in established TB programmes, to further understand the role that context plays in its implementation.

I designed my study to focus on exploring the barriers and facilitators for implementation of a mental health intervention to diagnose and treat depression in people with drug-susceptible TB in Karachi. I addressed this overarching research aim through the following research objectives:

1. To identify and compare the components of the mental health intervention for depression implemented in public and private services.
2. To explore the barriers and facilitators to implementation, defined for the purposes of this study as the delivery of the intervention for depression, at private and public care facilities. Barriers and facilitators were explored by assessing the influence of the intervention, the outer setting, the inner setting, the participants, and the implementation process activities on the delivery of the intervention (Damschroder, *et al*., 2022). See section 3.3.3 Data analysis for the definitions of these terms.
3. To explore the sustainability of the implementation of the intervention for depression following the end of the study in 2018 to date. For the purposes of this study, I defined sustainability as the sustainment of an intervention, an implementation outcome assessing whether “an intervention continues to be implemented over time” (Moullin, *et al*., 2020).

The following sections described the TB and the mental health services in Pakistan as the context in which the intervention for depression was implemented.

5.2 Background: TB and mental health services in Pakistan

5.2.1 Prevalence of TB and depression in Pakistan

The Islamic Republic of Pakistan is a country in South Asia. It has land border with India, Afghanistan, Iran, and China. It has a coastline along the Arabian Sea and the Gulf of Oman. It is the fifth most populous country in the world, with a population of 231.40 million (World Bank, 2021). The country is organized in four provinces (Punjab, Khyber Pakhtunkhwa, Sindh, and Balochistan) and three territories (the capital territory of Islamabad, Gilgit-Baltistan, and Azad Jammu and Kashmir).

Pakistan is considered a TB “high burden country” (WHO, 2023a; WHO, 2023b). The STOP TB Partnership ranks Pakistan as the 5th country in the world with the highest TB burden, contributing 5.8% of the new cases of TB worldwide (Stop TB Partnership, 2024). According to national data, in 2019 the incidence of TB in Pakistan was 562,000 (National TB Control Program Pakistan, 2019a). The country accounts for 61% of the TB burden in the WHO Eastern Mediterranean Region (WHO, 2023b).

Pakistan has the highest prevalence of common mental disorders, including depression, in South Asia (Naveed *et al.,* 2020). A recent umbrella review estimated that the prevalence of depression in the general population can vary from 10% to 24% (Vidyasagaran, *et al*., 2023). Another study estimated that 33.62% of the general population (n=2658) has depression symptoms (Mirza and Jenkins, 2004). Thus, there is wide variation in the estimates of prevalence of depression in the country. This can be due to lack of routine data collection on mental health statistics in healthcare services, and the lack of high-quality surveys with a sample size representative of the general population.

A few studies have assessed the prevalence of depression in people with TB in different provinces. In Punjab, a cross-sectional study of 12 treatment sites estimated that the proportion of MDR-people with TB with depression at baseline was 42.8% (n=1279; 95% CI) (Walker, *et al.,* 2018a). Other study found that 48 out of 60 in people receiving TB treatment in hospital had depression symptoms (Sulehri, *et al*., 2010). In Khyber Pakhtunkhwa, it was estimated that 65% MDR-people with TB had depression at baseline (Mehreen *et al.,* 2015). One study in Sindh reports that 51 out of 100 people with TB had moderate to severe symptoms of depression in the PHQ-9 scale (Rizvi, 2015). Other study in Sindh reports that 50 out of 108 people presented depression symptoms (Husain *et al.,* 2008). However, the results of these studies cannot be generalized to the wider TB population due to their non-representativeness, and, without such information, TB services are unprepared to address the mental health needs of people with TB.

5.2.2 National TB services

The National TB Control Programme (NTP), part of the National Institutes of Health, oversees and regulates the strategies and technical guidance of the national TB control activities. The provincial TB programmes deliver TB control activities designed at the national level (National TB Control Program Pakistan, 2014). The current structure of TB services in the country is the result of the devolution of control to the provinces in 2011

(National TB Control Program Pakistan, 2014). The NTP also provides monitoring and reporting of programmatic and financial performance to the Global Fund as it is the largest external donor for TB control in the Country (National TB Control Program Pakistan, 2014). The NTP and TB control activities are mostly funded by international donors. According to national sources, 85% of TB control funding is from international donors (National TB Control Program Pakistan, 2014). The WHO estimates that international donor funding contributes between 52% to 61% of the national TB spending in low-income countries with high TB burden (WHO, 2023a).

The NTP has thus designed and defined roles at the national, provincial and district levels to support the provinces in the delivery of programmatic TB control. TB treatment and surveillance is carried out in different types of private or public healthcare facilities: tertiary care hospital, district headquarter hospital, tehsil headquarter hospital, civil hospital, rural health centre, basic health units located in the TB patient's district of residence, or medical dispensaries (Department of Health Sindh, 2014). There are four different agreements with the private sector that establish collaborations between the NTP and private providers to provide TB care (National TB Control Program Pakistan, 2014).

The role of the private sector in TB control in the country is quite relevant. At least 50% of the basic health units, akin to primary care centres, are managed and owned by NGOs or the private sector (National TB Control Program Pakistan, 2014). There are different privately owned facilities providing TB treatment in the country, including pharmacies, solo practitioners, NGOs, private clinics/hospitals, amongst others. According to NTP reports, the first contact people have with the health system is through private providers, which often includes traditional healers (National TB Control Program Pakistan, 2014). An example of collaborations between the private sector and the NTP is the agreement with the Indus Hospital & Health Network (IHHN). IHHN is a non-for-profit organisation which provides free healthcare services at the point of access for a range of treatments, including TB. IHHN became a NTP partner through the establishment of public-private partnerships (PPM) so they have access to and manage financial and human resources necessary to the delivery of TB control programmes in their facilities (Indus Hospital and Health Network, 2021). The IHHN is one of the main recipients and administrators of national and international financial resources targeted for TB control programmes in Pakistan: they are one of the only Global Fund grant recipients in Pakistan for the control of HIV, TB and malaria (Indus Hospital and Health Network, 2021).

Although nationally and internationally TB care practices are meant to be standardized, the TB care that people in Pakistan actually receive varies in quality and there are typically inadequate PPPs that do not always meet the needs of local populations (Braham, White, & Arinaminpathy, 2018). There are still issues to address such as under-reporting, loss to follow-up, and childhood TB (Stop TB Partnership, 2023). There are accessibility barriers such as long waiting times, cost of initial tests and travel to clinics, limited clinic hours, and unsuitable infrastructure without privacy (Stop TB Partnership, 2023). Furthermore, there are discriminatory attitudes in society against people with TB, including amongst healthcare workers, which contribute to impede access to TB care. These barriers, compounded with the underfunding of the wider health system, lack of healthcare staff, high poverty rates in the general population (and in people with TB), and the aftermath of the COVID-19 pandemic have exacerbated the incidence of TB in the country (Khan, 2017; Shaikh, et al., 2022).

5.2.3 Mental health services

Mental health services in Pakistan and their legislation were decentralised and transferred to the provinces on April 2010; the laws in each province had to cover three core tenets: *"(1) the government has to maintain and establish psychiatric facilities for treatment rehabilitation and assessment; (2) separate units for men and women, geriatrics, children and adolescents, substance rehabilitation and those convicted of a criminal offence; (3) community-based mental health services will be established to provide support to persons with mental illness, their families and caretakers*" (Shah *et al.,* 2022). However, people often opt for traditional practices such as faith-based interventions, "*hakeem*", homeopathy, and unlicensed medical stores (Shah *et al.,* 2022). Although awareness of mental health has increased in Pakistani society, stigma persists as a challenge to diagnosis and treatment (Sikander, 2020).

Pakistan's mental health services and their performance is underreported (WHO, 2022a). It appears that mental health service improvement and development is not a priority for the recent government even in a context of high mental illness burden and comorbidities (Javed *et al.,* 2020). Given the lack of specialized mental health workforce and the deficiencies in infrastructure, it is considered that the best approach to address the mental health needs of people in Pakistan is through interventions delivered by non-specialists, peers, or community healthcare workers, through outreach and community-based initiatives (Sikander, 2020; Todowede, et al., 2023; Zavala et al., 2023).

5.2.4 Integrated mental health and TB services

In Pakistan, TB and mental health conditions are not treated together in public services part of the NTP. Both conditions can be treated separately in public or private healthcare services but not as an integrated approach (Muhammad, *et al.,* 2023). Mental health interventions for depression in people with TB are not officially part of the management programme for drug-susceptible TB in Pakistan but they are included in the programmatic management of DR-TB (National TB Control Program Pakistan, 2014). To my knowledge this was the latest government publication available on the matter. For example, the monitoring of DR-TB treatment includes monitoring of adverse effects and psychological side effects (National TB Control Program Pakistan, 2017). When a comorbidity is identified in the initial TB assessment, the patient should be referred to the appropriate health service. Additionally, all TB healthcare workers working in DR-TB are supposed to receive training for providing counselling to people about TB treatment, infection control measures, and to provide psychosocial support (National TB Control Program Pakistan, 2017).

5.2.5 An intervention for depression in people with TB in Karachi, Pakistan

The implementing organisation and its role in national TB services

In 2017, one non-for-profit and non-governmental organisation designed and implemented an intervention to provide psychological counselling for people with drug-susceptible TB and symptoms of depression in Karachi, Sindh. This organisation (from here on referred to as the implementing organisation) describes itself as a developmental organisation working in low-and-middle-income countries and describes its participation on diverse public health initiatives such as diabetes control, antenatal TB care, smoking cessation, immunization, community mental health, and deworming in Pakistan. Before the implementation period for the intervention described below, the implementing organisation had partnered with the Government of Sindh province, the Indus Hospital and Health Network, and other international NGOs such as Médecins Sans Frontières and Partners in Health to provide TB control activities in Karachi.

The implemented intervention

The intervention designed and implemented by the implementing organisation aimed to reduce symptom severity for depression and anxiety and to improve treatment adherence for people with drug-susceptible TB (Pasha, *et al.,* 2021). The name of this intervention was “IPUs” which stands for “Integrated Practice Units.” The Aga Khan University Anxiety and Depression Scale (AKUADS) was used for initial diagnosis, monitoring progress, and assess recovery of depression and depression symptoms. This is a 25-item indigenously developed, Urdu language screening tool measuring depression and anxiety, and validated with the local population. The implementation team assessed depression and anxiety outcomes at baseline and at the 4th session. If people were still symptomatic at the 4th session, they were offered additional sessions and re-assessed with AKUADS at each of these additional sessions. Figure 5.1 is a graphic description of the intervention as described in (Pasha, *et al.,* 2021).

The results of the IPUs intervention

The study reported that 1,012 people with drug-susceptible TB and with depression symptoms received the intervention. Participants were 51.4% men and 48.6% women; their mean age was 34.8 years (Pasha, *et al.,* 2021). The results of the intervention showed statistically significant decrease in depressive symptomatology and severity, with an average decrease of 16 points (p-value <0.0001) for people who received the intervention (Pasha, *et al.,* 2021). The TB treatment completion rates for participants with depressive symptoms who received the intervention were similar to those of non-symptomatic participants at baseline. Of people who received 4 counselling sessions, 92.7% completed TB treatment; of people who received 6 or more counselling sessions, 95.5% completed TB treatment. Thus, the authors of the published study of the intervention concluded they observed an improvement on people’s clinical outcomes for TB and mental health as a result of their participation in the intervention.

However, the study did not collect information on the barriers and facilitators for delivering depression care as part of routine TB services as it was not its original aim. The analysis of barriers and facilitators for implementation of this intervention can provide useful insight into the process and experience of implementing this type of interventions for depression in established TB programmes in LMICs. The implementation experience of this intervention can provide useful insight to other settings in LMICs aiming to do the same. The IPUs provide an opportunity to explore the implementation process of a non-public organisation working with public TB services.

I approached the authors of the published study and established professional relationships with them. These discussions held with the implementation team and conversations with my academic supervisors informed the design of the research methodology I used, described in the following section.

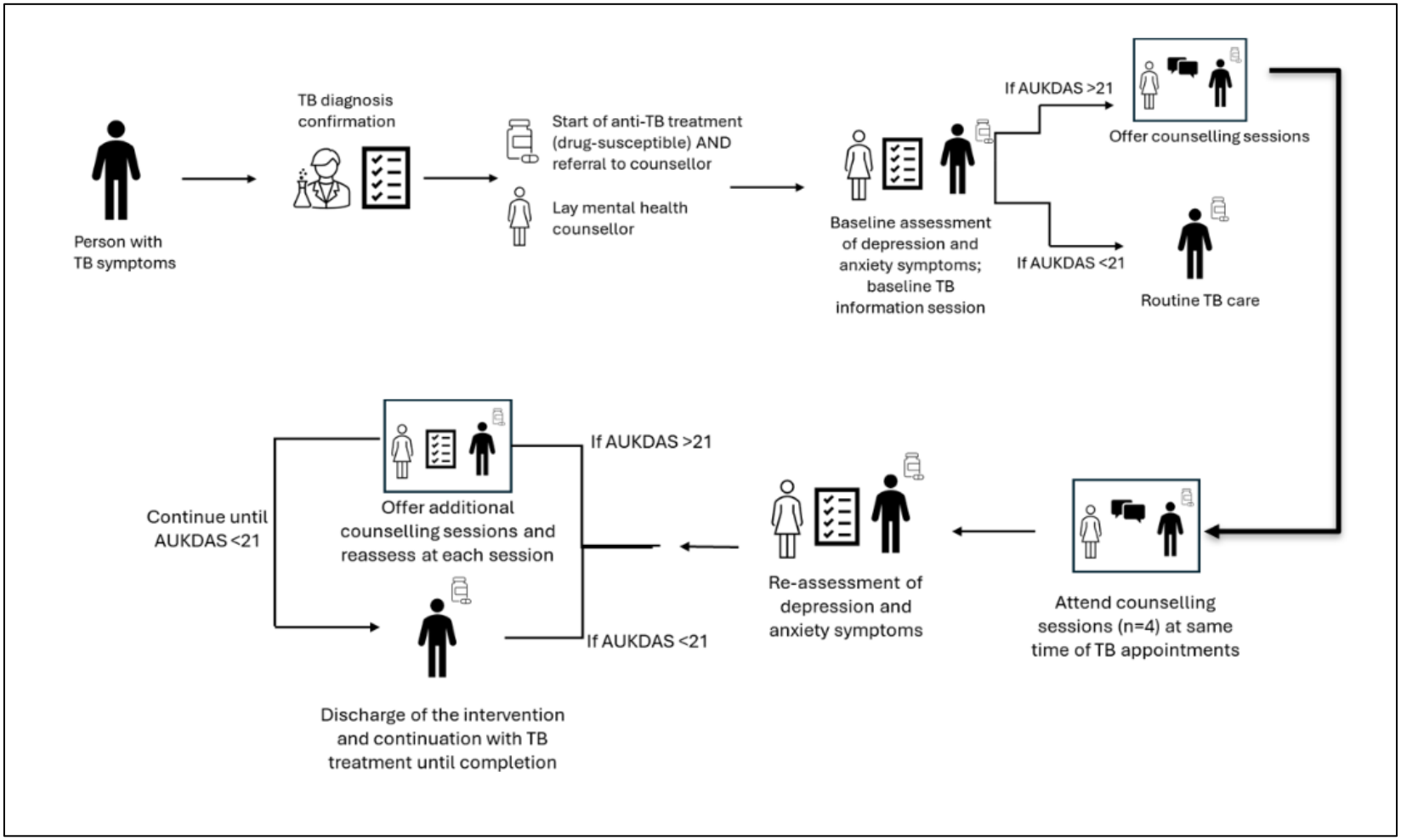

Figure 5.1 Care pathway for people with TB receiving the "IPUs" intervention

5.3 Materials and methods

5.3.1 Research methodology and study design

I decided to use qualitative case study research methodology to address the research objectives in 5.1. Case study methodology allows to explore how this intervention was implemented and gain in-depth knowledge about the implementation process as it is an "*empirical method that investigates a contemporary phenomenon (i.e., the case) in-depth and within its real-world context*" (Yin, 2017). Case study research as an epistemology aims to understand the context and the mechanisms that explain the observed phenomena (Yin, 2017; Emmel, *et al.*, 2019; Creswell, 2017). The relevance of case study methodology for research in health services research interventions is increasingly being recognized as a helpful methodology to understand the factors that influence implementation in complex healthcare systems. Examples from nursing and community health disciplines allude to the usefulness of case study methodology in understanding context-specific factors that can increase the likelihood of success of implementation programmes (Fabregues & Fetters, 2019; Heale and Twycross, 2018; Sibbald, *et al*., 2021).

The understanding of the contextual conditions around the phenomenon of interest, i.e., the case, is one of the key features of case study research. Case study research methodology can accommodate, and encourages, the use of multiple sources of evidence to address a research objective that focuses on a contemporary phenomenon and situate the phenomenon of interest within its context (Yin, 2017). It can also allow for comparison within and across cases which is compatible with my research objective of exploring, analysing, and comparing barriers and facilitators in public and private facilities (Creswell, 2017; Yin, 2017). In case study research methodology, the comparison and cross-case analysis of two or more cases can help to identify patterns, relationships, and theoretical insights by improving variation and representation of different underlying mechanisms and contextual factors unique to each case (Bartlett & Vavrus, 2016).

At the time I conceived this study as case study research, it was 2020 and the phenomenon of interest was still contemporary and relevant. Case study research methodology has distinct advantage when they deal with contemporary events (Yin, 2017). Furthermore, case study research methodology allows to focus in-depth on a case while retaining a holistic view of the interactions with its wider national and international

institutional context, using exploratory and descriptive approaches (Yin, 2017; Patton, 2002; Creswell, 2017). Thus, I considered that the epistemology of case study research methodology and its ability to include multiple methods and data sources would help me to address the research objectives by collecting and analysing data from different evidence sources and address the exploratory nature of the research questions described in 3.1.

One of the disadvantages of using case study research methodology is the intensity of resources required for data collection and data analysis. This risk can be mitigated by establishing clear selection criteria for the data sources included (Yin, 2017). I aimed to mitigate this risk by defining clearly the “Case,” the “Conte,””, the selection criteria, and the data sources I would include. This process was iterative. First, I scoped the existence and relevance of data to address my research questions, and second, I scoped the access I would have to this data and its availability. As much as possible, I carried out these two activities prior to fieldwork and prior to the definition of “Case” and “Context”.

Adapting case study methodology to my research questions

I used the five components for case study research design outlined by Yin (2018) as a guide to adapt this methodology to my research objectives. Their purpose is “to avoid the situation in which the evidence does not address the research questions” (Yin, 2017). The five elements are (i) a case study’s questions; (ii) its propositions, if any; (iii) its case(s); (iv) the logic linking the data to the propositions; and (v) the criteria for interpreting the findings. Below I explained how I used these elements to design my research methodology:

1. Case study’s questions. Case study research is most appropriate to “how” and “why” questions, but this is only a blueprint for design; according to Yin, it is possible to define the research questions iteratively doing literature reviews and preliminary fieldwork to identify the relevant questions for the methodology (2018). I defined the case study’s questions as the research objectives outlined in section 3.1. These were formulated and defined after I did some preliminary fieldwork by discussing with a contact in the field what kind of data was available and accessible. Thus, I ensured that data available in the field would be relevant to answer the research questions. The research objectives in 3.1. were also based on existing research gaps and the findings of the previous chapters, which include literature reviews. I carried out the process of defining

the research objectives iteratively, along with discussions with fieldwork contacts and my academic supervisors.

2. Case study's propositions. The propositions of a case study serve to direct the attention to what should be examined and included in the scope of study (Yin, 2017). The propositions of the case study can be exploratory, as long as the purpose is explicit and there are criteria to delimit the exploration (Yin, 2017). For adapting the case study methodology to my study, I defined the following propositions: a) the implementation of the IPUs have varying degrees of fidelity and adherence to protocol in the implementation sites, therefore warranting the exploration of the implementation process from the perspective of relevant stakeholders; b) the implementation of IPUs in TB services faced barriers and facilitators, and these varied across implementation settings; and c) the implementation of a mental health intervention for depression in any given setting can be explored by using different sources of data, such as observations of the site, interviews with relevant stakeholders, and documents that were routinely used during the delivery of the intervention.
3. The cases. According to Yin, there are two elements in identifying the cases to be studied, which are defining the case and bounding the case (2018). As it is possible to define the cases as organisations, I decided to use this classification given the information publicly available about the intervention I was interested in exploring. In the peer-reviewed article describing the intervention, it was described how the IPUs were implemented in public and private facilities; I chose the organisations the facilities were affiliated to as the cases to be studied. This definition of the "Cases" allowed me to have clear boundaries from other organisational stakeholders that might be part of the "Context" and extend this distinction between "Case" and "Context" to the data collected. Thus, helping to keep the case study delimited and feasible.
4. Linking data to propositions. Yin suggests different techniques to achieve this: pattern matching, explanation building, time-series analysis, logic models, and cross-case synthesis (2018). I chose a qualitative analytic approach similar to the analytic approach I used in the previous chapter as it is consistent with pattern matching and explanation building. Plus, the case design would allow me to do cross-case analysis in relation to the research objectives.

5. The criteria for interpreting the findings. This design element refers to the ability of the researcher to be critical of their methods and findings (Yin 2018). It is suggested that rival explanations should be considered when designing and analysing designing a case study to avoid pitfalls of confirmation bias or observer effect (Yin, 2017). I addressed these elements in the sections 3.3.4 Reflexivity, and 3.5.2 Reflections. My fieldwork log and the reflective log I kept during the analytical stages are available upon request but were not included in this thesis due to space limitations. Furthermore, I also addressed elements of trustworthiness of data and reliability and validity of my research methods using the Standards for Reporting Qualitative Research (SRQR) and Consolidated criteria for Reporting Qualitative research (COREQ) (O'Brien*, et al.,* 2014; Tong, Sainsbury, & Craig*,* 2007).

The case

I defined further the cases according to the case study design principles outlined by Yin (2018). The cases within this case study are the facilities where the mental health intervention for depression was implemented in Karachi, Pakistan in 2017 - 2018. The phenomena of interest that were explored within these cases were the activities carried out during, and after, the implementation of the IPUs. See Figure 3.2 for a graphic description of the analytical relationship between the phenomenon of interest, the cases, and the context.

I established the following boundaries to delimit the "Case":

- The cases, or units of analysis: This was a multiple-site case study. The intervention was implemented in two types of facilities, public and private. Thus, Case A was defined as private facilities (n=3 facilities) and Case B was defined as public facilities (n=3 facilities). This case study design as a multiple, two-case study, follows a replication rather than sampling logic (Yin, 2017). This means I designed the case study as to have two similar cases (i.e., the private and public TB facilities acting as implementation sites) that would allow comparison between them.
- Spatial boundaries: I defined these as the facilities, and the organisations they belonged to, where the IPUs were implemented, i.e., the implementation sites. These facilities were three public tertiary care facilities and three private facilities,

two primary care facilities, and one tertiary care facility. For the purposes of this study, I defined public organisations as those belonging to the NTP and/or funded entirely by the national government. I defined private organisations as those organisations funded by out-of-pocket payments, charity, and/or international donors. This classification was developed iteratively during the data collection and data analysis stages as I became more familiar with the structure of national TB services.

- Time boundaries: The design and implementation of the intervention, as described in (Pasha *et al.,* 2021), had clear start and end timepoints of 2017 and 2018, respectively. I defined the time limits of the Case to span 2017 to 2022 to allow the inclusion of relevant data collected during my fieldwork in 2022.

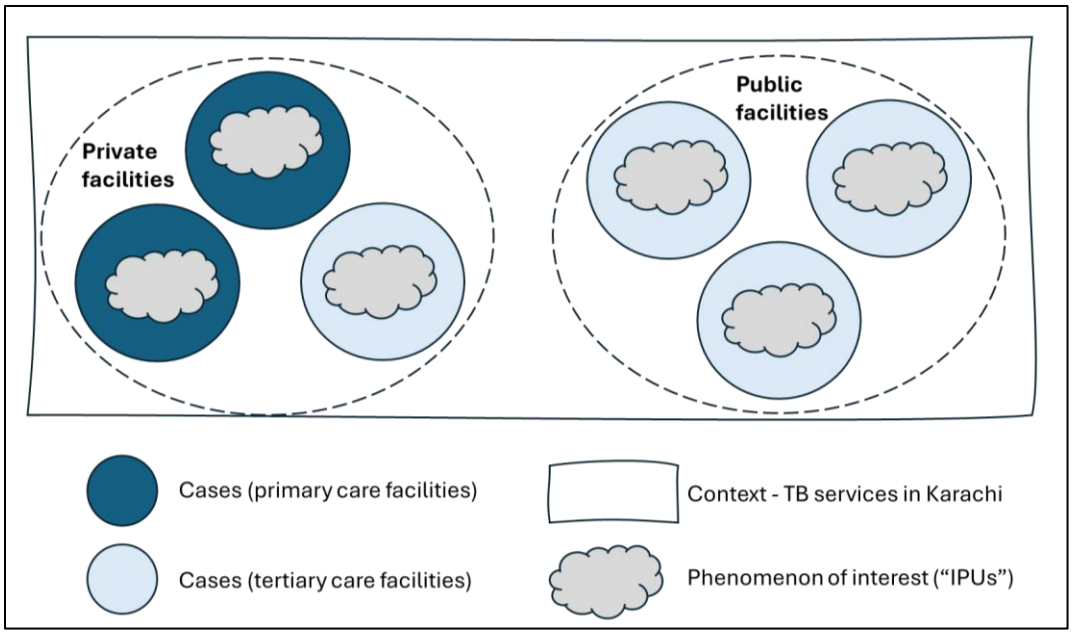

Figure 3.2 Illustration of the planned analytic relationship in my case study design; adapted from (Yin, 2017).

The Context

There is less definitive guidance on how to define the context of a case study as opposed to the definition of the case. Context can be defined as "*data external to the case*" (Yin, 2017). One feature of case study methodology is that boundaries between the context and the phenomenon of interest might not be clear, which is a characteristic feature of real-world situations (Yin, 2017). However, I chose to define the Context using similar

boundaries, as applicable, for defining the Case in order to keep this research study manageable.

- Spatial: The Context boundaries of the Cases were limited to other organisational stakeholders of the NTP in Sindh. This included non-governmental organisations (NGOs), unilateral or multilateral donors, and other national and international stakeholders working in or funding TB service delivery in the province. Only the data relevant to these stakeholders was collected. I considered the international and national TB-related policies as part of the Context, whilst the organisations , and internal organisational policies, to which the implementation sites were affiliated to were part of the Inner Setting and Outer Setting of the CFIR domain as appropriate (Damschroder, et al., 2022).
- Time: I defined the time boundaries of the context in the same manner to the time limits of the case, thus including data from 2017 to 2022 to allow the inclusion of relevant data collected during my fieldwork in 2022. However, I acknowledged that the analytical approach would be retrospective given the time elapsed since implementation and likely descriptive as I would not be able to observe the implementation process *in vivo*.
- Socio-cultural: I defined the socio-cultural context as that of the city of Karachi, at the time of fieldwork, i.e., 2022.

5.3.2 Methods for data collection

I collected data during fieldwork in January 2022 and February 2022. Before starting fieldwork, I contacted a person working at the implementing organisation. This contact helped me identify and have access to key informants for the interview studies; they also helped me identify and access the organisational documents used in the design and implementation of the intervention; and lastly, they helped me identify the sites where the intervention had been implemented, as this data was not publicly available in the published results of the intervention (Pasha, *et al.,* 2021).

I followed a relativist data collection procedure (Creswell, 2017; Yin, 2017). I employed qualitative methods to collect the data for answering the research questions of this study whilst representing the different perspectives of the stakeholders involved in implementation and the different implementation settings. I created a table (Table 5.1) to

keep track of the type data collected, date of collection, description, and its potential contribution to the research questions to increase transparency (Lincoln & Guba, 1985; Yin, 2017). The approach I used to collect data was informed by the principles suggested by Yin for case study research (2018) which emphasize the use of multiple sources of data. I used semi-structured interviews with key stakeholders, documentary analysis, and observations and site visits as data collection methods. The data collection and data analysis processes for each method are described below.

Semi-structured interviews

Based on the information publicly available about the intervention, I created four interview guides (Appendix 9) for the different types of participants I identified in the published results of the intervention (Pasha, *et al.,* 2021). The participants for this study were defined as healthcare workers, study leads, facility managers, and policymakers that were involved in the design and implementation of the depression intervention for people with TB between 2017 and 2018. It was not possible to interview people with TB who received the intervention as my contact in the implementing organisation said they had no way of contacting any people as a lot of time had passed since the implementation process.

Sampling, target group, and identification of participants

I used purposive sampling, i.e., I only interviewed people who had been part of the implementing organisation at the time of the IPUs implementation and had an active role in it, people who worked at the implementation sites at the time of the implementation period, and people who had knowledge of the TB system in the region. I limited the number of participants to a minimum of 11 and a maximum of 20 given the difficulties of access to participants, fieldwork costs, and my time availability. This sample size aligned with the concept of information power, which I considered appropriate for this study (Malterud *et al.,* 2016). For each type of participant I had identified, I established the following sampling criteria:

- Healthcare workers: defined as the people who were trained to deliver the intervention for depression in people with TB. I had aimed to interview between four and eight participants of this group.

- TB facility managers: defined as the managers of the TB department of the facilities where the intervention was implemented. I had aimed to interview between two and four participants of this group.
- Study leads: defined as the authors of the publication where the intervention and its outcomes are described (Pasha *et al.,* 2021). I had aimed to interview at least two and maximum six participants of this group.
- Policymakers: defined as policymakers working in TB control and/or mental health in Karachi, Pakistan, during the time of the intervention's implementation. I had aimed to interview at least one participant of this group and a maximum of two. The reason for the underrepresentation of this group was due to the feasibility of contacting elite interviewees in a foreign context and my lack of contacts with senior TB officials in the country.

Access to participants and recruitment

I gained access to the groups of study leads in the months prior to the start of my fieldwork by contacting them through email. The access to facility managers and policymakers was through fieldwork by visiting the implementation sites to introduce myself and the study; my contact at the implementing organisation could not facilitate this access. The access to local policymakers was facilitated by local contacts working in national and regional TB programmes with access to policymakers in Sindh. The access to the healthcare workers was mediated by my contact working at the implementing organisation. They explained that healthcare workers had limited access to email or other means of digital communication, and the best method to approach them would be over the phone. My contact at the implementing organisation arranged and carried out introductory phone calls with the healthcare workers, through which they agreed to read the participant information sheet and consent form before their participation in the interview. I am unaware of the number of introductory phone calls my contact made. I met with three healthcare workers face-to-face and had phone calls with the other three healthcare workers.

17 interviews were carried out using a mix of face-to-face, telephone, or videocall (via Zoom) methods. The interviews lasted between 30 and 80 minutes, and were mostly carried out in English, except for the interviews with the healthcare workers (n=6) which

required the help of a local translator. I employed two students from a local university fluent in English and Urdu to help with in-vivo translation before and during the interviews with the healthcare workers. All participants received an information sheet with the information of this study and signed a consent form before their participation; see 3.3.5 Ethical approvals.

Data management

All the interviews were recorded using a voice recorder, a mobile application, or video recording features, depending on the medium of the interview. After the interviews, I created verbatim transcripts and removed identifiable data such as people's names and names of the facilities.

During face-to-face interviews I collected the consent forms signed by participants. These forms are secured and only accessible to me. The videos and audio recordings of the interviews are kept in a secure external storage device, encrypted and only accessible to me. For videocalls, only the audio recordings were used as data for this study; the videos were not included in the analysis. All data is also secured in my personal file store within the University of York's central network file store which guarantees confidentiality and protection of participants' data. In line with the University Research Data Management Policy, all the data that is used to support the published research findings of this study will be kept for 10 years from the date of last requested access.

Documentary analysis

Eligibility criteria

Eligible documents described and represented how the IPUs were designed and implemented (i.e., the case) and described and represented the context in which it was implemented (i.e., the context of the case). I created an eligibility criteria list based on the premise that documents in an organisational setting are situated products which are used and consumed and can help to make organisational processes and systems visible (Prior, 2003). Thus, I wanted to identify the documents that were used routinely during the intervention by people involved in the delivery of the components of the intervention (i.e., diagnosis, treatment, follow-up, referral) as a mean of describing the intervention through

the use of routine documents (e.g., logs of intervention delivery, logs of healthcare workers routine activities, meeting logs and notes, routinely collected data at the facility level, data collection forms with anonymised patient data, follow-up forms with anonymised patient data) and other documents used for the development, implementation and evaluation of the intervention (e.g., research reports, indicators for TB and/or mental health services delivered at the facility). I was also interested in documents possibly relevant to the design and implementation of the intervention, such as national TB and mental health guidelines and reports, to gain more knowledge about the context of the Cases. The source of these documents were national and/or provincial government websites, and national and international donor reports. I also included grey literature published by the implementing organisation or by the organisations that the implementation sites were affiliated with. I excluded any patient data contained in the documents as this was not relevant for the purposes of this study.

Sampling criteria

I anticipated that my eligibility criteria were too broad, for which I decided to create sampling criteria for the documentary analysis that would be compatible with my aims and research methods. *"…[Q]ualitative sampling for case study research is about appropriateness, purpose, and access to good information rather than representative and random/probability sampling, as with quantitative studies*" (Fletcher & Plakoyiannaki, 2010). I used the SPICE framework to translate this definition into clear sampling criterion for the Setting, Perspective, Phenomenon of Interest/Intervention, Comparison, and Evaluation (Harris, *et al.,* 2018). Although there are different frameworks that can be used for sampling and defining eligibility criteria, I selected SPICE because it addressed the setting and perspective elements around the phenomenon of interest, the IPUs of where the intervention of interest was implemented:

- Setting: Private, public, primary care, secondary care, and tertiary care facilities in the city of Karachi where the intervention was implemented.
- Perspective: Different stakeholders involved in designing and implementing the intervention, e.g., project leaders or managers, site managers, healthcare workers, working in the facilities where the intervention was implemented, working with the implementing organisation, or working with the organisation where the intervention

was implemented. This evolved iteratively as I identified additional stakeholders during the data collection process.

- Phenomenon of interest/intervention: Integrated Practice Units, implemented between 2017 and 2018.
- Comparison: None.
- Evaluation: Descriptive accounts of the intervention, barriers and facilitators for implementation, and the sustainability of the intervention after 2018.

I used six different search approaches to identify and retrieve eligible documents relevant for the implementation timeline of the IPUs. I categorized whether the document provided information about the Context or the Case, to clarify the use of this type of data in my analysis. The search approaches and a full list of the included documents are included in Appendix 6.

Data extracted from documents

The data extraction form I used to extract data from eligible documents was informed by the guidelines of using documents in social research (Prior, 2003). The data extracted consisted of the descriptive properties of the document (i.e., name, date of publication, date of analysis, author, purpose of document), descriptive accounts of the content (including intended audience), and descriptive accounts of the context (including the context of its creation, use, and consumption as a tool during the implementation process).

Observations and site visits

I visited the six implementation sites and the administrative offices of the implementing organisation. During the visits, I aimed to create descriptions of the activities, interactions, organisational context, facility characteristics, or any other observable aspect of the implementation sites (Patton, 2002). I approached the implementation sites with an introduction of my study, showing participant information sheets adapted from the ones used for interview participants, my credentials as a doctoral student from the University of York, and the associated ethical clearance for this project. During the observation visits, I used the following checklist to capture as much relevant information as possible: Place, participants, description of participants, chronology of events, material objects involved in

the setting, description of behaviours and interactions, records of conversations or other verbal interactions. See Figure 5.3 for a photograph of the observation form I used.

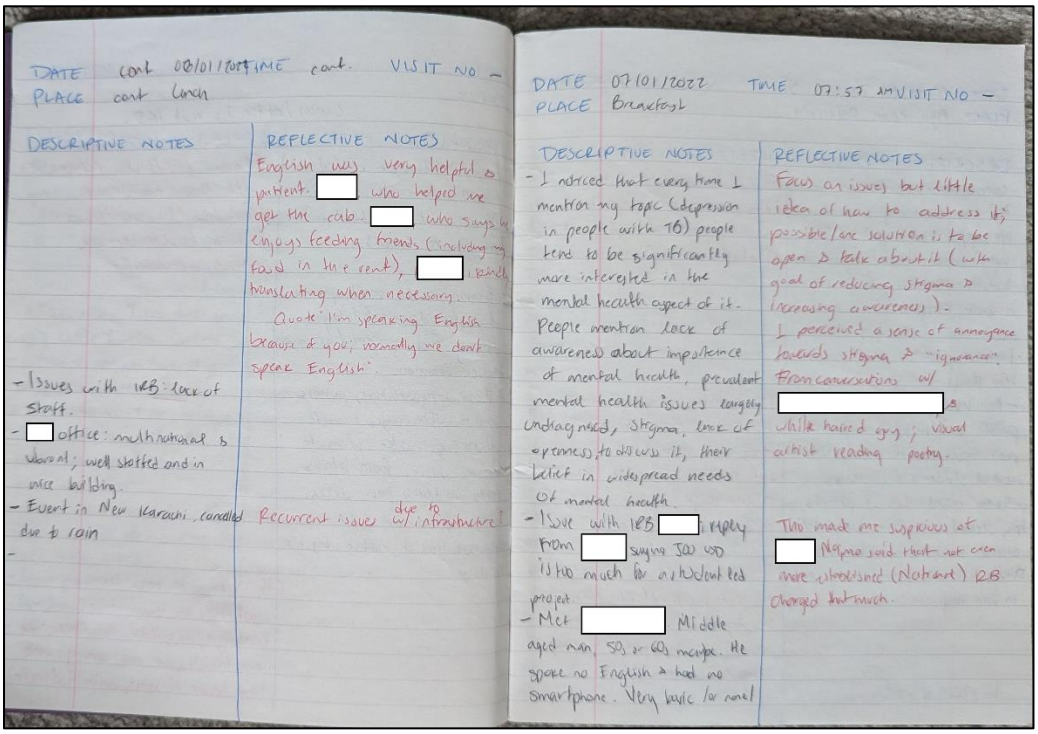

Figure 5.3 Photo of observation form used during site visits

Data management

During these visits I took written notes using the observation form. After the visits, I would record any thoughts using the audio recorder and compilated both notes, transcribed, in one electronic text file labelled with the name of the facility visited and the date of the visit. This helped me to improve the reliability of my notes by comparing written notes with audio recordings, and to create more detailed observation notes (Angrosino, 2007). The observation notes and audio recordings are kept in an encrypted external storage device.

5.3.3 Data analysis

In Table 5.1, I described all the data sources I used in the analysis and their contributions to the research objectives, including the name of the source, type, and source of the data, as well as their contribution to the Context or Case. I used NVivo for managing files during data analysis (QSR International, 2022). I imported all the documents generated from data collection such as interview transcripts, transcripts of fieldwork notes, and extant

documents. I coded the documents in January and February 2022, and again during February and March 2024, due to a break in my studies, and to familiarise with the data again.

To answer research objectives 1 and 2, I used the principles of iterative explanation building used in case study analysis to create a description of the intervention implemented (Yin, 2017). To answer research objective 3, I used a descriptive approach to the analysis of data collected. I used framework analysis as the main analytical approach (Gale et al., 2013; Pope, Mays, & Popay, 2007). The framework method is a flexible approach that can be used with many qualitative method, is consistent with pattern matching, an analytical technique suggested for case study research as it *"compares an empirical based pattern with a predicted one made before data collection*" p.175 (Yin, 2017). Framework analysis has been used in qualitative case studies exploring attitudes within health services (Munakampe *et al.,* 2024). I used the CFIR domains and sub-domains as *a priori* codes (the pattern) in the coding framework (Damschroder, et al., 2022). I coded the included data against the CFIR codes. I made the analytical decision to use the updated version of the CFIR framework instead of the previous version of the CFIR framework, which I used in Chapter 4, because the updated version included more sub-domains in the Implementation Process domain. Thus, I considered there was an advantage to use the updated version for the objectives of this study (Damschroder, et al., 2022).

For the purposes of this study, I adapted the definitions of the CFIR domains and constructs to specific definitions pertaining to my research questions and the phenomenon of interest (i.e., the intervention, innovation, or "IPUs"):

- I defined the innovation being implemented as the IPUs.
- The **Outer Setting** encompassed the national TB programmes, provincial TB services, non-for-profit organisations, and the socioeconomic, and political context in which these organisations sit at the provincial and national level.
- The **Inner Setting** referred to the private, public, primary, and tertiary care facilities where the IPUs were implemented. This was a total of 6 facilities, which means there were 6 Inner Settings.
- In the **Individuals** domain, I referred to the Individuals as those part of the implementation process for the IPUs. There are different individuals referred to in the original CFIR framework and the guidelines for its use specify that only those relevant

to the intervention should be used when applying the framework. Thus, I only adapted the definitions of the project implementation roles that were relevant to the implementation of the IPUs. These roles were high-level leaders, mid-level leaders, opinion leaders, implementation facilitators, implementation leads, implementation team members, other implementation support, innovation deliverers, and innovation recipients. For the **Characteristics of Individuals** subdomain, I adapted the definitions of the COM-B Model (Michie, Van Stralen, & West, 2011). in terms of the relevance of these characteristics to the project implementation roles described above.

- For the **Implementation Process** domain, I defined the implementing organisation as the organisation part of the Outer Setting that was responsible for the implementation process of the IPUs.

Trustworthiness of data

This can be defined as "*techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation)*" (O'Brien *et al.,* 2014). Trustworthiness of data can be akin to reliability and validity of data, covering four essential aspects of credibility, transferability, dependability, and confirmability (Morse, *et al*., 2002). As trustworthiness of data is a key element of quality in a case study, I incorporated activities through the data collection and data analysis stages of the case study that would help to ensure the member checking, audit trail, and transparency in triangulation processes. For example, after creating the transcripts, I sent them, password-protected, to some of the participants (when possible, as some of them did not have email addresses where I could contact them) to give them the opportunity to verify the fidelity of the representation of their answers into the transcript or express any discontent. I gave them a period of 30 calendar days from when I sent the email with the password-protected transcript. Two interviewees replied and agreed with the fidelity of the transcript; the rest of the interviewees I contacted did not reply.

To increase transparency on triangulation, the framework matrix output from NVivo (QSR International, 2022) with the summaries of data included in each code for each case is available. I have not included it in this document due to its size and length, but I would be happy to produce it if requested. in Appendix 11. I created and collated the analytic memos in an electronic text file and included them in as part of the case study data sources to help

establish the chain of evidence between research questions and findings (Yin, 2017). Furthermore, I have kept the quotes from the interviews exactly as expressed by interviewees and I chose not to edit grammatical inconsistencies to preserve their voice and to not interrupt the flow of quotes with “[sic]” notes.

Construct validity, internal validity, external validity, reliability.

This case study described the patterns of barriers and facilitators which were defined before data collection in the adaptations made to the CFIR framework for the purpose of this study, which was my method to strengthen the internal validity of this case study (Yin, 2017). The findings discussed in the results section represent the use of triangulation in two ways: first, triangulation of different data sources, and triangulation of different perspectives from participants. This was possible through the collection of different data sources, representative of a range of perspectives of people involved in the implementation process (Patton, 2002; Yin, 2017). Thus, the chain of evidence between the research questions, the methods outlined in the protocol, the specific citations in the case study database, and the findings outlined in this report, as it is suggested for a quality case study (Yin, 2017). Additionally, in the Reflexivity statement I address my particular position as a researcher and describe the social situations in which the research was done in order to improve the external validity and reliability of this project.

5.3.4 Reflexivity statement

During and after fieldwork, and while writing this chapter and the findings of my research, I reflected on how my own personal characteristics, beliefs, past experiences, and epistemological approach of my study influenced my work. This was my way to ensure that my research and this chapter met the criteria for reflexivity which means clarifying and making explicit the “*ways in which the researcher and the research process have shaped the collected data, including the role of prior assumptions and experience, which can influence… the inductive inquiries*” (Mays & Pope, 2000). My aim in writing this reflexivity statement is to clarify some of the experiences that shaped my research, particularly the data collection and analysis activities (Creswell, 2017; Flick, 2002).

I captured most of these reflections in a fieldwork log. I wrote on the fieldwork log almost every day during fieldwork, at night, after all the data collection and analysis activities were finished. I read back on these notes for writing this reflexivity statement and while doing the analysis.

One of the most note-worthy ways in which my attributes as a researcher influenced the study was the following: I established contact with the implementing organisation in 2021. I approached them with the idea of using one of their projects, the IPUs, as the focus of one of my doctoral studies. I shared with them the protocol for this study and, after we both were satisfied with it, we arranged logistics for me to travel to their offices in Karachi, Pakistan to conduct the study in January 2023. My main contact within the implementing organisation was part of the subject of my study thus I assumed that I would have full access to relevant materials and participants to carry out my research. Yet, after my arrival to their offices, I encountered organisational barriers to access documents and interview participants. This became a source of uncertainty and frustration during my fieldwork and led me to re-assess my relationship with the implementing organisation and their role in my study. Also, at the beginning of fieldwork, I began to acknowledge that some of my personal characteristics (being female, young, and a student) influenced my experience of fieldwork, my interactions with interview participants, and my ability to access sites for observations which in turn influenced the data I collected.

Another important factor that influenced my data collection were the social nuances of engaging with elite participants (i.e., policymakers and TB facility managers). I noticed that I had to emphasize and clarify consistently that I did not represent the implementing organisation as I was carrying out an independent, academic, study for my doctoral studies. I also noticed that, despite this reassurance, there were barriers to understanding and this resulted in me not having access to some elite participants and sites for observations. As a result of some of the elite participant's beliefs of my affiliations, I was denied access to one site where the intervention had been implemented due to conflicts between organisations that were related to my research study but outside of my control.

Finally, I want to acknowledge that, embedded in my data collection methods, is the acknowledgment that the phenomenon of interest for my study happened six years ago, before the Covid-19 pandemic, which influenced the way I phrased requests for collecting data, such as interview questions, site observations, and interpretation of documents.

5.3.5 Ethical approvals

I submitted an ethics review application as part of the requirements for studies with human subjects by the University of York (approval number: HSRGC/2021/466/F). The ethics

committee at the University of York considered that no further ethics review was necessary by a local ethic review board.

5.3.6 Quality assessment

I used COREQ and SRQR as guiding standards for reporting and documenting the design, process, and results of this study (Tong, Sainsbury, & Craig, 2007; O'Brien, *et al.,* 2014). These two standards are the most appropriate to use in the reporting of qualitative research (UK EQUATOR Centre, 2024). See Appendix 8 for the completed COREQ and SRQR checklists for this study.

5.4 Results

5.4.1 Data collected: the Cases and the Context

I created a case study database to clarify the data included in the analysis, its type and description, and its contribution to my research objectives, according to the principles of high-quality case study research (Yin, 2017). This informed the redesign of my analytical approach to the data analysis (Figure 5.5). The database is a table describing the collected documents (n=54), interviews (n=18), and site observations (n=5) (see Table 5.1 and Appendix 7). A contact within the implementing organisation helped me locate the six different types of facilities where the intervention had been implemented – four facilities were tertiary care level and two were primary care centres. Three facilities were privately owned and three were part of the Sindh public healthcare services. Figure 5.4 shows the approximate location of these facilities in the city of Karachi.

Data type	File name	Description	Anticipated contribution to research objectives	Actual contribution to research objectives
Documents	See Appendix 7	296 sources originally; 56 documents included after sampling; 54 could be retrieved and included (names and details in Appendix 7)	Context, R1, R2, R3	See Appendix 7
Interviews	ITW 1	Interview with project manager (implementation)	R1, R2, R3	Context, R1, R2, R3
	ITW 2	Interview with project manager (design)		
	ITW 3	Interview with Mental health lay counsellors (trainees)		Context, R1, R2
	ITW 4			
	ITW 5			
	ITW 6			
	ITW 7			
	ITW 8			R1, R2
	ITW 9	Interview with research associate		
	ITW 10	Interview with Principal investigator A (pre and during-implementation)		Context, R1, R2, R3
	ITW 11	Interview with Principal investigator B(pre, during, and post-implementation)		
	ITW 12	Interview with Project manager (implementation)		
	ITW 14	Interview with Head of TB department; public facility		Context, R3
	ITW 15			Context, R1, R2, R3
	ITW 17	Interview with TB doctor; private facility		
	ITW 18			
	ITW 20	Interview with Senior TB programme officer (NTP)		Context
	ITW 21	Interview with TB doctor; public facility		Context, R1, R3
Observations	Visit note 1	Site observation; public facility	R3	Context, R2
	Visit note 2			Context
	Visit note 3			
	Visit note A	Site observation; private facility		

Data type	File name	Description	Anticipated contribution to research objectives	Actual contribution to research objectives
	Visit note B			
Other	Meeting note - fieldwork logistics	Notes taken during a meeting about fieldwork	R1, R3	Context, R1, R2, R3
	Fieldwork log	Notes taken during fieldwork	R3	
	Context info about intervention documents	Notes taken during a conversation about some of the documents used in the intervention	R1	
	Analytic memos	Notes taken during data analysis phase; reflective log	Context, R1, R2, R3	

Table 5.1 Data included in the analysis and its contribution to the research objective.

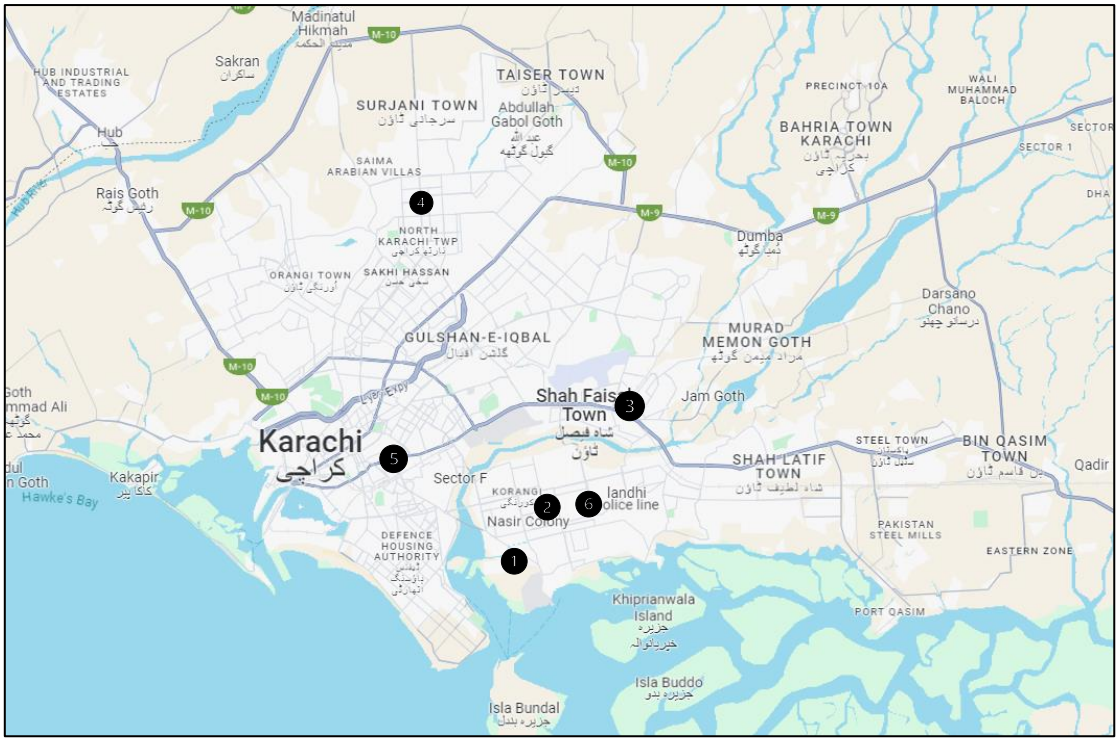

Figure 5.4 Approximate locations of the implementation sites (observation sites) for the intervention.

The number of visits to each facility was limited due to the length of fieldwork and the complex logistics of collecting data in the field. All collected data from different data sources contributed to address the research questions (i.e., triangulation), as described in Table 5.1. For reporting the results of this qualitative case study in relation to the research objectives in 5.1, I used the compositional format suggested by Yin (2018) which follows a question-and-answer format, using the research objectives as the guiding questions, and I added a preliminary section (see 5.4.2) describing the Context in which the Cases and the IPUs were situated.

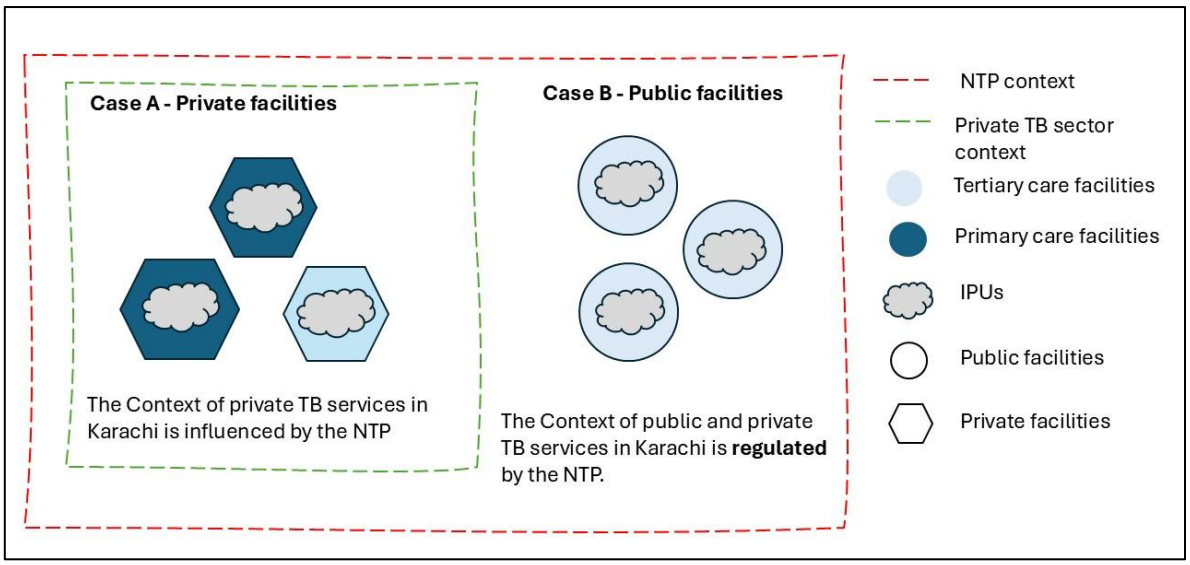

Figure 5.5 Actual analytical relationship conceptualized after data collection and analysis. The Context of the public and private TB services in Karachi.

5.4.2 Case study Context: TB burden and TB healthcare services in Pakistan

I organised the data I coded to the Context of the case study using the Outer Setting sub-domains of the CFIR framework as headings. During the data analysis stage, the included governmental documents showed that TB services in Pakistan were regulated, contracted, monitored, and evaluated mostly by the NTP, and their representatives at provincial level. Thus, most of the contextual characteristics of both cases, private and public facilities, were similar during the period 2017 to 2022.

There was a mix of tertiary and primary care facilities, public or private, used as implementation sites. All the public facilities used as implementation sites were tertiary care hospitals, part of the NTP and the Sindh Government. As for the private facilities used as implementation sites, the two primary care facilities belonged to a different organisation from the tertiary care facility. So, in total, there were 3 different organisations, two private organisations and one public organisation, represented in the Cases. Below is a description of the Context of the Cases using the CFIR Outer Setting domains as underlined sub-headings.

<u>Critical incidents</u>

All the data included in this case study referring to critical incidents affecting TB services in the city, private and/or public, was about the COVID-19 pandemic. COVID-19 had an important impact not only on the healthcare sector as a whole but particularly on TB services as most human and physical resources formerly allocated to TB control were redirected towards pandemic control activities. However, COVID-19 happened after the implementation period for the IPUs had ended (thus, happening outside the scope of this study) which is why I did not analyse the impact of the pandemic as an influencing factor for the purposes of describing Context at the time of implementation.

External Pressure (market, performance, societal)

There was an overall pressure on the NTP to meet the programmatic goals defined at national and international level. This was the responsibility of the provincial TB programmes which monitored and regulated the public facilities where TB control activities were delivered. The private sector is not subjected to the same regulations as the public sector due to lack of capacity and resource constraints in the provincial NTPs to monitor and evaluate private sector facilities participating in TB care. One exception was one of the private facilities acting as an implementation site for the IPUs. This was a tertiary care facility, part of a larger non-for-profit organisation, which reported yearly on their activities and results on TB control. The pressure, for this private organisation, was therefore more societal, as their reports had as an audience the general society, particularly those who had potential to become donors to the organisation as the donation details were included at the end of ever yearly report included in this study (Indus Hospital and Health Network, 2019; 2018; 2017). For the role of External Pressure as a barrier or facilitator for implementation of the IPUs, see Appendix 10.

Financing

The financing for private and public organisations working in TB control activities was intertwined. Public facilities were financed by the provincial TB control programmes which were themselves financed by the NTP. The NTPs were funded with domestic and international funds. On the other hand, the private primary care centres acting as implementation sites were for-profit organisations offering diagnostic and treatment services for individuals with TB free of cost, funded through a mix of Global Fund and NTP financing (Interview 17; Interview 18). The private tertiary care centre, as mentioned, was a non-profit organisation funded through private donations, international donors, and PPPs

with the NTP (Indus Hospital and Health Network, 2019; 2018; 2017). The financing of the IPUs, the intervention, represented how TB services were financed in public and private sectors. The implementation for the IPUs received funding from international donors who also funded the NTP, namely the Global Fund (Interview 11, principal investigator; Interview 12 project manager). Thus, the Global Fund funded TB control activities in Pakistan by funding the NTP and private organisations working in TB control activities locally.

A conflict of interest was documented in 2021 between the Global Fund, the implementing organisation, and one of the private implementation sites. The verdict of the internal review committee of the Global Fund as of non-compliant use of approximately US$2 million in grant funds which was proposed to be recovered by the Secretariat (Global Fund, 2021). These funds were described as having been allocated to the implementation site (not to the implementing organisation) for TB-related activities. The report's findings described the activities of a psychosocial support project as "*poorly implemented, reached too few people and/or were implemented too late*". It is possible this finding referred to the implementation of the IPUs given the timeline of the investigation and the implementation timeline of the IPUs. This conflict of interest highlights the complex and changing nature of TB services' financing in the country since private and public stakeholders received and managed TB-related funds from international donors often with inadequate oversight to identify conflicts of interest or underperformance. Although it is outside of the scope of this study to report further on such conflict of interest, it is worth mentioning that the implementing organisation disputed the report's findings and engaged in a legal conflict with the Global Fund.

Local conditions

TB programmes in Karachi (and arguably in other countries) had been run historically as silos (Interview 10, principal investigator). This meant that the TB programmes were run vertically, with human, financial, physical, and political resources exclusively dedicated to the control of TB in the country. During the devolution, the control of TB programmes transferred from a national, centralized, office, to the provincial departments of health, who had their own TB programme directors to liaise with the NTP, and were in charge of the monitoring and evaluation of the TB programmatic goals in their region (Government of Pakistan, 2014; 2022). In public facilities, the TB doctors reported information on patient volume, diagnostic outcome, type of TB, TB treatment follow-up, and TB treatment

outcome to the NTP representative in Karachi, (Visit note 1-3; Interview 14, Interview 15, Interview 21, TB doctor in public facility). TB doctors in public Cases emphasized the importance of disease surveillance aspect for their role, and their responsibility for accurate data collection and adherence to national guidelines for TB control for reporting (National TB Control Program Pakistan, 2019b; 2019c). In private Cases TB doctors also collected and reported this data to the NTP, as it was mandated by the national guidelines, but was not mentioned by them during the interviews.

Local attitudes

The local attitudes of staff in private facilities were described mostly as open and accepting towards the intervention by the implementation team. The implementation team sometimes described staff employed at the implementation sites using "*us*" and "*them*" terms, meaning the implementation team felt as outsiders in the implementation sites. In private Cases, staff was described by interview participants as generally positive or neutral towards the implementation team and/or the intervention. In contrast, staff in public Cases were described as neutral or hostile towards the implementation team, the intervention, and/or mental health screening and treatment (Interview 3, Interview 6; mental health lay counsellor trainee).

> *"Some of the medical officers or people in good positions… thought that, if a patient comes in, you diagnose them, you give them the medicine for tuberculosis, and that's' it. They don't need counselling. They used to think that this counselling is not going to help them at all, it's just an added thing that they are doing. They felt it had no advantage…it was only some medical officers and not all of them… some medical officers were pretty understanding."*
> (Interview 7, mental health lay counsellor trainee)

The implementation team described the people receiving the intervention, i.e., people with TB, as being similar in private and public Cases. This was not a surprising finding given that all the facilities used as implementation sites provided TB care for free and were spread out across the city of Karachi. People with TB possibly attended whichever healthcare centre was more convenient for them which meant that all the implementation sites received a fairly similar group of people with TB. The implementation team described people with TB's attitudes as "*unlearned*", "*suspicious*", "*superstitious*" towards TB treatment (Interview 3-8, mental health lay counsellor, trainee). In some cases, they would

be in denial. A TB doctor described other attitudes of people with TB such as their use of unlicensed private practitioners (i.e., traditional healers), language barriers (i.e., speaking a language that was not Urdu or Sindhi), and illiteracy (Interview 18, TB doctor, private).

Partnerships and Connections

The collaborations established before the implementation period as PPPs (public-private partnerships) and PPMs (public-private mix) shaped the collaborations between private and public sectors in TB control activities in the country (Department of Health Sindh, 2014). PPMs are a form of PPPs: they support the delivery of TB care through public and private facilities by providing human resources (medical doctors) and facilities (clinics, mobile clinics) to the TB programme so TB control activities can be delivered using the private sector infrastructure. For example, in Sindh there are 399 basic management units where TB control activities are provided at the community level, 342 are owned and managed by public healthcare sector and 57 by private healthcare deliverers (Interview 20, TB policymaker). The burden of TB control activities fluctuates between private and public healthcare facility, and PPMs helps to address issues of underreporting and service unavailability in public sector by engaging the private sector.

> *"…in the Sindh cases registered at least 49.5% is PPM, public private mix. Because due to the closure of the hospitals of public side, all people divert to clinics, because clinics are even open in the night-time and the evening time. The burden of the public side goes to PPM."*
>
> (Interview 20, TB policymaker).

Policies and Laws

The policies and laws that governed TB provision in public and private healthcare facilities aligned, in theory, with NTP guidelines. In practice, there was little to no oversight of private sector provision and particularly of informal or traditional healers (Interview 18, TB doctor). Only two policy documents mentioned mental health as a component of TB control as they encouraged the involvement of psychologists in multidrug-resistant (MDR) and drug-susceptible (DS) provincial teams. In these documents, depression was described as an adverse side effect in people with TB caused by socioeconomic circumstances, chronic disease, and anti-TB drugs. Depression was described as a psychiatric disorder in these documents, which could inadvertently increase the stigma associated with mental health conditions amongst people with TB and/or TB healthcare workers. The policies for

managing depression as an adverse side effect in people with DR-TB suggested healthcare workers to assess and address underlying socioeconomic issues acting as risk factors for depression, i.e., substance abuse, and to refer people with TB to substance abuse services.

> *"[T]here is higher incidence of depression with MDR TB treatment especially associated with chronicity and lower socioeconomic status" and "socioeconomic conditions and chronic illness should not be underestimated as contributing factors to depression*"
> (National TB Control Program Pakistan, 2017).

Summary

The Context of TB services and mental health services for people with TB in Karachi is complex. The interactions between the private and public sectors within TB control activities were particularly complex to discern due to Financing arrangements and national and international funders. Although private and public sectors might appear as distinct units, their participation in TB control activities meant they have more commonalities than differences between them and such division of "private and public" might not be relevant. However, a difference between private and public sectors is the lack of capacity for monitoring and regulating private sector activities in TB control. This could be concerning for the NTP and international donors given the large proportion of service users, and providers, in the private healthcare sector in Pakistan. Given that both sectors should be governed at the national level by the NTP and the Ministry of National Health Service, Regulations and Coordination, this is an area of opportunity for government agencies to improve reporting activities of all providers receiving funds to deliver TB control programme activities.

3.4.3 Research objective 1: Description of the intervention

After comparing the initial description of the intervention in published peer-reviewed literature with the data included in the analysis, I created a revisited, description of the intervention, reflecting both the initial description and the input of the case study data. I used the TiDiER guidelines (Hoffmann *et al.,* 2014) to organise the description of the core elements of the intervention; see Table 5.2.

There was one major discrepancy in the initial and revisited descriptions of the intervention. The peer-reviewed article which as used as the only source for creating the

initial description reported different numbers of participants at different points of the intervention:

- Participants in the initial screening: 3,500 in peer-reviewed article vs 53,289 in documentary source of the case study data.
- Number of symptomatic participants: 1,057 in peer-reviewed article vs 2,527 documentary source of the case study data.
- Number of participants receiving counselling by mental health lay counsellors: 1,012 in peer-reviewed article vs 1,462 in documentary source of the case study data.

It is possible the differences between the reported numbers are due to the different nature of the documents in which they are reported. The requirements to have a peer-reviewed article published might make authors report data only on participants for whom they have complete information or data sets. For documents whose purpose is dissemination for a general audience, the methodological rigour is not the same and there might be an incentive to over-report, or extrapolate, operational successes particularly if their objective is to attract donor funding. Thus, I did not consider this as a significant difference, and I used the figures reported in both documents as part of the final description of the intervention.

Another finding was that the goals of the intervention addressed diabetes and mental health in people with TB. One of the participants mentioned that the intervention was designed as to have a diabetes and glycaemic control element added to it (Interview 10, principal investigator). In one of the data collection forms, one of the fields asked for patient's "HbA1C result and date" (Document "Mental health screening data format"). Haemoglobin A1C (HbA1c) is a blood test used to diagnose diabetes. Thus, the IPU intervention was not designed to be a standalone mental health intervention for depression as it had the additional objective of assessing diabetes in people with TB. Lastly, an additional finding was that the design of the intervention and its implementation received funding from different sources (Interview 11, principal investigator) but this did not have an impact on the original or revisited descriptions of the intervention. Outside the differences mentioned above, there were no significant differences between the initial and the revisited descriptions of the intervention.

Revisited description of the intervention including case study data	
Brief Name	Integrated Practice Units (IPUs).
Why	Describe the rationale, theory, or goal of the elements essential to the intervention.
	The document reporting the study as a peer-reviewed article describes the rationale for the intervention the increased risk for mental health illness amongst people with TB, poor medication adherence in people with TB and comorbid depression, and poverty as an exacerbating factor of all the above (Pasha, *et al.,* 2021). *"…there was a clear need identified…there was an understanding and a realisation within programme teams implementing the TB programme on the need for mental health services"* (Interview 11, principal investigator). One of the documents (Document "TB and mental health training manuals") makes reference to a study "*conducted within* [implementing organisation] *TB control program indicate significant rates of depression and anxiety amongst people with TB*" but there was no reference or further information provided to retrieve said study. This claim about the prevalence of depression in people with TB in Karachi, receiving TB care through the implementation organisation's TB programme was thus difficult to prove. When I asked to access the mentioned study, to understand more of the implementing organisation's role in TB programmes, my request was denied as they considered that as confidential material and not pertaining to this qualitative case study. The essential goal of the training part of the intervention was described as " [to provide] *a structured and comprehensive approach to organizing trainings on basic mental health counselling skills for lay mental health counsellors."* *"It is important to note that* ***this training does not qualify the mental health counselor*** [sic] ***to become a registered and independent counsellor, psychotherapist, or mental health practitioner*** *as additional study and training is mandatory for these positions"*. (emphasis in original; Document "Mental Health Training Manual").

What	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers.
	They used two manuals (Document “Mental Health Training Manual” and “TB and mental health training modules”) to train mental health lay counsellors and one intervention protocol. The “Mental Health Training Manual” covered the following content: – “Introduction to mental health and problems associated with mental health” – “Introduction to mental health counselling” – “Interpersonal communication skills” – “Other effective communication skills” – “Phases of mental health counselling” – “Other considerations in mental health counselling” – “Assessment and screening tools” – “Common mental health problems” – “Revisiting the basics of mental health counselling” – “Basics of interpersonal communication” This training manual includes the following appendices: – Appendix 1: Competency Assessment Toolkit – Appendix 2: Ice-Breaker Activities – Appendix 3: Pre-Test Measure – Appendix 4: Role-Play Script for Empathy – Appendix 5: Role-Play Content for Non-Judgmental Attitude – Appendix 6: Content for Practising Reflection – Appendix 7: Content for Practising Paraphrasing – Appendix 8: Open-Ended and Closed-Ended Questions Worksheet – Appendix 9: Role-Play Script for Funneling Technique – Appendix 10: Brainstorming Bubble – Appendix 11: Cost-Benefit Analysis – Appendix 12: Post-Test Measure

	The “TB and mental health training modules” covered the following content: – “Background/rationale” – “Purpose of the training” – “Target groups” – “Outline/structure of the module” – “Module 1: Mind body connection” – “Tuberculosis” – “Module: TB-Basics” – “Module: Management of TB” – “Module: TB - adherence to treatment” – “Module: Drug-resistant TB” – “Module: Role of nutrition in TB” – “Module: TB prevention.” Data collection forms were designed to be used manually, i.e., all data collection was done manually by the mental health lay counsellor trainees. The data collection forms I was able to access were: – Screening forms with AKUDAS scale – Re-screening for follow-up forms – Patient information sheet with contact details – Appointment schedule for the implementation site – Data summaries for symptomatic people with TB – Data summaries for non-symptomatic people There was a discontinuation form, but I was not able to access this as the file was corrupted during saving, and I was not able to restore it after fieldwork ended.
	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.
	The intervention was described as IPUs, providing psychological counselling for depression for people with drug-susceptible TB

	(Interview 11, 12). It also included information about TB, medication side effects, and mental health (Interview 3-8; Document "TB and mental health training manual"). It consisted of use of task-shifting approach, relying on lay health counsellors for the provision of all mental health services (Interview 11). Mental health lay counsellors were employed by the implementing organisation explicitly for this intervention and were not routine employees of the TB treatment sites (Interview 3-8). All eligible people received a baseline session and follow-up sessions. The baseline session covered two main elements which were TB health education and mental health screening (Document "Protocol for intervention – integrated practice units"). This is not mentioned as such in the peer-reviewed publication as the description of the baseline session in it emphasizes the mental health components of the baseline session such as identifying sources of mental distress and establishing coping strategies to address it (Pasha, *et al.,* 2021). The follow-up sessions were provided to people scoring 21 or more in the AKUDAS scale (Document "Protocol for intervention – integrated practice units"). This cut-off point was consistent with what is described in the peer-reviewed publication of the intervention (Pasha, *et al.,* 2021).
Who provided	For each category of intervention provider describe their expertise, background and any specific training given.
	The training provided to the mental health lay counsellors to equip them for the delivering counselling to people with TB consisted of 6-to-8-day face-to-face training sessions. These sessions were lectures and role-playing activities, to teach lay health counsellors how to deliver counselling to people. It was delivered by implementing organisation staff, but it was unclear what role they had, such as project manager, principal investigator, or their qualifications to provide training in mental health counselling (Interview 3-9). The content of training sessions covered basics of TB and mental healthcare, basic cognitive behavioural therapeutic techniques, core communication skills, and

	ethical considerations required for counselling (Document: “TB Training Modules”; “Mental Health Training Modules”; Interview 3-8)
How	Describe the modes of delivery (e.g., face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.
	The counselling sessions were delivered in person, at the site of TB treatment delivery, in an adjacent room or a dedicated space adjacent to the TB treatment site. All sessions lasted between 45 minutes to 1 hour (Interview 6, Document “Protocol for intervention – Integrated Practice Units”). The 1st session was called a Baseline session (Document “Protocol for intervention – Integrated Practice Units”; Interview 11-12). This was a counselling and educational session offered to all people with DS-TB initiating TB treatment; it provided information on the link between TB and mental health and people were screened for depression and anxiety using the Aga Khan University Anxiety and Depression Scale (AKUADS); 25-item questionnaire in Urdu. People scoring 21 or more on the AKUADS scale were offered further counselling sessions. The 2nd to 5th sessions were counselling sessions. Every session there was re-assessment using AUKDAS at 4th session of counselling. If people were still symptomatic after 4th counselling session, they were offered additional sessions, up to the patient’s discretion, and re-assessed at each subsequent session. People were considered to have received the full intervention if they received 4 counselling sessions and scored less than 21 on the AUKDAS scale at the end of this session, or at completion of TB treatment (or cured), whichever was first (Pasha, *et al.,* 2021).
Where	Describe the types of locations where the intervention occurred, including any necessary infrastructure or relevant features.
	The intervention, including baseline and follow-up sessions, was delivered at the same facility where people received TB care (Document “Protocol for intervention – integrated practice units”).
When and how much	Describe the number of times the intervention was delivered and over what period of time, including the number of sessions, their schedule, and their duration, intensity, or dose.

	The Protocol describes the structure of the intervention as "comprised of 6 counselling sessions which can be broken down into one baseline session and five follow-up sessions" (Document "Protocol for intervention – integrated practice units). This seems to be somewhat at odds with what was published in the peer-reviewed article as they described a complete intervention as 4 sessions rather than 6 (Pasha, *et al.,* 2021). The rates of attrition after the baseline and counselling sessions were not reported in any of the included documents so it is unclear the number of sessions each participants received which is important given the stigma associated to TB and mental health in local society.
Tailoring	If the intervention as planned to be personalised, titrated, or adapted, then describe what, why, when, and how.
	One mental health lay counsellor trainee reported having adapted the location of the counselling session to allow more privacy for their male clients. *"[The counsellor] says that the locations and everything that he mentioned, that was only for gents. He says that within our society, within their practice, gents would counsel gents. As for female counsellors, they would have the access to the people' home, if they were female, and their families. He says that it's not about the facility, it's not about anything else, it's just the community and the society that we live in. It's relatively harder for men to easily interact with women, and women with men, vice versa. So, he says that all of that he has talked about it's just for gents."* (Interview 7, mental health lay counsellor trainee). These provisions to deliver the intervention allowing for gender preferences and adapting to local social dynamics was not mentioned in any training documents or the protocol of the intervention.
Modifications	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).

	In the interviews with some mental health lay counsellor trainees, they mentioned how they would rotate between implementation sites. This means that counsellors were not always stationed in the same implementation site through the implementation period described in the protocols, training documents, or peer-reviewed publications of the study's results. *"There was another person already doing the job before me"* (Interview 05, mental health lay counsellor, trainee) Additionally, in the data collection form "Appointment schedule for the implementation site" the handwriting was different at different dates, even though the schedule belonged to the same implementation site.
How well	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.
	There was no evidence of a planned evaluation for fidelity assessment in any of the data sources included in this study. The intervention adherence monitoring was carried out by counsellors, as evidenced in the data collection forms "Appointment schedule for the implementation site", "Re-screening for follow-up forms", and "Data summaries for symptomatic people with TB". The data collected to assess intervention adherence were patient name, identifier, and contact details, as well as number of session and place, and content of counselling session.
	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.
	The data collection forms I had access to report a variable number of follow-up sessions, between zero and five, which raises questions about the monitoring of drop-outs or people who refused the intervention as these forms were not available due to lack of access or inexistence. Some of the data fields in the forms are used inconsistently, particularly those who would require the counsellor or whoever was doing the data collection to write in them (e.g., father or husband's name, location of the session, refusal or acceptance of the

	counselling intervention) as opposed to selecting an option in the form (e.g., yes, no, session number, AKUDAS scale).

Table 5.2 Description of the intervention after data analysis using TiDieR checklist, adapted from (Hoffmann, et al., 2014).

5.4.4 Research objective 2: Barriers and facilitators for implementation

There were few differences in the barriers and facilitators for implementation at public and private facilities (see Table 5.3). In most domains of the CFIR framework, the experience of implementation in both cases is quite similar. Further, the data coded to the domain of **Implementation Process** shows that the experience of implementation between cases was almost identical. This can be due to the nature of the constructs included in that domain, or that the similarity in implementation experiences is due to the high fidelity of implementation strategies applied to both settings. From the description of the intervention in Table 5.2 and the findings of this section, some of the implementation strategies used were dedicated funding and contracting for the implementation process and development of the intervention, “alter patient/consumer fees” (as the intervention was provided free of charge), facilitation of the implementation process, centralization of technical assistance for implementation support and intervention delivery, training (including the development and distribution of educational materials, such as the training manuals), creation of new clinical teams (as the role of the counsellor was created and funded by the implementing organisation), involvement of executive boards of the organisational affiliations of the implementation sites, and promotion of networking and relationship-building at the implementation site (Powell *et al.,* 2015).

It seemed that all the implementation strategies were consistently applied to all the implementation sites. The lack of significant differences between cases could also be due to the scope and nature of the framework I used for analysis. The CFIR framework is used for analysing contextual characteristics of the implementation setting and their influence on the implementation process, rather than identifying differences between similar implementation settings. This hypothesis is supported by the analysis of barriers for implementation in this case study since during data analysis there were no barriers unique to private Cases and all the barriers described in the data were shared across private and public Cases. Similarly, there were no facilitators unique to the implementation experience in public Cases as all facilitators experienced by the stakeholders were shared across

private and public Cases as reported in the included data. Thus, it is possible that some nuance is missing in the description of the implementation experience described in the following sections. Table 5.3 describes the overview of barriers and facilitators experienced in private and public Cases.

Due to space limitations, I will only describe the **differences** in implementation experiences between Cases. That is, sub-domains that acted as facilitators for one case whilst being barriers for the other, or vice versa. A detailed narrative description of each of the CFIR domains is included in Appendix 10.

Innovation domain: pre-implementation pilots were done only in private facilities

The construct of **Trialability** was the only difference observed between the implementation of the IPUs in the Innovation domain. The intervention was only trialled and piloted in the private facilities, which had considerable facilitators pre-existing to the intervention's implementation such as IT infrastructure, reputability, adequate staff numbers with adequate training, and adequate space and physical facilities.

> *"… this is in the initial stages, where we were just starting piloting it at* [private facility] *hospital as a site… and obviously challenges kept popping up, and we tried to troubleshoot, trying to find different ways in which certain ways would work."*
>
> (Interview 10, principal investigator*).*

There was no reference made to a similar trial in public facilities which is why this domain is marked as "ND" in Table 5.3.

Outer setting domain: regulation was considered important only in public Cases

The construct of **Policies and Laws** had different effects in the implementation cases. For private facilities, it was unclear whether existing TB-related legislation influenced the implementation of this intervention. In the public cases, the then current legislation for TB services was a barrier for implementation which interviewees experienced and interpreted as bureaucracy and governmental red tape associated with the size and patient volume that public facilities received.

> "*The bureaucracy and the red tape... That was more present in the larger facilities than the smaller ones. Longer chain command, shorter chain of*

command, and more people enrolled…".

(Interview 12, project manager)

Inner setting domain: infrastructure and working relationships made the biggest difference between private and public Cases

The **Inner Setting** was the domain where most differences between implementation cases were evident. The differences were attributed to the **Physical infrastructure, IT infrastructure,** and **Relational Connections** of each implementation setting. For private settings, their **Physical infrastructure** and **IT Infrastructure** acted as facilitators for implementation in contrast with the infrastructure available at public settings where these characteristics were a barrier.

"… private facilities, probably had the resources from what I could see, they also had more electronic systems versus public facilities having more manual, hand-written systems."

(Interview 9, research associate).

In public facilities there was no privacy or reprieve from the heavy patient flow during opening hours which impacted on the quality and confidentiality of the face-to-face counselling sessions (Interview 8, mental health lay counsellor trainee).

"There was some sort of issue of confidentiality when it comes to the space. And we had to ask people to go out when we were conducting the counselling sessions."

(Interview 4, mental health lay counsellor trainee).

During a visit to a private implementation site, I observed the disruptive impact that heavy patient flow can have on the physical space within the facility (Visit note B). Similarly, the difference between the **IT infrastructure** available in public and private sites influenced the participants' experience of delivering the intervention. In public facilities was certainly a barrier for the implementation of the intervention, particularly for data collection and monitoring activities.

"*I think like the infrastructure of the facilities was definitely one. And the fact that data maintenance at the public facility level, public facility level, it was more outdated, there was on paper, it wasn't electronic. And there was a lag in terms of how frequently, or how soon they completed their data. So you know, we would have to - if I were to collect data right now, I would be told that 'oh we don't have complete data, we only have complete data until the past few quarters or so'… Public facilities, public facility level."*
(Interview 9, research associate).

This description is consistent with what I observed during fieldwork. I observed how public facilities carry out most administrative tasks using paper-based systems, such as patient registers, referral forms for laboratory or diagnostic tests, referrals to pharmacy for anti-TB medications (Visit note 1; Visit note 3). I observed how, in private settings, the patient register and other information would be kept using computers (Visit note A, Visit note B).

The **Relational Connections** between staff from the implementing organisation and the implementation sites had a mixed impact on private facilities, and a negative impact on public facilities. In the private sector, there was a mismatch between the collaborative relationships established at high seniority levels and the lack of collaboration at the frontline. The mental health lay counsellors from the implementing organisation described the hostility from the staff employed by the organisation towards them and described their reluctance to cooperate and "share" people.

"*… there was a problem of cooperation at* [private implementation site]*. We were outsiders … we had to be cautious with our relationship with the staff. … we had to keep our own team safe... Because we were partners … not insiders."*
(Interview 3, mental health lay counsellor trainee).

In public settings, there was a lack of support for the implementation team at all levels of the organisational hierarchy. The hostilities faced by implementation team members working in public facilities were similar, if more frequent, as the ones experienced by those working in private facilities and came from different members of staff at different seniority levels.

"There were some difficulties. Especially since it was a government site. We had to tolerate the government officials… The government officials and the staff had this nature that they were hesitant to send people to us. And they had this idea that this our place, why do we provide information to you. The government employees were hesitant and rude about sending people to us…It's not nice. It's really difficult for us."
(Interview 4, mental health lay counsellor trainee).

Individuals domain: TB department managers were more amenable to the intervention in private Cases

Mid-level leaders, i.e., TB doctors or TB department managers**,** were a facilitator in private setting but had mixed impact in public setting. In the private setting their role was a facilitator for implementation, and it is unclear if the pre-existing collaborations between the implementing organisation and the implementation sites was what influenced these stakeholders to facilitate the intervention's implementation.

"…in the private setting because [the implementing organisation] *also had a connection with them, I wonder if that has to do anything with this, that basically allowed us more - bigger room and it facilitated us more. But even, as if I kind of take that aside, put that aside, people or management in the private facilities were more accommodating to our requests and were willing – were way definitely much more willing to collaborate…So that could have been one reason why the management of those hospitals would cooperate."*
(Interview 9, research associate).

In public facilities, the managers and staff of TB departments were not helpful or welcoming during the implementation process.

"…sometimes, some of the medical officers or people in good positions, … They used to think that this counselling is not going to help them at all, it's just an added thing that they are doing. They felt it had no advantage."
(Interview 7, mental health lay counsellor, trainee).

When compared to implementation in private facilities, members of the implementation team mentioned that, in general, it was easier to implement the intervention in private facilities vs public facilities, where they would face more challenges.

"*We had various kinds of doctors, right? There were some that were interested and motivated that something like this was coming to the facility. There was some who were indifferent, and there were some who were actively hostile. So, kind of managing all of that, that was a barrier that we eventually overcame."*
(Interview 12, project manager).

Other barriers: attitudes toward gender influenced the experience of the implementation team

There were other barriers that did not fit the criteria of the CFIR framework nor could be coded to any of the domains in Table 5.3.

"…*gender bias was not particularly a huge challenge. That's just one-off case where it was, at another public facility… I had the support of my brother, my counsellor, that was already working at the facilities."*
(Interview 9, research associate).

The closest construct this can be attributed to, as a barrier, would be perhaps **Local Attitudes,** but the interviewees' answer described these as not related to the intervention and rather just societal norms. In other interviews, the participants did mention how societal gender dynamics influenced negatively on the delivery of the intervention to male vs female participants (Interview 4, 7, mental health lay counsellor trainee) but since this was not the research objective of the interviews, I did not explore further this barrier during the interviews.

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	Case A Private facilities	Case B Public facilities
Innovation	Source	The group that developed and/or visibly sponsored the use of the innovation (i.e., the implementing organisation) is reputable, credible, and/or trustable.	2	
	Evidence base	The IPUs have robust evidence supporting its effectiveness.	1	
	Relative advantage	The IPUs are better than other available innovations or current practice.	1	
	Adaptability	The IPUs can be modified, tailored, or refined to fit local context or needs.	1	
	Trialability	The IPUs can be tested or piloted on a small scale and undone.	2	ND
	Complexity	The IPUs are complicated, which may be reflected by their scope and/or the nature and number of connections and steps.	X	
	Design	The IPUs are well designed and packaged, including how they are assembled, bundled, and presented.	X	
	Cost	The IPUs purchase and/or operating costs are affordable.	ND	ND
Outer Setting	Critical incidents	Large-scale and/or unanticipated events can/have disrupted(ed) implementation and/or delivery of the IPUs.	ND	ND
	Local attitudes	Sociocultural values (e.g., shared responsibility in helping people with TB) and beliefs (e.g., convictions about the worthiness of people with TB) encourage the Outer Setting to support implementation and/or delivery of the IPUs.	-2	
	Local conditions	Economic, environmental, political, and/or technological conditions at the provincial or national level enable the Outer Setting to support implementation and/or delivery of the IPUs.	1	

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	Case A Private facilities	Case B Public facilities
	Partnerships and connections	The Inner Setting (i.e., facilities) are networked with external entities, including referral networks, academic affiliations, and professional organisation networks.	2	
	Policies and laws	Legislation, regulations, professional group guidelines and recommendations, or accreditation standards support implementation and/or delivery of the IPUs.	0	-2
	Financing	Funding (e.g., grants, reimbursement) from external entities (e.g., international NGOs, academic institutions, international donors, etc.) is available to implement and/or deliver the IPUs.	2	
	External pressure:	External pressures drive implementation and/or delivery of the IPUs:		
	- Societal pressure	Mass media campaigns, advocacy groups, or social movements or protests drive implementation and/or delivery of the IPUs.	ND	ND
	- Market pressure	Competing with and/or imitating peer entities drives implementation and/or delivery of the IPUs.	ND	ND
	- Performance Measurement Pressure	Quality or benchmarking metrics or established service goals drive implementation and/or delivery of the IPUs.	ND	ND
Inner Setting	Structural characteristics:	Infrastructure components support functional performance of the facility where the IPUs were implemented:		

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	Case A Private facilities	Case B Public facilities
	- Physical infrastructure	Layout and configuration of space and other tangible materials features support functional performance of the facility where the IPUs were implemented.	1	-1
	- Information Technology infrastructure	Technological systems for tele-communication, electronic documentation, and data storage, management, reporting, and analysis support functional performance of the facility where the IPUs were implemented.	2	-1
	- Work infrastructure	Organisation of tasks and responsibilities within and between individuals and teams, and general staffing levels, support functional performance of the facility where the IPUs were implemented.	X	
	Relational Connections	There are high quality formal and informal relationships, networks, and teams within and across the facility's boundaries (e.g., structural, professional).	X	-1
	Communications	There are high quality formal and informal information sharing practices within and across the facility's boundaries (e.g., structural, professional).	-1	
	Culture:	There are shared values, beliefs, and norms across the facility where the IPUs were implemented:		
	- Human-Equality Centeredness	There are shared values, beliefs, and norms about the inherent equal worth and value of all human beings.	ND	ND
	- Recipient-centeredness	There are shared values, beliefs, and norms around caring, supporting, and addressing the needs and welfare of recipients.	1	
	- Deliverer-centeredness	There are shared values, beliefs, and norms around caring, supporting, and addressing the needs and welfare of deliverers.	ND	ND

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	**Case A Private facilities**	**Case B Public facilities**
	- Learning-centeredness	There are shared values, beliefs, and norms around psychological safety, continual improvement, and using data to inform practice.	**0**	
	Tension for change	The current situation in the facilities is intolerable and needs to change.	2	
	Compatibility	The IPUs fit with workflows, systems, and processes in the facility.	X	
	Relative priority	Implementing and delivering the IPUs is important compared to other initiatives in the facility.	-1	
	Incentive systems	Tangible and/or intangible incentives and rewards and/or disincentives and punishments support implementation and delivery of the IPUs.	ND	ND
	Mission alignment	Implementing and delivering the IPUs is in line with the overarching commitment, purpose, or goals in the facility.	**0**	
	Available resources:	Resources are available to implement and deliver the IPUs:		
	- Funding	Funding is available to implement and deliver the IPUs.	2	
	- Space	Physical space is available to implement and deliver the IPUs.	-1	
	- Materials and equipment	Supplies are available to implement and deliver the IPUs.	ND	ND
	Access to Knowledge and information	Guidance and/or training is accessible to implement and deliver the IPUs.	2	

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	**Case A Private facilities**	**Case B Public facilities**
Individuals' domain:	High-level leaders	Defined as individuals with a high level of authority, including key decision-makers, executive leaders, or directors, e.g., national, or provincial NTP directors. This type of individual sits within the Outer Setting as defined for the purposes of this study.	**0**	
Project roles subdomain:	Mid-level leaders	Individuals with a moderate level of authority, including leaders supervised by a high-level leader and who supervise others. For example, TB facility directors, private hospital TB managers. This type of individual can sit within the Outer or Inner Setting as defined for the purposes of this study.	2	X
	Opinion leaders	Individuals with informal influence on the attitudes and behaviours of others. For example, health policy decision-makers, individual donors, traditional medicine practitioners (e.g., hakeems, herbalists, etc). This type of individual sits within the Outer Setting as defined for the purposes of this study.	-2	
	Implementation facilitators	Individuals with subject matter expertise who assist, coach, or support implementation. This type of individual can sit within the Outer or Inner Setting as defined for the purposes of this study.	1	
	Implementation leads	Individuals who lead efforts to implement the IPUs. This type of individual sit within the Outer Setting as defined for the purposes of this study.	2	
	Implementation team members	Individuals who collaborate with and support the implementation leads to implement the IPUs, ideally including Innovation Deliverers and Recipients. This type of individual can sit within the Outer or Inner Setting as defined for the purposes of this study.	2	

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	Case A Private facilities	Case B Public facilities
	Other implementation support	Individuals who support the Implementation Leads and/or Implementation Team Members to implement the IPUs. This type of individual can sit within the Outer or Inner Setting as defined for the purposes of this study.	1	
	Innovation deliverers	Individuals who are directly or indirectly delivering the IPUs. This type of individual can sit within the Outer or Inner Setting as defined for the purposes of this study (i.e., counsellors).	2	
	Innovation recipients	Individuals who are directly or indirectly receiving the IPU. This type of individual sits within the Inner Setting as defined for the purposes of this study (i.e., people with TB and/or family members).	ND	ND
Characteristics subdomain:	Need	The degree to which the relevant individual(s) have deficits related to survival, well-being, or personal fulfilment, which will be addressed by implementation and/or delivery of the IPUs. Applicable to Innovation Recipients.	ND	ND
	Capability	The degree to which the relevant individual(s) have interpersonal competence, knowledge, and skills to fulfil Role, as described above. Applicable for Implementation facilitators, Implementation Leads, Implementation Team Members, Other Implementation Support, and Innovation Deliverers).	2	
	Opportunity	The degree to which the individual(s) have availability, scope, and power to fulfil Role, as described above. Applicable to all roles, except Innovation Recipients.	ND	ND

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	Case A Private facilities	Case B Public facilities
	Motivation	The degree to which the individual(s)is committed to fulfilling Role, as described above. Applicable to all Roles.	1	
Implementation process domain:	Teaming	The degree to which individuals from the implementing organisation join together, intentionally coordinating and collaborating on interdependent tasks with employees at the facility-level, to implement the IPUs.	X	
	Assessing needs:	The degree to which individuals from the implementing organisation collected information about priorities, preferences, and needs of IPUs recipients and deliverers:		
	- Innovation deliverers	The degree to which individuals from the implementing organisation collected information about the priorities, preferences, and needs of deliverers to guide implementation and delivery of the IPUs.	ND	ND
	- Innovation recipients	The degree to which individuals from the implementing organisation collected information about the priorities, preferences, and needs of recipients to guide implementation and delivery of the IPUs.	-2	
	Assessing context	The degree to which individuals from the implementing organisation collect information to identify and appraise barriers and facilitators to implementation and delivery of the IPUs.	1	
	Planning	The degree to which individuals from the implementing organisation identify roles and responsibilities, outline specific steps and milestones, and define goals and measures for implementation success in advance.	1	
	Tailoring strategies	The degree to which individuals from the implementing organisation chose and operationalized implementation strategies to address barriers, leverage facilitators, and fit context.	2	

Domain	Construct	**Definition of the updated CFIR (2022 version) for the purposes of this study**: This is defined as the degree to which…	**Case A Private facilities**	**Case B Public facilities**
	Engaging:	The degree to which individuals from the implementing organisation attract and encourage participation in implementation and/or the IPUs:		
	- Innovation deliverers	The degree to which individuals from the implementing organisation attract and encourage deliverers to serve on the implementation team and/or to deliver the IPUs.	2	
	- Innovation recipients	The degree to which individuals from the implementing organisation attract and encourage recipients to serve on the implementation team and/or to deliver the IPUs.	ND	ND
	Doing	The degree to which individuals from the implementing organisation implement in small steps, tests, or cycles of change to trial and cumulatively optimize delivery of the IPUs.	**0**	
	Reflecting and evaluating:	The degree to which individuals from the implementing organisation collect and discuss quantitative and qualitative information about the success of implementation and/or the IPUs:		
	- Implementation	The degree to which individuals from the implementing organisation collect and discuss quantitative and qualitative information about the success of implementation.	ND	ND
	- Innovation	The degree to which individuals from the implementing organisation collect and discuss quantitative and qualitative information about the success of the IPUs.	1	
	Adapting	The degree to which individuals from the implementing organisation modify the IPUs and/or the Inner Setting for optimal fit and integration into work processes.	2	

Domain	Construct	Definition of the updated CFIR (2022 version) for the purposes of this study: This is defined as the degree to which…	Case A Private facilities	Case B Public facilities
Legend:				
Barriers: Shaded in red; with a notation of-1 or -2				
Facilitators: Shaded in green; with a notation of 1 or 2 1				
Barrier and facilitator (mixed impact): Shaded in yellow, marked with ‘X’				
Unclear if barrier or facilitator: Shaded in grey; marked with a ‘0’				
No data: Not shaded; marked with ND				

Table 5.3 Barriers and facilitators for implementation of the IPUs intervention, adapted from (Damschroder, et al., 2022).

5.4.5 Research objective 3: Sustainability of the intervention after 2018

The main study which involved the implementation of the intervention “IPUs” was carried out from 2015/2016 to 2017/2018. By 2022, when I carried out the data collection and fieldwork, the implementation period had ended and there had been substantial changes to the facilities, the TB services, the country, and the world. The sections below describe the findings regarding the sustainment of the intervention during fieldwork.

After the implementation period ended, so did the working partnerships between the implementing organisation and implementation sites

By the time I carried out fieldwork, there were no existing working relationships between any of the organisations participating in the IPUs, i.e., the implementing organisation and the implementation sites’ organisations. At the individual level, most of the original implementation team involved in the implementation process was no longer working in the implementing organisation or in the implementation sites. Most individuals, according to my contact in the implementation organisation, had moved on to other roles in other regions and lost all contact with the implementing organisation. In terms of the participants in this study, 11 of 17 interviewees, members of the implementation team, had moved onto new roles in new organisations and cities. This meant that almost none of the interviewees had any knowledge or first-hand information on whether the IPUs had been sustained after the implementation period ended.

The change in people’s working circumstances could be partially attributed to the end of the working relationships between implementation sites and the implementation organisation at the formal end of the implementation process as there was no longer a rationale to keep people employed when the IPUs ended. The conflict of interest that was documented in the included data could also have influenced the sustainment of the intervention and the dissolution of the working relationship between the relevant organisations. Since working relationships and relational connections were important factors for the development and implementation of the intervention, it is possible that the lack of working relationships between organisations, exacerbated by a publicized conflict of interest, had a negative impact on any possible sustainment of the IPUs.

Mental healthcare for people with TB continued to be offered in some capacity in private settings but not necessarily because of the IPUs

Despite any lack of formal sustainment of the IPUs, some facilities continued to provide mental healthcare to people with TB after the formal implementation period ended. For example, some of the private implementation sites continued to deliver mental healthcare for people with TB after the IPUs ended in 2018. This was described by mental health lay counsellors (Interview 4, Interview 5) and one PI:

> "*…one or two of the private sector sites continued to integrate that. But I think there was a discontinuation of the study once the study duration ended. I know that the private sector sites, I do know, that they did, during that period, towards the end of the grant, they did recruit somebody with the programme manager with the background in mental health, who was able to take some of that work, and take it forward, and continue it. And I know for a fact that they continued it at the private sector sites. But of course, they were doing this on their own. We had the counsellors trained, we had the systems set up, so they kind of took it on from there. But I was not involved at that time after the study ended*."
> (Interview 11, principal investigator).

It was unclear for how long the sustained delivery of the intervention continued. In 2022, during fieldwork I visited two of the private implementation sites and I interviewed the TB doctors about the sustainment of the intervention. They described how the intervention was not continued after the implementation period. However, I observed they had escitalopram, an antidepressant, in their desks (Visit note A). When I asked if they currently provided any treatment for depression for people with TB they replied: *"antidepressants, antidepressants and antipsychotics"*. They mentioned they prescribed antidepressants for people when *"...they say they cannot sleep, they are restless, have anxiety, lose interest, then I prescribe them antidepressants"* (Visit note A; Interview 17, TB doctor, private). Alternatively, people with clear psychiatric symptoms were referred to tertiary hospitals at doctor's discretion.

> *"…if I need to observe this patient maybe a psychiatric treatment, along with a TB treatment, I refer them the patient to the psychiatrist. Not by me to advice something regarding psychiatric medicine, but we refer them, the patient, to the psychiatrist."*
> (Interview 18, TB doctor, private facility).

It was hard to establish whether these practices of treatment and referral were the result of the sustainment of the intervention. My observations, and interviewee's answers, showed that the treatment and referral processes did not align with the intervention's processes even if the staff at the implementation site remained the same after the implementation period ended. Thus, it is possible that any mental healthcare that was provided to people with TB was *ad hoc* and subject to the TB doctor's criteria, in private Cases.

The IPUs were not sustained in public implementation sites

In public Cases, the intervention did not continue to be delivered after implementation in the public sites. TB doctors in public facilities mentioned they are no longer associated nor receive support from the implementing organisation, or from the NTP, to provide mental healthcare for people with drug-susceptible TB. TB doctors give antidepressants and refer people to counselling services only for substance abuse issues (Interview 21, TB doctor, public).

During fieldwork, I observed how a few people attending public TB facilities being referred to non-for-profit private facilities to receive mental health support with psychiatrists and counselling (Visit note 3). I also observed packages of escitalopram, an antidepressant, and vitamin D in their desks, next to the ledgers used to keep track of people with TB (Visit note 1). The referrals to mental health services were made verbally, by the TB doctor. In one public facility it was clear that the referrals to mental health services or the prescriptions of antidepressants were not related to the IPUs as the TB doctor working in that particular facility was not in their employ at the time of implementation. Additionally, the referrals to mental health services and antidepressant prescriptions I observed are not the treatment protocol described in the IPUs protocols or by the interviewees, which means this was essentially a different form of providing mental healthcare to people with TB.

My impression of the referral process was that it is not a systematic process. There were no notes taken in the patient files, the process was done conversationally, there were no prescriptions or notes made to enact that referral, and there was not an assessment of the distress level in the patient that warranted a referral (Annotations). In public sites, it seemed that the only sustained outcome of the intervention was to increase awareness of the importance of people' mental health amongst TB doctors. The following quote is from one TB doctor who was working in one of the public implementation sites at the time of the IPUs implementation:

"*I think that it gave us a hope that at least we are aware of the problem. … Now, the team is not here but still, we in our behalf we try to counsel the patient.*"
(Interview 15, Head of TB department, public facility).

These findings on sustainment of the IPUs are consistent with findings in the literature assessing the effectiveness of training mental health providers to provide evidence-based psychological therapies. Training providers on psychological therapies increased their work satisfaction and their knowledge of mental health but training did not necessarily translate into sustained practice nor in adoption into routine practice (Valenstein-Mah, et al., 2020). Increased knowledge and awareness of mental health amongst frontline health workers is no small feat in contexts where there is widespread stigma towards TB and mental health as these attitudes can be expressed by the health workers during their practice (Mainga, et al., 2022a). Improved understanding should be supported with institutional initiatives that aim to increase provision and access to mental healthcare to promote the sustainability of increased awareness and mental health treatment access.

5.5 Discussion

In this study, I used a qualitative case study methodology to describe a mental health intervention for depression in people with TB in Karachi, Pakistan and explore its implementation process using the CFIR framework. The mental health intervention for depression was called Integrated Practice Units (IPUs) and consisted of baseline screening using a culturally appropriate tool, followed by four to six subsequent counselling sessions for symptomatic people delivered at the TB treatment facility. The following sub-headings discuss the findings of this case study's research questions, their implications for future work, and the strengths and limitations of this study.

This is the first study to describe in detail the training components of mental health interventions for depression in people with TB using lay health workers, but mental health interventions for depression should be better reported in peer reviewed literature

The first research objective of this case study was to describe the intervention implemented as IPUs and its relevant elements, building a description from the different data sources and the experiences of the interviewees. The trainees (mental health lay counsellors) and the intervention documents provided a comprehensive description of the training contents, mechanisms, and materials used for this intervention component. Peer-reviewed literature reviews on the training of lay health workers to deliver mental health interventions for

depression have focused on assessing effectiveness rather than describing the trainings' contents, mechanisms, and the experiences of the trainees in the same document and with the same detail as in this case study (Connolly, *et al.,* 2021; Bagchi, *et al.,* 2022; O'Donovan, *et al.,* 2018). The findings of this case study and the training used in the intervention can contribute to literature on the effectiveness of trainings for lay health workers to deliver mental healthcare interventions for people with common mental disorders such as depression and anxiety in LMICs. Particularly, the findings of this study detailing the adaptations made by the trainees when delivering the intervention can serve to inform the design of mental health interventions for depression which include training components.

There were some discrepancies between the peer-reviewed publication of the intervention and the data found in the documentary sources included in this case study. The final description of the IPUs in the Results section included information about the diabetes component of the intervention, funding, training materials used, and adaptations made while delivering the intervention. This underlines the importance of using one of the multiple frameworks available for reporting healthcare interventions to increase transparency, particularly in peer-reviewed literature. In the published peer-reviewed article documenting this intervention the goal was to report the effectiveness of the intervention on mental health and TB treatment outcomes. Increasing the transparency of reporting interventions that describe positive treatment outcomes can only improve the reliability and replicability of such studies to build upon their evidence and avoid designing studies that address research questions for which the evidence base has already been established. This is particularly important considering resource limitations associated with mental health research and intervention development in LMICs. Lastly, it is noteworthy that the journal article framed the mental health as the most important component of the intervention, while all the TB doctors interviewed considered the TB educational component of the intervention as the most useful aspect of it.

The implementation experience in public and private cases was similar. The organisational characteristics, and their differences, covered by the Inner Setting domain characterized most of the differences in the implementation process between sites

To address the second research objective of this case study, I retrospectively explored the implementation process of the IPUs intervention using the latest version of the CFIR framework, and framework analysis, as the analytical approach (Damschroder, et al., 2022). The analysis

showed that the implementation experience was very similar between private and public facilities, with the few differences mostly coded to the Inner Setting domain in the CFIR framework. The findings of this study showed that most differences in implementation process and most barriers to implementation were attributed to the Inner Setting characteristics of the implementation sites. This is consistent with other reviews of barriers and facilitators to implementation of mental health interventions for depression in LMICs, where barriers were mostly associated with factors that are difficult to modify or intervene with by the implementation team (Le, *et al.,* 2022). This study further proved the importance of assessing the internal organisational characteristics of implementation contexts, such as infrastructure, staff attitudes, and mid-level leaders, to anticipate and address any potential challenges to the fidelity of the implementation process, including intervention delivery. This can be particularly relevant when implementing interventions that aimed to be integrated within existing TB services, which have been historically structured as vertical programmes, as organisational characteristics might be deeply entrenched into routine operations and might pose barriers to change.

Other studies have mentioned the *"[l]ack of knowledge, training, and capacity to identify and deliver depression care to people*" as barriers to implementation of mental health interventions for depression in people with TB (Jarde, *et al*., 2022; Todowede, *et al*., 2023). This was consistent with the findings of this study as the same barriers were experienced by TB facility leaders/doctors, the implementation team, and policymakers. Thus, these findings suggest the that despite existing awareness regarding the role of organisational attitudes towards mental health as barriers or facilitators for implementation, these can remain unexplored and improperly addressed during pre- and implementation periods. Furthermore, lack of knowledge and hostile attitudes towards TB, i.e., social stigma, are considered to be important barriers for TB treatment success (Sweetland, et al., 2019). Future research that aims to integrate mental health interventions for depression within TB services should build upon these findings and explore organisational attitudes, including staff attitudes, towards mental health and mental health interventions, in general, as pre-implementation activities.

The facilitators for implementation experienced in public and private Cases were fairly similar. Most facilitators were coded to the Implementation Process domain, the Intervention characteristics domain, and the members of the implementation team in the Individuals domain. This is consistent with peer-reviewed reviews which argue that prevalent facilitators are those that are easily adaptable or modifiable by the implementation team, such as the providers' and intervention's characteristics (Le, *et al.,* 2022). A noteworthy finding was the facilitating role of

the expertise within the implementation team in the IPUs. This acted as facilitator for implementation since the implementation team, and the implementing organisation, had the necessary skills, knowledge, and relational connections to design, modify, and deliver the intervention in all the implementation sites. Further research could explore the core skills that need to be covered by implementation teams that aim to implement mental health interventions for depression in LMICs that include training components and navigating public and private healthcare infrastructures.

The sustainment of implemented interventions for depression was not properly addressed in the design of the intervention or the implementation process

The process by which the IPUs were funded and delivered meant that there was a clear timeline for the delivery of the project and reporting its results to donors. Clear start and end timepoints are not necessarily a barrier to include sustainment, or sustainability, as an implementation outcome. However, this study's findings show that neither the intervention nor the implementing organisation included any sustainability-related outcomes or measures in the design of the intervention and its implementation. This is not uncommon as sustainability and sustainment measures are underreported implementation outcome measures in studies reporting the implementation of mental health interventions for depression in LMICs (Verhey, *et al.,* 2020).

The lack of appropriate sustainability and sustainment plans embedded in implementation processes can be an important barrier to advance the quality of mental healthcare provision in LMICs. One method to address this is to make sustainability and sustainment evaluations mandatory elements of research proposals by research funding bodies. Furthermore, international, and national TB and mental health funding bodies should encourage and support local organisational partners to embed implementation sustainability outcomes in their current and future service delivery activities. National TB programmes can also address this by establishing regulatory frameworks that enforce the inclusion of sustainability-related outcomes in implemented projects and by providing onsite support that facilitates integration of interventions into routine clinical practice as this is an effective method to ensure sustainability of implemented interventions (Greene, *et al.,* 2021; Verhey, *et al.,* 2020). Lastly, relevant organisations in service delivery or research funding can allocate resources specifically aimed at exploring and developing the sustainability of mental healthcare delivery in existing services as this is a facilitator for the sustained delivery of mental healthcare in LMICs (Giebel, *et al.,* 2024; Ribic, *et al.,* 2022).

The impact of COVID-19 is still felt by people working in TB services in Karachi

COVID-19 and its impact on the health services was an inevitable part of all the conversations I held with the interviewees. For clarification, the COVID-19 pandemic happened outside the timeframe of interest for this case study. Yet, in all the interviews, there was at least one, unprompted, mention of COVID-19. TB doctors in particular would mention the impact of the pandemic on their approach to treatment for people with TB and health services for people with TB. The documented impacts of COVID-19 pandemic on TB services reported a decrease in TB cases notification rates, lack of personal protective equipment, and a disruption of the programmatic treatment of TB in all public sites (Khan, 2022). Public and private sectors integrated their TB and COVID-19 responses as much as they could, integrating testing, delivery of medication, provision of personal protective equipment to frontline clinical staff, and improving patient safety and sanitization protocols (Malik, *et al.,* 2022). As I interviewed participants in 2022, after all mandatory lockdowns related to COVID-19 had ended, it is understandable that such experience left an indelible mark on the memory of TB workers and people working in TB service delivery. It was not the purpose of this study to explore this important event but given the frequency with which this was mentioned by the interviewees, it warranted its inclusion in this section.

5.5.1 Strengths and Limitations

Case study as a research methodology was useful to explore implementation processes and health system-level influences on implementation

The main advantage of using a case study methodology was the ability to answer all the research questions I outlined in the introduction by using one single methodology. Thus, case study methodology is versatile, albeit time- and resource-consuming, and it should be carefully planned in advance to increase the quality of the study. More recently there has been increased guidance on how to minimise the resource intensity of qualitative research using interviews and the CFIR framework for analysis, which can help plan future research in this area (Nevedal *et al.,* 2021). Another advantage of using this methodology was to use multiple sources of evidence to answer my research questions and compare across cases the similarities and differences in the implementation process. It also helped to understand the Context of the implementation of this intervention from different perspectives, and the patterns of barriers and facilitators that occur in different settings.

The advantage of using documents was to corroborate and augment the details from other sources of data (Yin, 2017); it was also possible to make inferences from documents. It was very useful to define beforehand the criteria for selecting relevant documents available online as the searches retrieved a lot of documents that were not necessarily relevant to the phenomenon of interest and my research questions but were relevant for context.

Thanks to the site observations, I was able to observe the physical and social conditions of the settings where the intervention was implemented. I was able to observe things such as size of TB departments, furniture, availability of lab equipment, staffing levels, patient footfall, use of electronic and/or handwritten records, and general patient attitudes in the TB departments at the sites of implementation. This allowed me to corroborate or complement the information about the sites in other data sources.

Challenges and limitations

However, in the pursuit of understanding mental healthcare integration within tuberculosis (TB) services, I encountered several challenges related to data access and inherent limitations:

i. **Interviewee affiliation:** At least five interviewees were affiliated with the implementing organisation which may have influenced their responses. Other potential interview participants who were part of the implementation process were unavailable due to relocation or job changes and were no longer affiliated with the implementing organisation which made them, according to my fieldwork contact, unreachable. The experiences of such group remain unexplored.
ii. **Language Translation Dynamics:** The use of a third-party translator introduced complexities during interviews. Translating questions between Urdu and English influenced the interview process and the dynamics between interviewer and interviewee. Despite resource limitations, a local university student served as the translator. However, their lack of experience in conducting face-to-face semi-structured interviews occasionally hindered the quality of interactions.
iii. **Access Limitations:** Some intervention documents were deliberately withheld due to proprietary reasons or limited access. Consequently, my ability to analyse these documents was curtailed. Also, the documents I had access to were selected by the implementation organisation which means that there might be an inherent bias in the overrepresentation of this organisation and its role in the implementation process. It

cannot be said that these documents portray a complete or unbiased source of data for this case study.

A related limitation is the lack of participation from people with TB who received the intervention. My contact from the implementing organisation could not help me locate any of the people who had received the intervention and given the time elapsed since implementation, it would have been unfeasible for me to pursue contact with former people on my own. This means that the views of people who received the intervention are not properly addressed or elicited in the findings of this study.

iv. **Conflicts and restricted access:** The lack of access to documentary data and interviewees was further impacted by existing conflicts between the organisations involved in the implementation of the intervention, which resulted in interviewees (n=1) withdrawing their information and lack of access to site (n=2) for observation. This was an important limitation as these sites were referenced repeatedly by interview participants which meant they were important sites for the implementation process but due to the lack of access I could not gather any interview or observation data about the sites or the people working in their organisations at the time of fieldwork.

v. **Access and Time Elapsed:** Observations provided valuable insights into relevant social and environmental conditions during implementation. However, limitations arose due to:
    - Time Since Implementation: Conducting fieldwork in January and February 2022 meant that approximately 4 years had passed since the intervention's implementation. Recall bias was an There were challenges for remembering details which was an important issue for most interviewees. At least two years, and the global pandemic, had passed since the intervention and participants kept reporting how they could not recall their experiences of barriers and facilitators accurately.
    - Personnel Changes: Counsellors and TB facility managers had moved to new positions, sometimes outside the city, leaving no contact details.
    - COVID-19 Impact: The pandemic overlapped with the post-implementation period, affecting people's recollections and responses during interviews.

I acknowledge that the resources I had access to, including contacts in the field and self-funded monetary resources, did influence the data I could collect and the time-limits for fieldwork, but did not influence the methods I planned for data collection.

5.5.2 Reflections

During the write-up of this study, I realised that the methodology I chose was difficult and time-consuming. This gave me a renewed understanding of the demands and requirements that qualitative researchers must consider when designing a study. I thought that choosing an analytical framework I was familiar with would facilitate the undertaking of this study (see Chapter 4), but this was not the case. The inherent characteristics of the case study methodology, its research design, and qualitative research in general, required more time, data, and monetary resources that I had anticipated. Using a qualitative research approach in this chapter made this study the most complex in this thesis.

Doing fieldwork, as a lone worker, is emotionally and intellectually taxing. My experience was that being a researcher immersed in the field 24/7 was intellectually demanding, challenging, and stimulating as everything was new information and the environment was the setting of my study. This was an interesting experience but also tiring. The cultural context was different to what I was familiar with, and this also proved taxing. Particularly, the gender dynamics that were the social norm in that context were not familiar to me, and these often clashed with my own worldviews. My perspective was that these social norms permeated every personal and professional interaction I had during fieldwork and possibly influenced how locals acted towards me and what they *presented* to me. I was especially aware of this mismatch in interactions during interviews that required a translator. I felt like an outsider and an observer, not being able to understand the quips or remarks between locals due to the language barrier. This study left an indelible mark on me. I have my outmost admiration and respect for people who do high-quality qualitative research using fieldwork as now I have a little more understanding of what that entails.

A very specific situation arose during my fieldwork that I had not anticipated nor was I aware of it before my arrival to the country. Upon arrival, I became aware of a professional conflict between two organisational actors relevant to my case study, one of them was the implementing organisation, which was not mentioned during the preparation meetings I had with the members of the implementation organisation prior to my visit to the country. Before this conflict, the two organisations had been working partners for over 13 years but, at the time of my visit, the professional relationships were non-existent. During face-to-face conversations with the implementing organisation, I noticed the tension that would ensue when the former organisational partner was mentioned. For example, I noticed that members of the implementation team and staff of the implementing organisation were particularly reluctant,

hesitant, or uncomfortable to contact the organisational partner for brokering access and promote their participation in this study. One of their concerns was that I would be representing the implementing organisation negatively. Once I shared with them my data analysis plan and a detailed explanation of the studies objectives, the research methodology, the data analysis plan, and the data management plan, including anonymisation strategies, they agreed to participate in this study. However, they did not share all the information they had agreed to share in previous meetings.

5.6 Conclusion

5.6.1 What this study adds

This research sheds light on the intricate interplay between mental health services and TB care. While case study methodology provided rich insights, its limitations include potential biases and generalizability constraints. Future work should explore additional contexts and consider mixed-method approaches to enhance our understanding further.

Navigating the challenges I encountered during data collection required rigorous methodological transparency. Moreover, while data limitations exist, they underscore the need for rigorous research design and consideration of contextual factors. Future studies should explore alternative data sources and address biases inherent in real-world research.

Future work could focus on strengthening this study or similar studies by building logic models that describe the intermediate and ultimate outcomes of the implementation process of an intervention for depression for people with TB in LMICs. This would require adequate planning and data collection that occurs at the same time as the implementation process is undergoing, to be able to capture observed outcomes and events and compare with the data collected for the case study (Yin, 2017). The use of logic models as part of case study methodologies can help to address the “black box” of implementation that is often observed in the analysis and studies of implementation of public health policies and interventions.

Chapter 6 - Discussion

Chapter summary

The aim of this thesis was to assess the evidence for the effectiveness of treating depression in people with TB and explore the approaches that have been used to this end in LMICs. This chapter brings together the findings from the three studies included in this thesis and considers their implications for future research. The first section of this chapter summarizes the findings of the three studies included in this thesis and discusses the links between them. The second section of this chapter discusses the contribution of these findings to current knowledge and future research. The last section of this chapter summarizes the limitations of the studies and the limitations of their contributions to current knowledge and this thesis.

6.1 Summary of findings

This thesis aimed to address the following research objectives, based on existing research gaps outlined in the Background section:

1. To assess the effectiveness of interventions for treatment of depression in people with TB; addressed in Chapter 3.
2. To identify the various interventions and approaches to deliver depression care as part of TB care which have been implemented in LMICs, and to analyse the barriers and facilitators for the implementation of these interventions; addressed in Chapter 4.
3. To identify a mental health intervention for depression implemented as part of a national TB programme in a LMIC and explore the barriers and facilitators for its implementation; addressed in Chapter 5.

In **Chapter 3**, I used a systematic review study design to assess the effectiveness of interventions to treat depression in people with TB. I used a quantitative meta-analysis to pool the results of the individual studies included in the review. I identified two eligible studies, and both described the effectiveness of psychological interventions (cognitive behavioural therapy) for people with TB in China. Between both studies, the number of participants was 637. The meta-analysis showed that there was a greater reduction in the severity of depression symptoms compared to no-intervention or routine care (SMD -0.29, 95% CI -0.45 to -0.13). This is a small to moderate effect according to Schünemann and colleagues (Schünemann, *et al.*, 2022). One study reported health-related quality of life (HRQoL) outcomes in the intervention

participants. I calculated the SMD and 95%CI for this outcome using alpha=0.025 and assuming a normal distribution. The results were SMD = 1.02, 95% CI (0.83, 1.22). The results for HRQoL show the 95% CI of this outcome is very wide, crossing the line of no effect, which means the results for this outcome are inconclusive.

The results of this systematic review and meta-analysis showed that treating depression in people with TB using psychological interventions can be an effective way to improve people with TB's mental health and HRQoL. More RCT study designs which evaluate the effectiveness of psychological interventions and discern between different dose, intensity/frequency, and length can help to further our knowledge in the size of improvement on mental health symptom severity observed in people with TB. Future studies can also compare a range of mental health treatments' effectiveness and their impact on TB-related outcomes, particularly discerning between the effectiveness of using different pharmacological and psychological treatments, which vary in content, dose, frequency, and length.

In **Chapter 4**, I used a systematic review study design to explore the approaches that have been used to deliver care for depression for people with TB in LMICs. I also analysed the barriers and facilitators for their implementation using the CFIR framework (2020 version), and the framework method as the analytical approach. I identified 10 peer-reviewed articles that met the eligibility criteria and were included for analysis. They described three types of interventions for depression in people with TB: psychological, combined (psychological and pharmacological), and combined, with socioeconomic support. The intervention implemented most commonly was psychological care, alone or in combination with pharmacological components, or with socioeconomic support. I found that descriptions of interventions were often incomplete as they did not report the dose, length of treatment, or follow-up information about the mental healthcare interventions. These are factors that can mediate the efficacy of the interventions. I found that quality of reporting of the interventions was associated with the type of study design (e.g., feasibility and acceptability) rather than the intervention (e.g., psychological, combined), with the former having better reporting quality than the latter.

In this study I also found that the provision of mental health training to lay or community healthcare workers, the provision of mental health and TB knowledge to people/families/ communities, and human and financial resources facilitated implementation. This is further supported by the finding that all interventions and their implementation processes incurred in costs, related to the use of human resources, training, and physical spaces. Thus, showing that

dedicated resources available for implementation, and the intervention, will facilitate its process of delivery, specifically in low resource settings like LMICs.

In **Chapter 5** I retrospectively explored the implementation experience of an intervention for depression for people with TB in Karachi. This was, to my knowledge, the first study to explicitly use a qualitative case study research methodology to explore the implementation process of a mental health intervention for depression in TB services of countries with high TB incidence and prevalence. I used the updated CFIR framework (2022 version) and the framework method, as the analytical approach to explore the implementation process and the barriers and facilitators to it.

The mental healthcare intervention consisted of psychological counselling delivered by lay people explicitly trained to deliver it. A completed course of the intervention comprised a baseline assessment session followed by four to six sessions of counselling. The delivery of the intervention was designed to be co-delivered with TB care, meaning that people with TB attending TB healthcare centres would receive both TB care and the mental health intervention for depression at the same time during the same visit. The findings of my study described the intervention's components in detail, including the training contents, the administrative forms and processes used (describing the therapeutic pathway in further detail), and the adaptations made by intervention deliverers (i.e., the mental health lay counsellors, who were the trainees). The findings of the barriers and facilitators analysis showed the internal organisational characteristics were key influencing factors, as barriers or facilitators, in the implementation process in public and private facilities. Thus, although the implementation experience in public and private TB facilities was similar, the intrinsic organisational characteristics of the implementation sites' affiliations mediated the ease or difficulty by which the intervention was implemented in a given facility. Lastly, the findings of this case study showed that the implementation of this intervention was not sustained after the end of the official implementation period and people with TB in Karachi were no longer being offered mental healthcare systematically.

6.2 Contributions to the field

- **This thesis, along with other studies, has contributed to the evidence-base showing that addressing the mental health of people with TB can lead to improved TB treatment outcomes and better mental health outcomes**

The first study in this thesis was a Cochrane review which aimed to assess the effectiveness of interventions for TB and mental health outcomes for people with TB. There were few peer-reviewed and publicly available studies that complied with the required study designs (RCT and cRCT) that can test intervention's effectiveness. Other studies have tried to assess the effectiveness of psychological and pharmacological treatments for DS-TB and DR-TB but their inclusion criteria were not compatible with the assessment of interventions' effectiveness (Farooq, Tunmore, and Comber, 2021). Furthermore, the analyses presented in this thesis, and in other literature, have not been able to discern what are the necessary components of a mental health intervention for depression to ensure its effectiveness, in terms of their psychological components, length, dose, mode of delivery, use of antidepressants alongside psychological therapy, and the mediating role of socioeconomic and societal support(Farooq, Tumore, Comber, 2021; Van Rensburg*, et al*., 2020; *Barbui, et al*., 2020).

Nevertheless, available evidence, including the synthesis presented in Chapters 3 and 4, suggests a beneficial effect from treating depression in people with TB. One of the consistent findings across all the studies included in this thesis was the positive impact of providing mental healthcare for people with TB and depression. This was evident for all the psychological interventions identified and analysed in this thesis (Acha, et al., 2007; Khachadourian, et al., 2020; Li, et al., 2018; Walker, et al., 2018b; Das, et al., 2014; Vega, et al., 2004; Lovero, et al., 2019; Contreras, et al., 2017; Kaukab, et al., 2015, Pasha, et al., 2021, Zhang, et al., 2019, Li, et al, 2019). Additionally, the findings in Chapter 4 regarding the different types of interventions implemented to improve mental health outcomes for people with TB in LMICs are consistent with previously published literature, which has also highlighted the beneficial impact of psychological interventions and those combining psychological and socioeconomic support to improve TB treatment outcomes (Van Hoorn, *et al*., 2016; Farooq, Tunmore, and Comber, 2021). This could be a result of publication bias, as interventional studies are more likely to report better mental health status and outcomes compared to prevalence studies, and studies with positive treatment outcomes are more likely to be published (Agbeko, et al., 2022). Yet, the overwhelming consensus in the peer-reviewed literature is that mental health treatment should be routinely available for people with TB in LMICs, given the socioeconomic and psychological needs of this particular population before, during, and after TB diagnosis and treatment.

- **This thesis, and previous research, have proven that it is possible to address the mental health needs of people with TB with multiple approaches which can be tailored to local needs and available resources.**

The results of Chapter 3, Chapter 4, and Chapter 3of this thesis contribute to research on the different mental health interventions for depression in people with TB. Other studies that have also reviewed and analysed the different interventions for mental health in people with TB have also included studies which are a result of one-off projects focusing on improving TB treatment outcomes or mental health outcomes in the participants (Van Rensburg, et al., 2020; Farooq, Tunmore, and Comber, 2021; Van Hoorn, et al., 2016). This means that possibly none of the individual studies included in the reviews in this thesis and in other peer-reviewed literature are a result of programmatic changes to the delivery of TB in the countries reflected in the studies. This is a significant finding given the increasing awareness and support for the integration of mental health diagnosis and treatment programmes in international guidance for TB treatment and primary healthcare. For example, the management of co-morbidities is a core component of the updated pillars of the End TB strategy of the WHO (WHO, 2022b). The diagnosis and treatment of mental health comorbidities in people with TB, including depression, are now a core part of the framework for addressing comorbidities in TB promoted by the WHO (WHO, 2022c; 2022d). “[The] *WHO recommends the provision of psychological support for people with TB*” (WHO, 2022c). However, these guidelines do not provide further guidance as to how to provide such psychological support. Yet, with international support and the mandate from the WHO, it is possible to leverage support at the national level to embed the treatment of mental health comorbidities programmatically.

- **Despite growing literature on the sustainability of mental health interventions for depression in LMICs, the healthcare delivery settings and the interventions examined in this research still show deficiencies in sustaining these interventions.**

In Chapters 4 and 5, the findings suggest that, despite the implementation of effective mental health interventions for depression in people with TB, these interventions were not sustained by the time this thesis was written. The sustainment of interventions analysed in Chapter 3 is unknown as it was not the objective of that chapter to explore that question. The sustainability of such interventions is crucial, given that mental health needs can persist long after TB treatment, depending on underlying risk factors for depression, such as poverty, lack of education, substance abuse, and female gender (Van Rensburg et al., 2020).The syndemic relationship between TB and depression can continue beyond the initial diagnosis of TB, necessitating longer-term, structured support that includes mental health components (Sweetland et al., 2017). This can be a strategic decision by national TB programme (NTP) leaders to improve

treatment adherence and prevent the recurrence of TB and the emergence of drug-resistant strains in at-risk populations.

An umbrella review of 19 meta-analyses evaluating the effectiveness of psychosocial interventions for various mental health illnesses in LMICs argues that there is no shortage of evidence for the clinical effectiveness of such interventions in low-resource settings (Barbui, et al., 2020). In fact, there is strong evidence supporting the need for mental health interventions for depression delivered through approaches that include sustained and adequate training programmes for non-specialist healthcare workers. However, long-term outcomes (e.g., sustainment) were absent from the 19 meta-analyses included in the review (Barbui, et al., 2020). The findings of this umbrella review, along with the findings from Chapters 4 and 5 of this thesis, emphasize that research should shift its focus toward the sustainability of implementation approaches, rather than solely assessing the clinical effectiveness of mental health interventions for depression (Barbui, et al., 2020). Health systems in LMICs are ill-prepared to adopt the care for non-communicable diseases into primary care services other than cardiovascular and chronic-respiratory diseases (Kabir, et al., 2022). This is particularly worrisome considering the burden of mental health illnesses and the comorbidities between non-communicable diseases and mental illness.

Few countries with high TB morbidity include routine screening for depression in their national TB guidelines, despite widespread support for integration of mental health into TB treatment by policymakers (Sweetland, et al., 2019). The findings in this thesis, which include studies undertaken in LMICs, are particularly relevant for research funding bodies, international donors, and national policymakers, as it provides evidence-based arguments for allocating more resources to implementation research and for the integration of explicit guidance on screening and treatment for depression into national TB guidelines could possibly support the implementation of mental health interventions in the frontline and more importantly, support the sustainability and long-term delivery of mental health services for people with TB. Alongside and sustained by programmatic support as budget and resources and increased mental health awareness can help to facilitate the integration of mental healthcare into TB services, as described by the experience of integrating the care of non-communicable diseases in the TB services of 15 LMICs (Foo, et al., 2022).

- **This thesis has contributed to the field of implementation science by comparing the use of the same analytical framework in the analysis of implementation**

barriers and facilitators for mental health interventions for depression using different research designs.

The use of two versions of the CFIR framework enhanced the implementation science focus of the research in Chapters 3 and 5 by allowing a comparison of the analytical approaches used in each study design and the application of the CFIR framework across different study types. There are versions of the CFIR Framework developed especially for its use in LMICs (Means, et al., 2020). I decided to use the 2022 version of the CFIR framework as it had been developed, or updated, through a consultation process with implementation science researchers (Damschroder, et al., 2022). Further research could compare the relevance of the Means, et al., version and the Damschroder, et al., 2022 version for LMICs as, due to resource constraints, I could not pursue this research direction myself.

From my experience using the CFIR framework for two study designs, I concluded that the CFIR framework is better suited for primary data collection studies, like the one in Chapter 5. However, I consider that its use is more relevant when exploring implementation processes as they occur (i.e., concurrently) rather than retrospectively. In both Chapters 4 and 5, I applied the framework retrospectively, using secondary data in Chapter 4 and primary data in Chapter 5, which provided a similar experience in terms of framework application. The particular contribution of Chapter 5 is the use of the CFIR framework within a qualitative case study research methodology for mental health services research. Other examples of the CFIR use for health services research in case study methodology have found that it can be time-consuming and resource intensive (Keith, et al., 2017; Inguane, et al., 2022). This is consistent with my experience, but it was my research objective to carry such an in-depth exploration of the context of implementation for a mental health intervention for depression in people with TB.

There are other frameworks that aim to evaluate the implementation of interventions in complex contexts. For example, the Normalisation Process Theory is a framework that focuses on exploring the factors needed for routine delivery, i.e., normalisation, of a new intervention (Murray, et al., 2010). The Theoretical Domains Framework is also a known implementation science framework for exploring factors determining behaviours and examine possible barriers and facilitators for implementation (Atkins, et al., 2017). These two implementation frameworks, along with the CFIR framework, share as a goal the exploration of implementation processes which determine the adoption, or failure, of a change in routine practice. Each framework has their own distinct advantages and disadvantages which can be inherent to the frameworks' conceptual model, and to the research questions they are applied to. Furthermore, it is possible

to combine the use of implementation frameworks as their conceptual domains often overlap or complement (McHugh, et al., 2022). As their conceptual models can be similar, and can be used in conjunction, the choice of implementation framework for analysis can be a question of preference for the researcher in terms of the frameworks' orientation, the audience of the results, and the analysis depth required of certain concepts (Moullin, et al., 2015). There is no single framework which covers all possible elements that can influence implementation of an intervention. For this thesis, I decided to use the CFIR framework as it allowed the detailed unpacking of the contextual factors which can influence implementation. In this, the CFIR framework is one of the few frameworks who addresses the macro-level context of implementation processes, despite the disadvantage of not addressing the sustainability or penetration of an intervention (Wang, et al., 2023).

Despite the limitations of using the CFIR framework retrospectively, it has much to offer the field of implementation science. First, it helps to standardize the language used when discussing barriers and facilitators to implementation. Second, it facilitates comparisons across different settings and interventions by using CFIR domains as a shared conceptual language for analysis. Third, the CFIR framework is comprehensive without being overwhelming, offering flexibility by allowing researchers to focus on specific domains as needed. The newer version of the CFIR framework, used in Chapter 5, addresses some of the criticisms of the previous version. I found the updated version particularly useful in Chapter 5, where I had to describe different organisations, their characteristics, and the role of individuals as barriers or facilitators to implementation. This flexibility and adaptability of the framework suited my research design and objectives, which would have been more complex had I used the older version applied in Chapter 4.

6.3 Future research

Although only Chapter 3 had as an objective to assess the effectiveness of mental health treatment for depression in people with TB, the studies included in Chapter 4 and Chapter 5 also reported beneficial outcomes for both mental health and TB-related outcomes. Future research could build on the work presented in Chapter 2 by incorporating more recent trials on mental health treatments for depression in people with TB. Although Cochrane reviews are considered the gold standard for evaluating effectiveness, this should not diminish the value of other studies that quantitatively synthesize results from peer-reviewed trials (Barbui, *et al*., 2020; Farooq, Tunmore, and Comber, 2021; Van Rensburg, *et al*., 2020). Mental health

outcomes, in particular, may be inherently biased and thus may not always meet Cochrane's quality criteria for evidence.

The updated version of the CFIR framework represents an improvement, but it could be further refined to better capture the nuances of the relationships between the implemented intervention, the implementation team, and the implementing organisation—especially in complex settings such as multi-donor programmes like TB services in LMICs. This refinement could be achieved by individuals experienced with the updated CFIR, who are familiar with stakeholders in LMICs' healthcare systems, and approach such task through an implementation science perspective.

One of the key findings from Chapter 5 was the influence of gender on the delivery of mental health interventions for depression in women with TB in Pakistan. For women, the delivery of the intervention for depression described in the case study was not always equivalent to that received by their male counterparts. Peer-reviewed literature on the relationship between gender, depression, and TB has established that being a woman is a risk factor for developing depression among people with TB in LMICs (Van Rensburg, et al., 2020; Koyanagi, et al., 2017). However, other reviews have found gender-specific dynamics that can hinder access to TB diagnosis and treatment, such as patriarchal attitudes amongst men and caregiving commitments in women (Teibo, et al., 2024). The findings of Chapter 5 elucidate the mechanisms by which women with TB may not receive adequate mental healthcare, even when such interventions are available and accessible, but the influence of male gender on acceptability of the mental health intervention for depression was unexplored. Therefore, further research could explore gender-specific mechanisms that could facilitate the delivery and acceptability of mental healthcare amongst different genders, and in different cultural settings.

Future research could also focus on continuing exploring the prevalence of mental health illnesses, including depression, in people with TB. The aftermath of the COVID-19 pandemic and its impact on TB services and people receiving treatment for TB during the pandemic is not yet fully understood. It is possible that the pandemic exacerbated the cases of TB and increased the risk for comorbid depression. Thus, future studies could conduct meta-analysis or umbrella reviews including the studies conducted post-COVID-19.

6.4 Research limitations and thesis limitations

The main limitations of Chapter 3 include the small number of studies reviewed and the limitations inherent in those studies (Li et al., 2019; Zhang et al., 2021). Notably, these limitations include the restricted age range of the study populations and the lack of information

on the type of TB (drug-susceptible or drug-resistant). These factors are significant because the mental health needs of people with TB vary based on age, gender, type of TB, and the type of anti-TB treatment received (Dartois and Rubin, 2022; Koyanagi, et al., 2017). Therefore, the findings from Chapter 13 should be interpreted with caution and used as a foundation for future research. This future research should include more recent studies and emphasize the importance of reporting age, gender, and TB type in randomized controlled trials (RCTs) of mental health interventions for depression.

Moreover, there should be further discussion about the use of RCTs as the gold standard for evaluating the effectiveness of mental health interventions. Mental health interventions often involve self-assessed outcomes, which introduces an inherent risk of bias (Juul, et al., 2021; Savovic, et al., 2015). Additionally, these interventions are challenging to assess through double-blinded, placebo-controlled studies, which are typically considered of higher quality. Future discussions should explore alternative methods better suited to evaluating mental health interventions. Such discussions should also be framed within the broader context of shifting focus from effectiveness to implementation and sustainability research for mental health interventions in LMICs. As other reviews and studies have highlighted, research priorities should align with implementation-oriented outcomes to ensure the sustainability of interventions (Wagenaar, et al., 2020; Means, et al., 2020).

Lastly, a significant limitation of this thesis is the lack of perspectives from people with TB who received mental health interventions for depression. Their views could only have been incorporated in Chapter 5, given the study designs of Chapters 3 and 4. Including the perspectives of individuals receiving healthcare interventions is crucial, and this thesis did not address this aspect.
Retrospectively, one of the ways that people with TB could have been involved in my thesis is by co-designing the research questions and the methods used to answer those questions. By co-creating the research questions, I would be adhering to the principles of collaboration, relevance, and empowerment of patient and public engagement (Troya, et al., 2019; Dawson, et al., 2020). Furthermore, I could have involved them through the research process (i.e., design, overview, analysis, interpretation, and dissemination of findings) to empower them to be part the research cycle and democratizing their access to the research process. By doing this, I believe my thesis could have improved not only in its relevance and quality but also in its contribution to me as a researcher and a human being. It would have helped me to learn to explore difficult

experiences in peoples' lives, and to advocate for balanced research relationships between people and researchers and promote inclusive and relevant research practices that reflect real-world priorities and concerns. I consider that patient and public engagement in my thesis would have made me a better researcher and with additional resources and time, I would have included people with TB in the design of the research objectives, particularly of chapter 4 and chapter 5. The main reasons for not involving people with TB in the design of my research was lack of awareness of this possibility and constrained financial and time resources that meant that I had limited time and financing to undertake my research, relying on scholarships and personal savings. I consider this a limitation to people with TB's engagement with my research as they should be adequately remunerated for their contributions.

Future research should aim to incorporate the views of people with TB alongside the implementation analysis of mental health interventions for depression. Co-created research objectives should be integrated into future study designs aimed at delivering and evaluating mental health interventions to people with TB in LMICs.

Chapter 7 - Conclusion

7.1 Summary of key findings

As a whole, this thesis contributed to the field of depression comorbid with TB, particularly in people in LMICs. The findings of the studies included in this thesis showed that treating depression in people with TB using psychological treatments could improve depression-related and TB-related health outcomes in people with TB, but more evidence is needed to assess the size of this effect and their impact on other health outcomes such as health-related quality of life. The delivery of psychological and other types of interventions for people with TB and depression is possible, including in resource-constrained settings such as LMICs. However, adequate training, physical spaces, human resources, and financial resources need to be available to facilitate implementation. These findings stemmed from the research in Chapter 4 and 5 in this thesis. Implementation teams and relevant organisations should adopt measures that ensure and promote the inclusion of sustainability and sustainment plans in any future projects that aim to deliver mental healthcare for people with TB.

7.2 Recommendations for improvement

There are a few ways in which this thesis could be improved, other than those addressing the limitations of the individual studies here included which I will not repeat here. One of the ways in which this thesis can be improved is to update the systematic reviews in Chapter 3 and Chapter 4 to include recently published literature and ensure their contributions to the field are up to date.

A second way in which this thesis can be improved is by using the study design and analytical approach of Chapter 5 to study an intervention as it is implemented, rather than retrospectively. This approach can be particularly beneficial given the focus on implementation processes which are easier to observe as they happen rather than reconstruct them from documentary sources and participants' recollections.

This thesis can be further improved by analysing, or discussing, the applicability of this research to other countries with high TB prevalence and incidence. This was not a research objective in any of the studies included but it merits further exploration given the world TB burden remains high. It can also be improved by exploring the relevance of these findings to the sub-sets of people with TB, as they are not a homogeneous group. Future work could focus on the

relevance of these findings for children with TB, homeless populations, people in prisons, people with more than one comorbidity, amongst others.

Lastly, this thesis can be further improved by exploring the relevance and applicability of this research considering recent events such as the COVID-19 pandemic and the updated treatment guidelines for TB which call for more people-centred care and shorter courses of treatment.

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ZHANG, K., WANG, X., TU, J., RONG, H., WERZ, O. & CHEN, X. 2019. The interplay between depression and tuberculosis. J Leukoc Biol, 106, 749-757.

Appendices

Appendix 1 – Search strategy for Medline (Cochrane Review; Chapter 3)

Appendix 2 – Search strategy for exploratory systematic review (NIHR review; Chapter 4)

Appendix 3 – Qualitative and quantitative data extracted from included studies (NIHR review; Chapter 4)

Appendix 4 – List of excluded studies (NIHR review; Chapter 4)

Appendix 5 – Detailed description of barriers and facilitators for implementation of interventions for depression in people with TB in LMICs according to the CFIR domains (NIHR review; Chapter 4)

Appendix 6 – Search approaches to identify documents for qualitative case study (Chapter 5)

Appendix 7 - Complete list of data included in qualitative case study (Chapter 5)

Appendix 8 – COREQ and SRQR checklists for qualitative research reporting (Chapter 5)

Appendix 9 – Interview guide for study participants (relevant stakeholders), (Chapter 5)

Appendix 10 – Detailed description of barriers and facilitators for implementing the mental health intervention “IPUs” in Karachi, Pakistan (Chapter 5)

Appendix 1 - Search strategy for Medline (Cochrane Review; Chapter 3)

Date of search: 19/05/2021

Results: 138

Database: Ovid MEDLINE(R) ALL <1946 to May 18, 2021>

Search Strategy:

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1 Mycobacterium tuberculosis/ (52118)

2 exp Tuberculosis/ (195688)

3 Tuberculosis, Multidrug-Resistant/ (8251)

4 Tuberculin Test/ (13886)

5 (tubercul* or TB or MTB or Koch* disease).ti,ab,kf. (270395)

6 1 or 2 or 3 or 4 or 5 (298864)

7 Depression/ (127618)

8 exp Depressive Disorder/ (112620)

9 Mood Disorders/ (14820)

10 (depression or depressive? or mood? or affective disorder? or affective symptom?).ti,ab,kf. (463042)

11 depressed.ti,ab,kf. (95864)

12 (mental* or psych*).ti,kf. (552631)

13 7 or 8 or 9 or 10 or 11 or 12 (1017145)

14 6 and 13 (2732)

15 controlled clinical trial.pt. (94165)

16 randomized controlled trial.pt. (530996)

17 clinical trials as topic/ (195882)

18 (randomi#ed or randomi#ation or randomi#ing).ti,ab,kf. (688452)

19 (RCT or "at random" or (random* adj3 (administ* or allocat* or assign* or class* or cluster or crossover or cross-over or control* or determine* or divide* or division or distribut* or expose* or fashion or number* or place* or pragmatic or quasi or recruit* or split or subsitut* or treat*))).ti,ab,kf. (607983)

20 placebo.ab,ti,kf. (224316)

21 trial.ti. (240167)

22 (control* adj3 group*).ab. (572417)

23 (control* and (trial or study or group*) and (waitlist* or wait* list* or ((treatment or care) adj2 usual))).ti,ab,kf,hw. (27755)

24 ((single or double or triple or treble) adj2 (blind* or mask* or dummy)).ti,ab,kf. (181309)

25 double-blind method/ or random allocation/ or single-blind method/ (288603)

26 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 (1823634)

27 exp animals/ not humans.sh. (4830396)

28 26 not 27 (1583282)

29 14 and 28 (138)

Appendix 2 – Search strategy for exploratory systematic review (NIHR review; Chapter 4)

The general search strategy consists of using relevant terms for tuberculosis, depression, and approaches to integration listed in bold in at least one of 3 modes - as MeSH terms, as subject headings, or as keywords in the title or abstract. Their usage will depend on the indexing rules of each database.

(Relevant terms for pulmonary tuberculosis):
tuberculosis as *MeSH* OR **tuberculosis** as *subject heading* (i.e., *exp*) OR **tuberculosis** as *keyword* in title or abstract (i.e. *.mp .kw .ti. .ab*)
AND (relevant terms for depression):
depression as *MeSh* OR **depression** as *subject heading* (i.e. *exp*) OR **depressive disorder** as *MeSh* OR **depressive disorder** as *subject heading* (i.e. exp) OR **depress*** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **((psych*** OR **emotion*** OR **mental*** OR **socio*** OR **behavio#r*** next/adj1 (**disease*** OR **health*** OR **problem*** OR **state*** OR **aspect*** OR **ill*** OR **disord*** OR **disturb*** OR **condition*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti. .ab*) OR **((‘mental health*’ OR ‘mental illness*’ OR ‘mental disorder*’)** as *subject heading* (i.e., *exp*) OR **(‘mental health*’ OR ‘mental illness*’ OR ‘mental disorder*’)** as *MeSh* OR **(‘mental health*’ OR ‘mental illness*’ OR ‘mental disorder*’)** as *keyword* in title or abstract (i.e. *.mp .kw .ti. .ab*)
AND (relevant terms for approaches to integration):
((patient* OR person* OR people*) adj1 cent*) as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **(outpatient* adj/3 (care* OR service* OR clinic*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **(team* adj2 (care* OR treat* OR assess* OR consult*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **(care adj2 (coordinat* OR co-ordinat* OR program* OR continu*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **continuity of care** as *MeSH* OR **continuity of care** as *subject heading* OR **‘continuity of care’** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **integrated care** as *MeSH* OR **integrated care** as *subject heading* OR **‘integrated care’** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **integrated healthcare system** as *MeSH* OR **integrated healthcare system** as *subject heading* OR **‘integrated health*’** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **integrated services** as *MeSH* OR **integrated services** as *subject heading* OR **integrated services** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **referral and consultation** as *MeSH* OR **referral and consultation** as *subject heading* OR **refer*** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*)

OR **consult*** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **comprehensive care** as *MeSH* OR **comprehensive care** as *subject heading* OR **(integrat* adj3 (care* OR service* OR deliver* OR strateg* OR program OR manage*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **(deliver* adj3 (with OR within OR together))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **(multi* adj2 (care* OR service* OR clinic* OR disciplin*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **(multicare OR multiservice* OR multiclinic* OR multidisciplin*)** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **((collaborat* OR manage* OR integrat* OR link* OR join* OR co#rdinat* OR comprehensive OR contin*) adj3 (health* OR care* OR therap* OR intervent* OR treat* OR program* OR service* OR strateg* OR deliver*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **case management** as *MeSH* OR **case management** as *subject heading* OR **(case adj1 manag*)** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*) OR **((psych*** OR **emotion*** OR **mental*** OR **socio*** OR **behavio#r*) adj3 (educat* OR therap* OR support* OR program* OR intervent* OR service* OR train* OR consult* OR refer* OR treat*))** as *keyword* in title or abstract (i.e. *.mp .kw .ti .ab*)

Appendix 3 - Qualitative and quantitative data extracted from included studies (NIHR review; Chapter 4)

Qualitative data extracted as reported in the included studies

Study	Population**	Intervention	Results	Qualitative method
(Acha, *et al.,* 2007)	N= 285	Psychological only	Narrative description of attendance patterns and participants; description of therapeutic strategies; description of thematic content of the sessions; description of workshops for recreation and family members.	Participant observation, focus groups, documentation (session summaries and transcripts).
(Diez-Canseco., et al. 2018 *)	N= 127/143 people. N= 21/22 primary healthcare practitioners	Screening-only	Narrative description of study participants, description of the implementation of the screening, description of positive cases detection and referrals; help-seeking and access to mental healthcare; primary healthcare practitioners' assessment of the project, delivery of results and referral, feasibility of integrating a mental health screening.	Documentation (routinely collected data); interviews with people; interviews with primary healthcare practitioners.
(Lovero, *et al.,* 2019)*	N= 5	Combined	Participants' description of integrated mental health service provision, challenges to implementation of integrated mental health services in primary care.	Interviews with TB programme managers.

(Walker, *et al.,* 2018b)*	N=11	Psychological-only	Feasibility and acceptability of the psychosocial package (the screening process, the counselling, the group support, other challenges, and benefits), narrative description of depression symptom outcomes for people.	Documentation (counsellors' diary); interviews with people; interviews with TB health workers; observations.

*Studies with mixed-methods design; only qualitative data is reflected in this table.

** Refers to the number of participants from whom qualitative data was obtained.

Quantitative data extracted as reported in included studies

Study	Population description	Intervention	Comparator	Quantitative outcomes	
				Process outcomes	Clinical outcomes
(Contreras, et al. 2017)	N=192	Combined, with socioeconomic support. Cut-off scores for mental health scales: SRQ18 >=1 (on the psychotic and alcoholism section) PHQ9>=10;	None; not applicable.	> Number of people screened for comorbidities (including mental health) = 135/192 > Number of people referred to mental health services (including those at risk for all mental health conditions including depression) = 47/62 > Number of people who refused mental health screening = 57/192 > Number of people who attended the mental health appointment = 41/47 > Number of people screened for socioeconomic assistance = 126/192 > Number of people who declined or did not complete socioeconomic assistance assessment= 66/192. > Number of people that required follow-up to initial assessment = 192 (100%)	> Number of people with poor adherence to TB treatment = 192/192***. > No measurement of mental health outcomes at the end of the intervention, only measured attendance to psychological services. > Number of people at risk of depression = 36/192 > Number of people without mental health condition identified at screening point = 80/192

				> Number of people receiving socioeconomic assistance = 76/192	
(Das, *et al.,* 2014)	N=61	Combined. Cut off scores for mental health scales: PHQ-9 >=4.	None; not applicable.	> Number of eligible people screened for depression 45/61	> Number of people with depressive symptoms at baseline = 7/45 > Number of people without depressive symptoms = 38 at baseline > Number of people without depressive symptoms at follow-up (3 months) = 41/44 > Number of people with depressive symptoms at follow-up (3 months) = 3/44 > Number of deaths =1
(Diez-Canseco, *et al.,* 2018)*	People N=85 Primary healthcare providers (all female) = 22	Screening-only Screening tool and cut-off scores not reported.	None; not applicable.	> Number of people screened = 733 > Number of screenings in TB services = 85/733 > Number of positive cases of mental health illness and suicide risk in people with TB = 13/85.	None reported.

				> Number of cases of detected mental health illness and suicide risk in all types of people = 159/733 > Number of referrals to psychologist (includes number of people with conditions other than TB) = 143/159 > Number of people who sought help after positive diagnosis of mental health illness or suicide risk = 92/127 > Number of people who had access to specialised care = 70/92.	
(Kaukab, et al. 2015)	N=70	Combined, with socioeconomic support. Cut-off scores for mental health scales: BDI >=9	Intervention n= 35 Control n=35	None reported.	> Number of participants with depression at baseline, intervention = 35/35 > Number of participants with depression at baseline, control = 35/35 > Number of participants with depression at end of intervention = 20/35

					> Number of participants with depression at end of intervention = 35/35
(Khachadourian, *et al.,* 2020)**	N=385	Psychological-only Cut-off scores for mental health scales: CES-D; no cut-off point; higher scores indicate higher levels of depression symptoms.	Intervention n=187 Control n=198	> TB knowledge score intervention M (SD) = 23.9 (3.1) > TB knowledge score control M (SD) = 23.1 (3.5) > Support score intervention M (SD) = 43.2 (5.3) > Support score control M (SD) = 41.8 (7.5)	> TB treatment success intervention = 172/187 > TB treatment success control = 184/198 > Lost to follow-up intervention = 12/187 > Lost to follow-up control = 10/198 > Failure intervention = 0/187 > Failure control = 0/198 > Death intervention = 3/187 > Death control = 3/198 > Not evaluated intervention = 0/187 > Not evaluated control = 1/198

					> Depression score intervention M (SD) = 4.3 (7.5) > Depression score control M (SD) = 4.7 (7.6)
(Li, et al. 2018)	N= 201	Psychological-only Cut-off scores for mental health scales: SDS; no cut-off point; higher scores indicate higher levels of depression symptoms.	Intervention n=69 Control = 132	None reported.	> Number of deaths intervention = 1/69 > Number of deaths control = 2/132 > Depression score baseline intervention M (SD)= 59 (7.49) > Depression score baseline control M (SD)= 57 (9.66) > Depression score end of intervention M (SD)= 43 (8.53) > Depression score end of intervention control M (SD)= 48 (9.13)
(Lovero, et al,.2019)*	Nurses =59	Combined	None; not applicable.	> Number of nurses who received mental health training = 46/59	None reported.

	Mental health practitioners = 17	Cut-off scores for mental health scales: PC101 (cut-off score not reported or ratings).		> Number of nurses who received training in primary care guidelines, including mental healthcare guidelines = 37/59 > Number of nurses that consider the primary care guidelines easy or very easy to use = 53/59 > Number of nurses who feel comfortable or very comfortable managing mental illness = 35/59 > Number of mental health screenings done by nurses in the past 3 months = 51/59 > Number of nurses who screen people at every visit = 43/59 > Number of nurses that use a tool to assess mental illness in people = 26/59 > Number of nurses who manage positive mental illness cases at clinic = 2/59 > Number of nurses that refer people to treatment elsewhere inside clinic = 34/59	

				> Number of nurses that refer people to mental health practitioners = 30/59 > Number of nurses that refer people to other clinic = 21/59 > Number of mental health practitioners that assess mental illness = 14/17 > Number of mental health practitioners that use a tool to assess mental illness = 5/14 > Number of mental health practitioners that offer treatment to positive cases of mental illness = 14/17 > Number of mental health practitioners that offer psychiatric medications = 7/14 > Number of mental health practitioners that offer individual therapy = 4/14 > Number of mental health practitioners that offer group therapy = 1/14	
(Vega, et al. 2004)	N= 75	Combined Based on DSM-IV criteria.	None; not applicable.	None reported.	> Number of depression cases at baseline (n=69) = 36

					> Number of incident cases of depression during anti-TB therapy = 10/75 > Number of hospitalizations due to depression during anti-TB treatment = 0/75 > Persistent psychiatric symptoms throughout MDR-TB treatment requiring psychiatric medications (new depression) = 8/10 > Persistent psychiatric symptoms throughout MDR-TB treatment requiring psychiatric medications (baseline depression) = 2/12
(Walker, et al. 2018)*	N=135	Psychological	None; not applicable.	> Fidelity, feasibility, acceptability of the intervention. > Number of eligible people referred to counselling = 29/30	> Number of people with positive anxiety and depression scores at

		Cut-off scores for mental health scales: HSCL (anxiety) >= 17 HSCL (depression) >= 24 MSPSS <= 3 PHQ-9 >=10		> Number of assessments made by counsellor after referral = 29/29 > Number of people referred to psychiatric care due to severity of symptoms = 6/29 > Number of people with low PHQ-9 scores (PHQ-9 <= 10) not eligible for counselling = 11/29 > Number of people that received information leaflet = 115/135 > Number of people that received one information and education session = 80/135 > Number of people who completed counselling sessions = 9/18****	baseline (HSCL and MSPSS) = 30/135 > Number of people with severe depression score at baseline (PHQ-9 >=19) = 6/29

*Studies with mixed-methods design; only quantitative data is reflected in this table.

** Data refers to per-protocol analysis.

*** Described as "Irregular attendance at health facility for TB treatment".

**** Defined as the 18 people who were eligible for counselling after scoring positive for depression in PHQ-9 scale and HSCL scale, including those with severe symptoms.

Appendix 4 – List of excluded studies (NIHR review; Chapter 4)

Eleven articles were excluded because they were based in high-income countries, mostly the US:

- CRANE GE. Further studies on iproniazid phosphate; isonicotinil-isopropyl-hydrazine phosphate marsilid. J Nerv Ment Dis. 1956 Sep;124(3):322-31. doi: 10.1097/00005053-195609000-00014. PMID: 13429360.
- Jentoft, B. (1949). Convulsive Treatment in 56 Tuberculous Mental Patients. Journal of Mental Science, 95(400), 651-654. doi:10.1192/bjp.95.400.651
- CHOI, Y. H. 1985. An experimental study of the effects of supportive nursing intervention on family support behavior and sick role behavior. *Taehan kanho. The Korean nurse,* 24**,** 10-20.
- DOCKHORN, J. M. 1960. The influence of social and emotional factors in the treatment of tuberculosis. *The American review of respiratory disease,* 82**,** 223-231.
- GRABENER, J. 1963. PSYCHOLOGICAL CARE OF TUBERCULOTICS FROM THE VIEWPOINT OF THE PUBLIC HEALTH PHYSICIAN. *Der Öffentliche Gesundheitsdienst,* 25**,** 606-612
- KIENAST, H. W., FISHER, R. A. & RODRIGUEZ, G. 1965. PSYCHIATRIC TREATMENT OF TUBERCULOUS PATIENTS IN A STATE HOSPITAL SETTING. *Diseases of the nervous system,* 26**,** 284-287.
- Nagata Y, Urakawa M, Kobayashi N, Kato S. [Analysis on workload for hospital DOTS service]. Kekkaku. 2014 Apr;89(4):495-502. Japanese. PMID: 24908810.
- PLEASURE, H. 1954. 233 patients with mental illness treated with electroconvulsive therapy in the presence of tuberculosis. *The American Journal of Psychiatry,* 111**,** 177-183.
- RONCATI, C. 1952. Treatment of tuberculotics in psychiatric hospitals. *Rassegna di neuropsichiatria e scienze affini,* 6**,** 214-218.
- SILVERMAN, M. 1953. Electrical convulsive therapy in psychiatric patients with pulmonary tuberculosis. *The British journal of tuberculosis and diseases of the chest,* 47**,** 172-178.
- Crouzatier, A. 1969. Psychoanalysis and psychotherapy of recent pulmonary tuberculosis patients. *Cumulated Index Medicus*, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Library of Medicine.

One study was excluded because it did not include patients with pulmonary TB in its cohort:

- FORSYTHE AM, VENTER C. Behavioral Economics, Motivating Psycho-Education Improvements: A Mobile Technology Initiative in South Africa. Front Psychol. 2019 Jul

10;10:1560. doi: 10.3389/fpsyg.2019.01560. PMID: 31354576; PMCID: PMC6635590.

Two studies were excluded because they measured the prevalence of depression in people with TB:

- AYDIN IO, ULUŞAHIN A. Depression, anxiety comorbidity, and disability in tuberculosis and chronic obstructive pulmonary disease patients: applicability of GHQ-12. Gen Hosp Psychiatry. 2001 Mar-Apr;23(2):77-83. doi: 10.1016/s0163-8343(01)00116-5. PMID: 11313075.
- AMBAW F, MAYSTON R, HANLON C, ALEM A. Depression among patients with tuberculosis: determinants, course and impact on pathways to care and treatment outcomes in a primary care setting in southern Ethiopia--a study protocol. BMJ Open. 2015 Jul 8;5(7): e007653. doi: 10.1136/bmjopen-2015-007653. PMID: 26155818; PMCID: PMC4499723.

Five studies were excluded because they were discussion papers or reports:

- BORZENKO, A. S., ZUBOVA, E. I. & IAITSKII, I. A. 2007. [Evaluation of the efficiency of a hospital stage of treatment in delivering antituberculous care to mental patients with active pulmonary tuberculosis]. *Problemy tuberkuleza i boleznei legkikh***,** 37-40.
- KOSTNAPFEL, J. 1964. MENTAL HYGIENE SERVICES IN TUBERCULOSIS HOSPITALS. *Tuberkuloza,* 16**,** 454-456.
- MOHAN REDDY, M. 2019. An alternative model to combat mental illness: A collaborative approach. *Indian Journal of Psychiatry,* 61**,** S452.
- STRELTSOV, V. V., SIRESINA, N. N., ZOLOTOVA, N. V., BARANOVA, G. V., STOLBUN, I. V., DOLGOVA, I. V., PANKOVA, L. I., EROKHIN, V. V., ERGESHOV, A. E., CHERNYKH, N. A., KUZ'MIN, A. V., RODINA, O. V. & SEL'TSOVSKIĬ, P. P. 2009. Psychoemotional changes in patients with pulmonary tuberculosis during therapy using psychological and neuropsychological methods. *Problemy tuberkuleza i bolezneĭ legkikh***,** 31-37.
- WORLD HEALTH ORGANIZATION 2001. *The World Health Report 2001: Mental Health: New Understanding, New Hope*, World Health Organization.

Seven studies were excluded because they did not describe interventions to treat depression – they focused on adherence or psychosis (Egwaga *et al.,* 2009; Janmeja *et al.,* 2005; Liu *et al.,* 2017; Maas, 1957; Poleksic *et al.,* 1963; Streltsov and Zolotova, 2019; Tadesse *et al.,* 2013).

- Egwaga S, Mkopi A, Range N, Haag-Arbenz V, Baraka A, Grewal P, Cobelens F, Mshinda H, Lwilla F, van Leth F (2009). Patient-centred tuberculosis treatment delivery under programmatic conditions in Tanzania: a cohort study. BMC Med. 2009 Dec 21;7:80. doi: 10.1186/1741-7015-7-80. PMID: 20025724; PMCID: PMC2801503.
- Yan-Yan Liu, Hong-Mei Zhao, Zhao-Xia Zhang. (2017). Effects of comprehensive nursing intervention on the quality of life and prognosis of patients with smear-positive tuberculosis. Biomedical Research (2017) Volume 28, Issue 22.
- JANMEJA, A. K., DAS, S. K., BHARGAVA, R. & CHAVAN, B. S. (2005). Psychotherapy improves compliance with tuberculosis treatment. *Respiration; international review of thoracic diseases,* 72**,** 375-80.
- Maas, G. (1957). Psychotherapy in a tuberculosis sanatorium with special reference to autogenous training. *Der Tuberkulosearzt,* 11**,** 633-639.
- POLEKSIC, J., VUCKOVIC, S., BOGICEVIC, D., JOANOVIC, T. & LALEVIC, P. (1963). MODERN ACTIVE PSYCHIATRIC THERAPY OF TUBERCULOUS MENTAL PATIENTS. *Neuropsihijatrija,* 11**,** 97-101.
- Streltsov, V. V. and Zolotova, N. V. 2019 Streltsov V.V., Zolotova N.V. Psychological Support for the Patient with Pulmonary Tuberculosis: A Case Report [Elektronnyi resurs]. Konsul'tativnaya psikhologiya i psikhoterapiya = Counseling Psychology and Psychotherapy, 2019. Vol. 27, no. 1, pp. 102–118. doi:10.17759/cpp.2019270107. (In Russ., abstr. in Engl.)
- Tadesse Y, Yesuf M, Williams V. Evaluating the output of transformational patient-centred nurse training in Ethiopia. Int J Tuberc Lung Dis. 2013 Oct;17(10 Suppl 1):9-14. doi: 10.5588/ijtld.13.0386. PMID: 24020595.

Two articles were excluded because it was not possible to establish contact with the authors or national libraries in Brazil and Bolivia to access the full text:

- SUN, S. & ZHANG, L. 2020. Effect of drug combined with psychological intervention therapy on mental status of MDR-TB patients. Boletin de Malariologia y Salud Ambiental, 60, 431-436.
- VIEIRA, E. A. & CHEVITARESE, M. F. 1981. Investigacao diagnostica das caracteristicas psicossocias dos pacientes no hospital de tuberculose. HE rev, 8, 227-46.

Appendix 5 – Detailed description of barriers and facilitators for implementation of interventions for depression in people with TB in LMICs according to the CFIR domains (NIHR review; Chapter 4)

Other barriers across interventions

Complexity is part of the Intervention Characteristics domain. This was a barrier for psychological and combined interventions, but it had a mixed impact in interventions combined with socioeconomic support and screening-only. In psychological and combined interventions, the participant's perspective was that the initial screening component of the intervention was complicated to implement due to the additional time and paperwork required, or the number of steps required to implement some components of the intervention (Walker *et al.,* 2018). In one intervention, the feedback from healthcare workers made the implementing team change the original screening tool for one more acceptable to TB healthcare workers and their practices. TB healthcare workers also found challenging to deliver the psychological treatment component of the intervention (Acha *et al.,* 2007). In interventions where Complexity had a mixed impact, the studies report that participants expressed positive and negative opinions regarding the implementation of the intervention. In the screening-only intervention there was some flexibility to allow healthcare workers to implement the intervention as they saw fit but they still considered that the intervention was hard to implement, even though the technological elements of the intervention facilitated their paperwork activities (Diez-Canseco *et al.,* 2018). In some interventions, the processes of delivering the intervention components had been designed with the input of the healthcare workers and were adapted during implementation according to their feedback (Walker *et al.,* 2018;Diez-Canseco *et al.,* 2018).

Culture, part of the Inner Setting domain**,** was referred to as a barrier when organisational or people' culture clashed with the goals of the intervention. **Culture** as a barrier is best exemplified in the quote by (Lovero *et al.,* 2019), where they compare the goals of the intervention with the goals of people and the organisation (i.e., public TB services): "The goals of the intervention did not align with wider organisational goals, as these often conflicted with each other, causing the clinic staff to feel stressed by the competing directives and interests … most DPMs [district programme managers] highlighted a need for increased mental health literacy and awareness among district-level administrators to better facilitate mental healthcare integration". In the screening-only intervention, the cultural attitude towards mental health was reflected in people and healthcare workers discomfort when asking diagnostic questions regarding people' mental health (Diez-Canseco *et al.,* 2018). This challenge echoed in the implementation of two psychological interventions, which

affected the screening and treatment components of the intervention (Acha *et al.,* 2007;Walker *et al.,* 2018). **Culture** was a barrier for all types of interventions, except for combined interventions with socioeconomic support where there was no data available.

Other facilitators across interventions

Evidence strength and quality was defined as the belief, sustained by evidence, that the intervention would have the desired outcome. This was a facilitator in psychological, combined, and combined with socioeconomic support interventions. In studies that described these types of interventions, the interventions were justified on previous empirical research. In studies that reported quantitative outcome assessments, the interventions improved depression symptoms, decreased stigma scores, and improved TB knowledge in people and family members (Khachadourian *et al.,* 2020; Li *et al.,* 2018), which were the interventions' desired outcomes. In qualitative studies, people and participants expressed belief in the beneficial impact of the intervention, particularly in interventions where current and cured people interacted (Walker *et al.,* 2018b; Acha *et al.,* 2007) .

Cosmopolitanism, part of the Outer Setting, seemed to be a facilitator for all types of interventions, except for screening-only where there was no data to assess this. Cosmopolitanism, defined as the linkages between TB services and other public or private services, was an obvious facilitator in interventions that were implemented as part of collaborations between public TB services and private not-for-profit organisations or non-governmental organisations (NGOs) (Contreras *et al.,* 2017;Das *et al.,* 2014;Kaukab *et al.,* 2015;Vega *et al.,* 2004). In three combined interventions, NGOs where the main point of delivery of TB services, which acted as the main point of delivery of the intervention for depression (Contreras *et al.,* 2017;Das *et al.,* 2014;Vega *et al.,* 2004). The role of NGOs as the main community healthcare service delivery and their role as facilitators of the implementation for the depression intervention was more prominent in the studies that described interventions implemented in Peru (Acha *et al.,* 2007;Contreras *et al.,* 2017;Vega *et al.,* 2004).

External policy and incentives, part of the Outer Setting, seemed to be facilitators for all types of interventions, except for screening-only for which there was no data to assess this. We considered the influence of local, national, and international policies. In the implementation of psychological interventions, the existence of policies that supported the provision of mental healthcare to people with TB, or supported person-centred care, acted as a facilitator for implementation. For example, the description of one psychological intervention mentioned that the provision of mental healthcare to people with TB was "…a strategy that is well aligned with and supported by the people-centred model of care

advocated by the WHO" (Khachadourian *et al.,* 2020). In one combined intervention, the implementation of training, diagnosis, treatment, and referral components was enshrined in a national mental health policy which supported the integration of mental health services into primary care services. "One of the main objectives of the Strategic Plan is to scale up decentralized integrated primary mental health services, with the goal of including universal, routine screening and a stepped approach to management of mental disorders in primary care clinics" (Lovero *et al.,* 2019). In other combined intervention, implemented as part of NGO-provided TB services, the availability of external policies and incentives supported implementation and facilitated the delivery of screening and treatment. "People were also eligible for services provided by the municipality such as quarterly food baskets for people with TB… In Lima, Peru, all these interventions are available and supported by local or national policy. Thus, it is feasible to implement a comprehensive approach to managing the health issues…" (Contreras *et al.,* 2017). National and international policies acted as facilitators for implementation. International policies and guidelines, like the WHO, acted as facilitators at the local level.

Access to Knowledge and Information, part of the Inner Setting, acted as a facilitator for all types of interventions, except for combined interventions with socioeconomic support, where there was no data available to assess this. In all studies that described psychological, combined, or screening-only information, the Access to Knowledge and Information (e.g., training, provision of educational materials) for healthcare workers was a facilitator for implementation. This was particularly relevant for the implementation of the interventions' screening components as it was reported that some interventions provided training to healthcare workers to use mental health screening tools in their day-to-day practice in TB services. Only one study described the number of training sessions, along with the content of the training (Walker *et al.,* 2018b). One combined intervention recognised the importance of providing training to healthcare workers but also acknowledged that training was provided unevenly and it was hard to assess its impact as there were no indicators to measure its effect (Lovero *et al.,* 2019). In the screening-only intervention it was described that healthcare workers valued the mental health training they received to implement the intervention. "[Healthcare workers] believed the training made them more aware of the importance of caring for people's mental health... and offered them necessary skills to help their people" (Diez-Canseco *et al.,* 2018).

Individual stage of change, part of the Characteristics of Individuals domain, seemed to be a facilitator for all types of interventions, except for combined interventions with socioeconomic support, where there was no data to assess this. This construct refers to the stages that healthcare workers go through towards the sustained and skilled delivery of the

intervention, in terms of change in their confidence and knowledge to implement the intervention. In one psychological intervention, the progression of healthcare workers in their mental health treatment skills was considered a facilitator. “Primary healthcare workers showed willingness to learn to deliver the intervention either as co-facilitators alongside a mental health specialist or in the absence of one” (Acha *et al.,* 2007). In combined interventions, healthcare workers felt more comfortable providing screening and treatment components of the intervention after receiving training in mental health. “…though the majority [of healthcare workers] … responded they felt “very comfortable” or “comfortable” with the management of mental illness in people…” (Lovero *et al.,* 2019). A similar opinion was echoed in the screening-only intervention, in which healthcare workers felt more confident in their mental health screening abilities and decisions after receiving training (Diez-Canseco *et al.,* 2018).

The influence of **External change agents** as facilitators of implementation was present in all interventions, except for the screening-only intervention where there was no data available to assess this. External change agents were defined as individuals affiliated to other organisations that are not governmental or public TB services. The role of External change agents as a facilitator was more evident in studies describing interventions implemented in partnership with NGOs as these had collaborations with local public health authorities. For example, in one combined intervention with socioeconomic support that was implemented in the context of a pre-existing collaboration between NGOs and governmental health services, External change agents influenced the recruitment of participants for the intervention and its delivery, including the delivery of psychological treatment components and training for healthcare workers (Contreras *et al.,* 2017). This was also the case in two combined interventions (without socioeconomic support) where the role of External change agents was also to provide training to healthcare workers and provide the psychological and pharmacological treatment to participants in the intervention (Vega *et al.,* 2004;Das *et al.,* 2014;Li *et al.,* 2018). In interventions that were implemented solely by governmental services, the influence of External change agents in the implementation of the intervention was less clear or not mentioned at all (Khachadourian *et al.,* 2020;Diez-Canseco *et al.,* 2018;Lovero *et al.,* 2019).

Discrepancies in barriers and facilitators across intervention types

The construct **Needs of those served by the organisation** (i.e., people with TB’s needs), part of the Outer Setting domain, was a facilitator in psychological, combined, and combined with interventions with socioeconomic support. However, it was a barrier in the screening only intervention. In the studies that described interventions where this construct was a

facilitator, it was mentioned that the interventions were based on the care needs expressed or manifested by people with TB and their families. In one psychological intervention where depression treatment was delivered in a group setting, the intervention addressed non-clinical needs of people, like emotional support and reduction of stigma. "… for many people the support groups appeared to be one of the only places in which people could speak freely about their experiences and feelings and receive empathetic support from others." (Acha *et al.,* 2007). Two studies mentioned how the delivery of combined interventions was rooted in the mental health needs of people with TB that had been observed in pre-implementation years (Lovero *et al.,* 2019). Combined interventions with socioeconomic support were underpinned by the economic needs often expressed by people with TB and their family. One study described how socioeconomic support for the person with TB often involved helping them to provide for their families which the intervention supported by means of covering school fees, transport, food, or linking them to existing social assistance services (Contreras *et al.,* 2017). However, in screening-only interventions, this construct was defined as a barrier for the implementation as the people' needs were partially or not met at all. The study describing this intervention mentioned that, after screening, not all people were referred to mental health services even if they needed to and screening was not done consistently for all people; this was possibly because the depression screening activities were not included in performance assessments at the time the intervention was implemented (Diez-Canseco *et al.,* 2018).

The role of **Available resources**, a construct part of the Inner Setting domain, was a facilitator for implementation in combined interventions with socioeconomic support. However, this construct was described in the context of barriers for implementation in psychological and combined interventions. Additionally, this construct was one of the few ones to have a mixed impact, as a barrier and facilitator, in the implementation of screening-only interventions. In combined interventions with socioeconomic support the role of NGOs was a facilitator to improve the Available resources for the implementation of screening, treatment, and socioeconomic support components of the intervention. In these interventions, NGOs would provide the socioeconomic support, provide mental health training to TB healthcare workers, and offer support to link people with socioeconomic assistance available in their communities (Contreras *et al.,* 2017). This finding seems to overlap with the role of Costs of intervention and implementation: in the case of combined interventions with socioeconomic support, it was described that increased costs were mainly absorbed by the NGOs working locally, as they supplied sufficient human resources, training, socioeconomic support components, and other relevant components for the delivery of the intervention. In psychological interventions, one of the studies reported how physical

and human resources were constantly hard to obtain during the 5 years that the intervention lasted (Acha *et al.,* 2007). In combined interventions, the negative impact of the lack of available resources was echoed and it conflated reasons for lack of human and physical resources as a general lack of funding for mental health and primary care services. “Most [district programme managers] cited shortages in personnel and training opportunities, both of which often corresponded with a lack of funding.” (Lovero *et al.,* 2019).

Self-efficacy, part of the Characteristics of Individuals domain, was a facilitator for the implementation of psychological-only and screening-only interventions, but it was a barrier for implementation for combined interventions. One study describing the implementation of a psychological-only intervention mentioned the Self-efficacy of healthcare workers delivering the intervention was a facilitator. Healthcare workers were able to implement the intervention by themselves, with initial guidance by psychiatrists (Acha *et al.,* 2007). This was described as a progressive process in the study, meaning that healthcare workers were more confident in implementing the intervention with time. This echoes the findings described in the screening-only intervention study where the study discussed how healthcare workers were able to overcome challenges during the delivery of the intervention by applying their learning from the training provided to them. “Furthermore, some PHCPs reported referring people who, despite having negative screening results, showed symptoms that they deemed relevant.” (Diez-Canseco *et al.,* 2018).

Appendix 6 – Search approaches to identify documents for qualitative case study (Chapter 5)

I used six approaches to identify relevant documents as data for the qualitative case study:

i. I manually searched the website of Pakistan's Ministry of Health, called "Pakistan Health Knowledge Hub" to identify national guidelines for TB and mental health (Government of Pakistan, 2022). In the search box contained in their website, I entered the terms "Sindh", "tuberculosis" and "mental health" separately – the date of search was 10th January 2022. I downloaded the results retrieved with each search term from this website, which were a total of 85 documents, before sampling or removing duplicates. I also searched manually the website of the National TB Control Programme (Ministry Of National Health Services, Regulations, And Coordination; 2024.) where they have DS-TB data, publications, guidelines and training modules, annual reports, strategic plans, amongst other resources. From this website I downloaded the resources relevant to TB in Sindh (n=26). After sampling, I included 14 documents in the analysis for this study.

ii. I manually searched national and international donors' websites as listed in the National Tuberculosis Programme website on 7th October 2023 (Ministry of National Health Services, 2024). The list of donors referred to on the website were: the Global Fund (n=7), the World Bank (n=7), the World Health Organisation (n=0), Pakistan Chest Society (n=2), Stop TB partnership (n=11), USAID (n=1), DFID (now replaced by the Foreign, Commonwealth & Development Office; n=0), JICA (n=1), CIDA (now Global Affairs Canada; n=0), IUATLD (International Union Against Tuberculosis and Lung Disease; n=,1) KFW (Bankengruppe) (n=0), KNCV TB Foundation (n=1), GIZ Deutsche (n=5), Australian Aid (officially part of the Department of Foreign Affairs and Trade of the Australian Government; n=19), Indus Hospital (n=10), and Mercy Corps (n=1). I searched the websites of these organisations using their search engines to identify documents such as grant reports, datasets, or any other information relevant to their activities on TB and mental health during the relevant timeline for the implementation of the intervention. In all websites, I used the search string "Pakistan AND tuberculosis AND mental health" in the search field, and I also searched their mental health and TB sections manually. I only retrieved PDF and Word files, published on or after 2017. I retrieved (n=66) documents, before sampling. After sampling, I included 15 documents in the analysis for this study.

iii. I manually searched the implementing organisation's website to identify documents such as grant reports, datasets, or any other information relevant to their activities on TB and mental health during the relevant timeline for the implementation of the

intervention (Interactive Research & Development, 2024). I searched their website on 19th January 2022 and again on 07th October 2023, using Google Advanced Search to retrieve the words “Pakistan”, “tuberculosis”, and “(mental health)” and retrieved a total of nine documents, before sampling. After sampling, I included 8 documents in the analysis for this study.

iv. My contact at the implementing organisation helped me identify and access the routine documents that were used during the design and implementation of the intervention. We created a list of these documents and identified which of those documents still existed and I could have access to. This yielded a total of nine documents which my contact described as not publicly accessible and meant to be used only for the purposes of this study. These documents include patient files (one for non-symptomatic and one for symptomatic people), follow-up forms, calendar schedule for patient appointments, re-screening forms, mental health screening forms, patient information forms, patient screening logs, the protocol for the intervention, and the information covered in TB and mental health training modules. After sampling, I included 13 documents in the analysis for this study.

v. I carried out a structured search in electronic databases to identify relevant peer-reviewed literature. I used the search string (TB OR tuberculos*) AND (mental* OR depress* OR psych) AND (Pakistan* OR Karachi) and applied filters for date, according to my sampling criteria, to include results published on or after 2017. On 07th October 2023, I searched Pubmed (n=35), PsycInfo (n=1), Medline (n=7), Embase (n=34), and Web of Science (n=102). This yielded a total of 179 results, before sampling for the rest of the criteria I described above. I removed 43 duplicate references using EndNote (The EndNote Team, 2013). After sampling the remaining 136 records, I included 8 documents in the analysis for this study.

vi. I carried out a structure search to identify relevant doctoral dissertations that explored TB and mental health in Pakistan. The University of York has access to seven theses databases. I searched six of them as one was a musicology database which I excluded. I used the same parameters and search string that I used for retrieving peer-reviewed literature, described above. On 07th October 2023, I searched Dart- Europe e-theses portal (n=0), EThOs (n=0), ProQuest Dissertations and Theses (n=20), Open Access Theses and Dissertations (n=1), White Rose eTheses Online (n=0), and WorldCat (n=1). This yielded a total of 22 results, before sampling. After sampling, I did not include any doctoral dissertations in the analysis for this study

Appendix 7 - Complete list of data included in qualitative case study (Chapter 3)

Name	Notes
Training Module Doctors (Full - 2019)	Meets all SPICE criteria.
Research_Paper_PPA_TB_Care_Pakistan _2017	Meets all SPICE criteria; use for Context.
National_Guidelines_for_TB_Revised_2019	Published after the implementation timeline but relevant for outcomes of implementation; P.24 and 76/101 make reference to the management of psychological distress in TB.
DR-TB National Guideline 26-11-20	Meets all SPICE criteria; use for Context.
Desk_Guide_for_MDR_TB_Physicians	Meets all SPICE criteria; use for Context.
The Sindh Tuberculosis Notification Bill 2014	Published in 2014; maybe include if relevant for the time where the intervention was implemented .
Policy on Collaborative TB-HIV activtities WHO 2012	Published in 2012.
Phase 1 Operational Plan Health Strategy Sindh 2014-17	Relevant as it includes information on the outcomes for strategies to strengthen vertical programmes (TB)?; include in Context.
National End TB Strategic Plan 2017-20	Meets all SPICE criteria.
List of public TB centres Karachi 2-2	Meets all SPICE criteria.
List of Health Laws Pakistan	Snowballing; Find document "The Mental Health Ordinance, 2001 (last updated 06/06/2014).
Investigation report_the global fund	Meets all SPICE criteria.
Essential Package of Health Services Technical Component Sindh 2014	Meets all SPICE criteria.
Essential Medicines List Sindh 2017	Meets all SPICE criteria.
Global Fund_TB grants_data dashboard	Meets all SPICE criteria.
Global Fund_TB budget allocation	Meets all SPICE criteria.
Global Fund_investigation report on bad practices in Pakistan	Meets all SPICE Criteria

Global fund_grants recipients	Meets all SPICE criteria; two documents uploaded to Nvivo for analysis.
Global Fund_audit report grants in Pakistan	Meets all SPICE Criteria.
thefinancials2017-18	Meets all SPICE criteria. Relevant to the time and context of the phenomenon of interest.
thefinancials2016-17	Meets all SPICE criteria. Relevant to the time and context of the phenomenon of interest.
Indus annual-report-2017-18	Meets all SPICE criteria. Relevant to the time and context of the phenomenon of interest.
Indus annual report 2019 2020	P.36 Pursukoon Zindagi makes reference to the phenomenon of interest.
Indus annual report 2018-2019	P.26 Pursukoon Zindagi makes reference to the phenomenon of interest.
COVID-19_report indus	P.17 Pursukoon Zindagi makes reference to the phenomenon of interest.
AR-2020-21WebCompressed	P.86 makes reference to the funds of the phenomenon of interest.
Diagnosis_delay_LHW_Intervention_June2018_Final Mercy Corps	Meets all SPICE criteria; relevant to the analysis of lady health workers. Reference (MERCY CORPS 2018. Engagement of Lady Health Workers leading to early diagnosis - A cross sectional study. In: BUZDAR, N. (ed.). Islamabad, Pakistan: Mery Corps.)
country_profile_pakistan_0623	Relevant to phenomenon of interest (adjacent intervention, p.11).
Activating a Human Rights-Based TB Response - Technical Brief (November 2020)	Meets all SPICE criteria; relevant to the analysis of mental health provision for people with TB in Pakistan.
(redacted for anonymity) TB and mental health	Meets all SPICE Criteria.

(redacted for anonymity) - Global Ltd vs The Global Fund to Fight Aids Tuberculosis and Malaria Merits	Meets all SPICE Criteria.
(redacted for anonymity) - Building Support Systems within Communities to Prevent and Treat TB	Meets all SPICE Criteria.
(redacted for anonymity) - Adopting a Holistic Approach to Tackle TB comorbidities	Meets all SPICE Criteria.
(redacted for anonymity) - thatta Archives	Meets all SPICE Criteria.
(redacted for anonymity) - Innovative TB trial starts in Sindh Province, Pakistan	Meets all SPICE Criteria.
(redacted for anonymity) - Press Release: Update on (redacted for anonymity) legal action against Global Fund	Meets all SPICE Criteria.
(redacted for anonymity) - Press release: Global Fund report - (redacted for anonymity) taking legal action against sweeping, unfounded allegations	Meets all SPICE Criteria.
Protocol - Mental Health Services	Meets all SPICE Criteria.
Tuberculosis and Mental Health Training Modules	Meets all SPICE Criteria.
Basic Mental Health Counselling Skills Trainer's Manual	Meets all SPICE Criteria.
Discontinuation form	File corrupted and could not be restores. Not included in analysis.
Data extraction_PF NS	Patient files non symptomatic (patient information and screening form, AKUDAS). Available blank (translated to English; not include patient data; blue binder. SGH Korangi.
Data extraction _ FUP	Follow-up form.
Data extraction _ Cal	Calendar schedule. Paper based; one per facility; excel form available.
Data extraction RSC	Re-screening form.
Data extraction SC TRC	Mental Health screening data format. .

Data extraction Patient information form	Meets all SPICE Criteria.
Data extraction - MHS	AKUDAS (MH and Screening form). Notebook green with black bonding; excel blank form available. JPMC.
Documentary Sources list	Not available: Notes on counselling data at follow- ups, Power point presentation for app training for counsellors, Health and hygiene protocol, Checklist site for visits, Counsellors monthly performance evaluation, Data dump from the app, Monthly meeting minutes, Whatsapp daily reports from counsellors to project manager, Counselling notes, .
AHMER, A. 2021. Treatment outcomes among the people with mdr-tuberculosis in peoples medical college hospital Sindh Pakistan: A cross sectional and comparative study. *Latin American Journal of Pharmacy,* 40**,** 353-358.	Meets all SPICE criteria; check facilities where the study was carried out.
AMREEN & RIZVI, N. 2022. Psychiatric Co-Morbidity and its Associated Risk Factors among Tuberculosis People. *PAKISTAN JOURNAL OF MEDICAL & HEALTH SCIENCES,* 16**,** 67-69.	Meets all SPICE criteria.
JARDE, A., SIQUEIRA, N., AFAQ, S., NAZ, F., IRFAN, M., TUFAIL, P., ASLAM, F., TODOWEDE, O., RAKHSHANDA, S., KHALID, H., LIN, Y., BIERMAN, O., ELSONY, A., ELSEY, H., SIDDIQI, N. & SIDDIQI, K. 2022b. Addressing TB multimorbidity in policy and practice: An exploratory survey of TB providers in 27 high-TB burden countries. *PLOS Glob Public Health,* 2**,** e0001205.	Meets SPICE criteria; include as part of Context.
MALIK, A. A., HUSSAIN, H., MANIAR, R., SAFDAR, N., MOHIUDDIN, A., RIAZ, N.,	Meets all SPICE criteria.

PASHA, A., KHAN, S., KAZMI, S. S. H., KAZMI, E. & KHOWAJA, S. 2022. Integrated Tuberculosis and COVID-19 Activities in Karachi and Tuberculosis Case Notifications. *Trop Med Infect Dis,* 7.	
PASHA, A., SIDDIQUI, H., ALI, S., BROOKS, M. B., MAQBOOL, N. R. & KHAN, A. J. 2021. Impact of integrating mental health services within existing tuberculosis treatment facilities. *Med Access Point Care,* 5**,** 23992026211011314.	Meets all SPICE criteria.
TARIQ, A., ARSHAD, S. & EJAZ, M. 2018. Frequency of depression in tuberculosis people and its association with various sociodemographic factors. *Pakistan Journal of Medical and Health Sciences,* 12**,** 42-45.	Full text requested from authors, no response. Article was not included because it was unavailable from the journal website (404 file not found on server).
TODOWEDE, O., AFAQ, S., ADHIKARY, A., KANAN, S., SHREE, V., JENNINGS, H. M., FAISAL, M. R., NISAR, Z., KHAN, I., DESAI, G., HUQUE, R. & SIDDIQI, N. 2023. Barriers and facilitators to integrating depression care in tuberculosis services in South Asia: a multi-country qualitative study. *BMC Health Serv Res,* 23**,** 818.	Meets SPICE criteria; include as part of Context.

Appendix 8 – COREQ and SRQR checklists for qualitative research reporting (Chapter 5)

SRQR

Source: O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014 Sep;89(9):1245-51. doi: 10.1097/ACM.0000000000000388. PMID: 24979285.

Topic	Description	Place in Chapter 5
1. Title	Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	Page 94.
2. Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	Not applicable as it is not a publication. The chapter abstract was written as appropriate for a thesis chapter.
3. Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	Yes; section 5.1 Purpose of this study and research questions
4. Purpose or research question	Purpose of the study and specific objectives or questions	Yes; section 5.1 Purpose of this study and research questions
5. Qualitative approach and research paradigm	Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended, rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options	Yes, section 5.3 Research methodology and study design

	available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.	
6. Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	Yes, 5.3.4 Reflexivity
7. Context	Setting/site and salient contextual factors; rationale	Yes, section 5.4.2 The Context and 5.2 Background
8. Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale	Yes, section 5.3 Materials and methods
9. Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	Yes, section 5.3.5 Ethical approvals
10. Data collection methods	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale	Yes, 5.3.2 Data Collection.
11. Data collection instruments and technologies	Description of instruments (e.g., interview guides, questionnaires)	5.3.2 Data Collection.

	and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	
12. Units of study	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	Yes, section 5.3 Case study methodology, and 5.4.1 Results
13. Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/deidentification of excerpts	Yes, 5.3.3 Data analysis
14. Data analysis	Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale.	Yes, 5.3.3 Data analysis
15. Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale.	Yes, section 5.3.3 Data analysis includes a statement on Trustworthiness of data
16. Synthesis and interpretation	Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	Yes, section 5.4 Results
17. Links to empirical data	Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Yes, section 5.4 Results and Table 5.1 Data included in the analysis and its contribution to the research objective.
18. Integration with prior work,	Short summary of main findings; explanation of how findings and conclusions connect to,	Yes, section 5.5 Discussion.

implications, transferability, and contribution(s) to the field	support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/ generalizability; identification of unique contribution(s) to scholarship in a discipline or field	
19. Limitations	Trustworthiness and limitations of findings	Yes, section 5.5.1 Limitations
20. Conflicts of interest	Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed.	Yes, 5.3.4 Reflexivity
21. Funding	Sources of funding and other support; role of funders in data collection, interpretation, and reporting	Yes, in "Acknowledgement" section of thesis

COREQ

Source: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007 Dec;19(6):349-57. doi: 10.1093/intqhc/mzm042. Epub 2007 Sep 14. PMID: 17872937.

Item	Description	Place in Chapter 5
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	5.3.2 Methods for data collection, Semi-structured interviews
2. Credentials	What were the researcher's credentials? E.g., PhD, MD	5.3.4 Reflexivity statement
3. Occupation	What was their occupation at the time of the study?	5.3.4 Reflexivity
4. Gender	Was the researcher male or female?	5.3.4 Reflexivity
5. Experience and training	What experience or training did the researcher have?	Not mentioned
6. Relationship established	Was a relationship established prior to study commencement?	5.2 Background

7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g., personal goals, reasons for doing the research	5.3.2 Methods for data collection, Semi-structured interviews
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g., Bias, assumptions, reasons, and interests in the research topic	5.3.2 Methods for data collection, Semi-structured interviews (assumptions and interests in the research topic) and 5.3.4 Reflexivity (interviewer characteristics)
9. Methodological orientation and theory	What methodological orientation was stated to underpin the study? e.g., grounded theory, discourse analysis, ethnography, phenomenology, content analysis	5.3.1 Research methodology and study design
10. Participant sampling	How were participants selected? e.g., purposive, convenience, consecutive, snowball?	5.3.2 Methods for data collection
11. Method of approach	How were participants approached? e.g., face-to-face, telephone, mail, email?	5.3.2 Methods for data collection
12. Sample size	How many participants were in the study?	5.3.2 Methods for data collection and table 5.1 Data included in the analysis
13. Non-participation	How many people refused to participate or dropped out? Reasons?	5.3.2 Methods for data collection
14. Setting of data collection	Where was the data collected? e.g., home, clinic, workplace	5.3.2 Methods for Data collection
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	5.3.2 Methods for Data collection, Semi-structured interviews

16. Description of sample	What are the important characteristics of the sample? e.g., demographic data, date	5.3.2 Methods for Data collection, Semi-structured interviews
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Appendix 9
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	Not applicable
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	5.3.2 Methods for Data collection, Semi-structured interviews
20. Field notes	Were field notes made during and/or after the interview or focus group?	5.3.2 Methods for Data collection, Observations and site visits and 5.3.4 Reflexivity
21. Duration	What was the duration of the interviews or focus group?	5.3.2 Methods for Data collection, Semi-structured interviews
22. Data saturation	Was data saturation discussed?	Not discussed
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	5.3.2 Methods for Data collection, Semi-structured interviews
24. Number of data coders	How many data coders coded the data?	5.3.3 Data analysis
25. Description of the coding tree	Did authors provide a description of the coding tree?	5.3.3 Data analysis
26. Derivation of themes	Were themes identified in advance or derived from the data?	5.4 Results
27. Software	What software, if applicable, was used to manage the data?	5.3.3 Data analysis
28. Participant checking	Did participants provide feedback on the findings?	Not discussed
29. Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g., participant number	5.4 Results

30. Data and findings consistent	Was there consistency between the data presented and the findings?	Table 5.1 Data included in the analysis
31. Clarity of major themes	Were major themes clearly presented in the findings?	5.4 Results
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	5.4 Results

Appendix 9 – Interview guide for study participants (Relevant stakeholders) (Chapter 5)

The questions below were used as a guide for discussion, and were re-defined, or rephrased, accordingly depending on the flow of the interview, the attitude of the interviewee, their role in the intervention, their current role, their affiliation to the implementation organisation, and the use of a translator.

Interview guide for study leads (PI, project managers):

[Starting script]

1) Tell me about your motivation for developing this intervention. What was your motivation/rationale for designing and implementing the intervention? What was the rationale for choosing implementation sites? What kind of evidence or information sources did you consider for the design of the intervention and its implementation strategy? Was this intervention trialled before on a smaller scale in this or other organisations?
2) What were the main challenges you experienced during implementation of the intervention? Are there any challenges that were present before implementation or that continued to be present after implementation?
3) What worked well during implementation? Is there anything that you consider was an important facilitator for, or encouraged, implementation?
4) What was the role of IRD (your research organisation), the funder (Harvard Medical School) and other stakeholders external to the facilities and NTP in the design and implementation of the intervention?
5) Were there any policies or incentives that encouraged you to design and implement the intervention? Were there any incentives for participants (facility sites, providers, people)?
6) Tell me about how you developed the training component of the intervention. How was the training content and sessions designed? How were training participants recruited? What were the main challenges you encountered during the training sessions/process?
7) Tell me about how you engaged other participants in the intervention, like healthcare workers and facility managers. Who was engaged in the implementation process and delivery of the intervention and related activities at the facility level? Could you tell me what was your experience for the recruitment of all types of participants, from facilities to people, as well as healthcare workers and trainers?

8) Which resources would you consider critical for the implementation of the intervention?
9) Is there anything you would like to discuss that we have not covered in these questions?

[Ending script]

Interview guide for healthcare workers (trainees):

[Starting script]

1) Let's talk about your role in the intervention. Could you describe to me how you became involved in this intervention? What encouraged you to participate? What was your role in implementation, what were your activities and responsibilities?
2) Tell me about your experience delivering the intervention. What is your opinion of the intervention? How complex or easy do you consider this intervention or its implementation process was?
3) Was this intervention acceptable to you or are there any activities or characteristics of the intervention that are not acceptable to you?
4) Tell me about the training you received. What is your experience about the training sessions and materials you received to deliver the intervention? What encouraged you to take the training and participate in the implementation of the intervention? What were the main challenges you encountered during the training sessions/process?
5) What is your opinion on the communication between you and the other participants in the intervention, that is, with other healthcare workers, with the trainers, or with the study leads?
6) What do you think about the interventions' compatibility with this facility? Or with the existing workflows of the facility and the goals of the TB program?
7) What was your experience of delivering the intervention as part of TB treatment offered to people, or as part of your activities at the facility level? Did you have to make adaptations to the intervention or to your routine activities during the implementation process?
8) What is your opinion on how the intervention was received by people?
9) Which resources would you consider critical for the implementation of the intervention?
10) Do you consider this intervention should keep being implemented? Has it improved the status quo in any way?

11) What were the main challenges you experienced before, during, and after the implementation of the intervention?
12) Tell me about your role within this facility and in relation to the intervention. How would you describe the working culture and environment of this facility? How would you describe the working relationships between the different members working in this facility involved in the intervention's implementation?
13) Is there anything you would like to discuss that we have not covered in these questions?

[Ending script]

Interview guide for facility managers (TB doctors):

[Starting script]

1) Let's talk about the intervention. What encouraged you to implement this intervention in your facility? Was this or similar interventions trialled before on a smaller scale in this or other facilities? Who was engaged in the implementation process and delivery of the intervention and related activities at the facility level?
2) Do you think this intervention is compatible with your facility? Do you think it is compatible with existing workflows of the facility and the goals of the TB program?
3) Do you think the intervention is compatible with available resources (human, physical, financial) at the facility and TB-program levels?
4) Tell me about your experience implementing the intervention. Is this intervention acceptable to you? Are there any activities or characteristics of the intervention that are not acceptable to you?
5) What was your experience of delivering the intervention as part of TB treatment offered to people, or as part of your activities at the facility level?
6) Which resources would you consider critical for the implementation of the intervention?
7) Do you consider this intervention should keep being implemented? Has it improved the care routinely delivered to people in any way?
8) Did you experience any challenges during the implementation of the intervention, before or after?
9) Do you consider this intervention sustainable with the current resources and organisational structure? What are your suggestions to make this intervention

sustainable? Do you consider there are immediate challenges to sustain the implementation of this intervention in these facilities?

10) Tell me about your facility. Could you describe the working environment of your facility? What is the organisational structure, the TB and/or mental health services that you provide? How would you describe the attitude of those working in the facility on a day-to-day basis?
11) Is there anything else you would like to add?

[Ending script]

Interview guide for policymakers:

[Starting script]

1) Let's talk about the structure of the NTP at the local (Karachi), regional (Sindh) and national level. How would you describe the working relationships between different administrative levels?
2) How would you describe the collaboration between NTP and mental health services at these levels?
3) Tell me your views about the intervention. Are you aware that this intervention was implemented in your local area (Karachi)? Do you think it is compatible with existing workflows and the goals of the TB program?
4) Do you think the intervention is compatible with available resources (human, physical, financial) at the facility and TB-program levels?
5) Which resources would you consider critical for the implementation of the intervention?
6) Do you consider this intervention should keep being implemented? Has it improved the status quo in any way?
7) Do you consider this intervention sustainable with the current resources and organisational structure? What are your suggestions to make this intervention sustainable?
8) What would encourage you to improve the uptake of this intervention in more facilities?
9) What are the immediate challenges to sustain the implementation of this intervention in these facilities? What are the challenges to sustain the implementation at the district, regional and national level?
10) Is there anything else you would like to discuss?

[Ending script]

Appendix 10 – Detailed description of barriers and facilitators for implementing the mental health intervention "IPUs" in Karachi, Pakistan (Chapter 5)

Innovation domain

The constructs of Source, Evidence base, Relative advantage, and Adaptability of the IPUs were facilitators for implementation in private and public facilities. In this domain, it is reflected how the foundational elements of the intervention varied little, if at all, across implementation sites. This can be attributed to the characteristics of the intervention and also to the constructs covered in this domain. For example, the implementing organisation, the **Source**, of the intervention, was the same in all settings. This organisation, described in more detail in the Background section, was considered as a reputable and trusted source in all settings. The organisation had a reputable and credible team that had experience working in those settings. *"… we were already doing the work, we know what the components are in terms of the training that's required, the number of for example counselling sessions, the way that data would be collected and analysed, because that's what we were doing anyways. It was a matter of figuring out the process flows within public and private sector sites… it was really an extension of the work we were already doing in a more robust and rigorous manner."* (Interview 11, principal investigator). In all facilities the relevant stakeholders believed the intervention was an improvement to the routine care offered to people with TB. These beliefs were coded to the **Relevant advantage** of the intervention over the *status quo. "What we felt at that time was integration of some sort would be quite beneficial. … we should actively screen these people as well, because they won't come on their own for the mental health side of things, for sure."* (Interview 10, principal investigator). This quote also serves to illustrate how the **Evidence base** of the intervention was developed, including the analysis of other countries' experiences of integrating TB and mental healthcare. This combination of expertise, advantage, and previous experience of the implementing organisation facilitated the design and implementation of the intervention. Additionally, the **Adaptability** of the intervention was a facilitator for implementation better illustrated by the resourcefulness of the mental health counsellors. The intervention's delivery was adapted by the counsellors to fit the local needs of the staff, physical setting, and patient flow. *"*[The counsellor] *tried different methods…tried to go to peaceful environments, where they thought there a little quiet, or place where client could be comfortable…they would go to gardens, they would talk there, have longer discussions there, because there was no one disturbing them."* (Interview 7, mental health lay counsellor trainee). However, I observed that the accommodations this counsellor mentions were only available to male clients given the cultural attitudes towards interactions between males and females, so this was an adaptation unavailable to all the people with TB who might require it.

Unfortunately, the nuance of gender-related barriers and facilitators for the implementation process was hard to capture with this framework.

The constructs of Complexity and Design had a mixed impact on implementation, acting both as barriers and facilitators. For example, I observed that some of the fields in data collection forms used in all facilities, by all counsellors, were redundant, repetitive, or collecting unnecessary data. I coded this to **Complexity** of the intervention. However, only one counsellor mention paperwork as a difficulty in their daily activities during the intervention. "*…I didn't have the time… my paperwork would remain a bit disturbed. … a lot of things were going on. I was providing counselling, the paperwork was going on, I had to fill out the forms, and the clinic closed at 8 and that was the time when we would … there with the files.*" (Interview 8, mental health lay counsellor trainee). This was applicable to the paper-based data collection forms. At some point during the implementation process, intervention's data collection tools became digital and an app for data collection. I coded this as part of the **Design** of the intervention. *"I think the most important facilitator was that we were collecting data electronically through a mobile application. So that in itself was a facilitator"* (Interview 9, research associate). However, this also created issues when technology failed, creating double work for counsellors and members of the implementation team. *"Suddenly you are doing that, and the application crashes, and all systems are down. …* [The failures of the app] *interrupted the flow of the intervention, or they caused backlog, or they caused delays, or they caused issues when we extracted data, and there was no data because some bug happened. And then we had to re-do it based on our paper forms."* (Interview 12, project manager).

Outer setting

The constructs of **Local conditions**, **Partnerships and Connections**, and **Financing** had a similar effect of facilitating implementation across private and public facilities. All the implementation sites belonged to organisations participating in the NTP program at the provincial and national level which meant their economic, environmental, and political **Local Conditions** were very similar. For example, the precedent of integrating mental health in the DR-TB element of the NTP strategy was used as leverage to promote implementation in all sites part of the NTP who were delivering DR-TB services. *"…it's always been integrated in the DR-TB program but never in the drug susceptible program. So really the game changer was to integrate mental health services and bring in integrated practice unit for susceptible TB."* (Interview 2, project manager). The collaboration between the implementing organisation and the implementation sites was facilitated was facilitated by pre-existing and longstanding collaborations between partners. I coded this to **Partnerships and**

Connections. *"I think the collaboration just made the process easier… So even if there was even if there was any challenge the counsellors were accommodated. I think that also has to do with the fact that threw were other interventions that were being run at the same facility under the* [the implementing organisation] – [implementation site] *health network umbrella. So that could have been one reason why the management of those hospitals would cooperate."* (Interview 9, research associate). The availability of financial funding, coded to **Financing**, to support the implementation of the intervention as designed by the implementation team was an important facilitator. It is unclear how many financing bodies supported the implementation team, but interviewees mentioned two distinct international donors. One of them has longstanding collaborations with the TB control program in Pakistan. *"…we basically had managed to secure funding where we would create, we were creating these integrated practice units… we had* [international donor 1] *funds at the time. … And then we had applied for the* [international donor 2] *Grant as well…we knew that they were interested in this sort of interventions, these particular diseases, in this region. We sort of capitalised on that."* (Interview 10, principal investigator).

The construct of **Local attitudes** was a barrier for implementation in both cases. The local attitudes of TB managers and other frontline clinical staff employed by the implementation sites at the time was unwelcoming towards the integration of mental health services for people with TB. One of the reasons was that some TB doctors believed psychological counselling did not address people with TB' health needs and only represented additional work for them (Interview 7, mental health lay counsellor trainee). Some TB doctors referred to counselling in the context of the benefits or detriments it represented for the TB treatment of people rather than considering mental health as a component of people's health in a holistic way (Interview 18, TB doctor). People' attitudes towards their own mental health were also a barrier for receiving the intervention. TB doctors and counsellors attributed this to the widespread illiteracy of people with TB attending their clinics, and their attitudes of stigma towards TB and mental health illnesses. *"The first problem is the lack of education. People in Pakistan are unlearned. There is stigma and myths associated with the people of tuberculosis. When we talk about mental health it's the same issue. When we ask them about their mental health they say they are not … crazy. Mental health is one of the biggest challenges in Pakistan. There is also a gender issue associated with it. For example, I cannot talk to a female alone because their family will have issue with this even if it's a counselling session... And, on the other hand when I talk to the males they say that they don't need it."* (Interview 4, mental health lay counsellor trainee). I was not able to contact

any of the people who received the intervention, so their views and experiences are not represented in this study.

Inner setting

The constructs of **Recipient Centredness**, **Tension for change**, **Funding**, and **Access to Knowledge and Information** were facilitators across both implementation settings. This is not a surprising find as all organisations, regardless of affiliation, were motivated to improve the care that people with TB receive, which was coded to Recipient Centredness and Tension for change. There was a shared belief between the implementation team, the TB doctors, and the Head of TB departments in the implementation sites that people with any type of TB required psychological support to cope with the impact of the TB diagnosis, the side effects of treatment, and any underlying conditions that might be contributing to the distress of people with TB. TB facility managers saw their goal of good TB treatment outcomes as being aligned with the goals of the counsellors.*"… the challenges facing by the counsellor or by the doctor* [are] *almost the same. Because the doctor is focused on their disease, but if the patient there isn't cooperative, understandable, and they understand you, and think they follow your instructions, … these personal issues … I think, when addressed properly, on time, both of them,* [by the] *doctor and the counsellor, will have good outcome."* (Interview 18, TB doctor). There was consensus across multiple stakeholders that mental healthcare should be integrated into programmatic TB management for all people with TB, thus needing the overhaul of current practice. This opinion was expressed by counsellors, policymakers, and members of the implementation team. More explicitly, members of the implementation team mentioned that such change was needed given the historically vertical structures of TB programs in the country (Interview 10, principal investigator).

The data coded to the **Funding** and **Access to Knowledge and Information** constructs shows that these two resources were provided equally to all implementation sites by the implementing organisation and team. The data coded to **Funding** overlaps with the data in the construct of **Financing**, part of the **Outer Setting**. This is due to the implementing organisation being part of a distinct organisational structure from that of the implementation sites, hence its part of the **Outer Setting**, and acting as a non-governmental for-profit public health enterprise. The data coded to both **Funding** and **Financing** describes how the implementing organisation used the funds received through specific TB and public health development-related grants to cover the design and implementation costs associated to the IPUs. The data in this construct describes the difference in the funds used for the design of the intervention and the financing of the implementation activities. For example, the development of the training materials and context assessment activities implementation

activities were supported by one grant before the implementation timeline (Pasha *et al.,* 2021). A second, subsequent grant funded the operationalization and implementation of the results of the first grants' activities (Interview 11, principal investigator).

The training received by the mental health lay counsellors was an essential facilitator for the intervention's implementation process. This was coded to **Access to Knowledge and Information.** The training provided information on basics of pulmonary TB illness, mental health symptoms and causes, patient data collection, and guidance on troubleshooting if they had any issues during their face-to-face sessions with people (IRD private document: "Tuberculosis and Mental Health, Training Modules"). "*The purpose of this training is to build the capacity (knowledge, skills and attitudes) of counsellors regarding TB, and Mental Health. It aims to comprehensively train counsellors to understand the importance of using an integrated approach to management of these diseases. These modules will act as a guide to enable facilitators to cover essential aspects of TB and help them build their communication and counselling skills so they can best understand their clients' (people with TB suffering mental health problems) needs and effectively counsel them to be able to manage their condition."* (IRD private document: "Tuberculosis and Mental Health, Training Modules"). The training was delivered before the implementation, but trainee counsellors also received continuous support and supervision from the other members of the implementation team although the frequency of these support sessions is not mentioned. "*…the training started off with them knowing about the structure, the hospital, the services, then doctors and experts would come and would them what TB is, what causes it, how a patient is diagnosed, what are the symptoms, etcetera... the duration of their training was around one week or fifteen days … they would have these sessions with psychiatrists or psychologists where they would have case studies and they would have discussions. And every Friday they would have this session with the psychologist where they could take the problems that they were having, or new cases, or specific questions and they could work on the specific problems." (*Interview 6, mental health lay counsellor trainee).

Communication, Relative Priority and **Space** were barriers shared across cases. The interviewees described how internal **Communications** between the implementation site staff and the counsellors responsible for delivering the intervention was difficult and inconsistent. Specifically, counsellors faced challenges in tracking the people they needed to see daily. They had to actively seek out TB doctors for essential patient information, resulting in a time-consuming back-and-forth process (Interview 8, mental health lay counsellor trainee). This challenge in communication also extended to the collection of data from the implementation sites by the implementation team. "*… this is something that took the longest, which is to collect TB treatment outcomes from the facilities. So, we had to conduct multiple cycles of*

that data collection which was either by visiting the hospital, the facility, or it was by getting the data, having the health worker collect that data for us... That was the biggest … challenge, and it took the longest as well." (Interview 9, research associate). Although, in theory, all the stakeholders agreed on the importance of providing mental health treatment to people with TB, this was not translated into the **Relative priority** given to the intervention during the implementation process. In practice, the TB facility managers showed that mental health was not a high priority in TB treatment as opposed to treatment completion, adherence, loss to follow-up, and other programmatic goals. The mental health lay counsellor trainees considered that TB doctors gave little importance to the intervention and considered regular anti-TB treatment as more important and the intervention as additional work (Interview 7, mental health lay counsellor trainee). In the implementing organisation, the priority given to this intervention was at odds with other projects happening at the same time. *"I think in terms of barriers I would say we had a lot on our plate anyway, running our own individual programs. There's a lot that we had taken on, in a sense, this was an additional thing… But yeah, we were obviously working on a lot of different things at the same time (laughs) as we do at* [the implementing organisation] *and I would say that was always a bit of a barrier in terms of just focusing on just this particular one. This was a small project that we took on, in a sense…"* (Interview 10, principal investigator). Also, other interventions were being delivered for people with TB in the same facility as the IPUs. *"In the same setup, HIV people would also come. So we had a worker from the HIV department who would be doing tests over there. But since they were in close proximity a lot of the times when we were asking people and the people were explaining the HIV people would be very easily be able to hear whatever it was being talked about".* (Interview 8, mental health lay counsellor trainee). This corelates with the issue of **Space** availability for delivering the intervention at the implementation sites. *"I think getting space for our counselling was a challenge everywhere, whether it was private or public, because we were trying to integrate within the facilities' existing systems so to - without give us a small area for counselling was a challenge."* (Interview 9, research associate). The mental health lay counsellor trainees referred to how the spaces provided to have face-to-face sessions with people were not private, were crowded, or sometimes in corridors (Interview 5); in some instances, the lack of space forced them to have face-to-face sessions in nearby parks or local tea shops (Interview 6).

Compatibility and **Work Infrastructure** had mixed impacts on both private and public settings. The intervention was largely compatible with the processes and workflows for TB treatment existing in the implementation sites. I coded this to **Compatibility**. The implementation team would try and adapt to the facilities, processes and systems of the

implementation site which was a positive influence on implementation (Interview 9, research associate; Interview 10, principal investigator). However, it was challenging to adapt to the existing workflows in large facilities due to the physical area and the larger patient volume, and counsellors mention they had to adapt to the facility's characteristics such as patient pathways and patient volume constantly. *"I tried my best to ensure that no patient was missed. I would sometimes even come outside the doctors' office to ensure that I don't miss out on a single patient… it did happen sometimes, that the patient goes missed."* (Interview 8, mental health lay counsellor trainee). This aligns with the data coded to **Structural characteristics - Work infrastructure**, as the inherent infrastructure characteristics of public and private facilities, related to space and patient volume, influenced implementation in a mixed way. According to interviewees, the larger size facilities had higher patient volumes and this hindered counsellors in their delivery. *"I think some would have to do more with size. Like, we also worked with a private tertiary care hospital, but that was huge, and it was a charity based, so it had a huge influx of people. Even the facility, the way it was structured, it was very open, and airy, so there were multiple points of exits. And because it was so much larger, that algorithm or that flow, where we had different touch points, and we were reinforcing the system, that was much larger. So that was harder to navigate".* (Interview 12, project manager). In comparison, it was easier to implement and deliver the intervention effectively in smaller facilities. "*The easier ones were the* [implementation sites]*... Because the way they were structured they were much smaller. So, you have to build the system with less people, like five as opposed to twenty-five. And also because the clinic is small, right? So it is, it was far more feasible for the counsellor to be situated centrally... People were harder to miss."* (Interview 12, project manager). I observed how the space in private facilities allowed for a clear view of the entry and exit points of people in the building (Visit note A, Visit note B). In public facilities, there are large open areas where there are lot of people waiting to be seen, accompanying people, queuing up, asking questions, or selling food and chai (Visit note 1, Visit note 2, Visit note 3). In these sites, it was hard to establish where the service started and where it ended as the crowds at different locations and the high volume of people around obscured any information available.

The intervention's goal was to provide psychological counselling to people with TB, which I assigned to the **Mission alignment** construct in the CFIR framework. The mission of the implementation settings, the individual TB treatment centres and the organisations they were affiliated with, was to provide anti-TB treatment for people with diagnosed TB in accordance with the NTP guidelines for diagnosis and treatment (National TB Control Program Pakistan, 2019b). It was unclear if there was alignment between the goal of the intervention and the goals of implementation sites. TB doctors employed at the facilities and policymakers

considered the benefits of counselling to be improved TB-related education for people with TB and their families. Thus, they only considered counsellors as important because they fulfilled the role of educating people and their families (Interview 15, Head of TB department, public facility). Some doctors considered depression was a side-effect presented after people received a TB diagnosis or started on the medication. They did not consider depression as a condition that merited screening at the onset of TB illness. *"They don't know the importance of the mental health of the patient. Because mental health, education, (when the patient) know he is now suffering from TB, (he) is under depression. And it is the responsibility of the doctor to improve his mental health and guide them, and (tell them) no problem, you will be managed, and it is a 100% curable disease like this. But it is very important. When he (the patient) is mentally strong, so he will complete the treatment, and be helpful in the contact management, and preventive stuff." (*Interview 20, programme officer NTP).

This aligns with the prevailing culture within the facility, which one respondent noted as an influence in the acceptance of the intervention. At the facility level, senior buy-in was considered as the most important factor that would determine the sites' **Learning Centeredness** that would ultimately facilitate implementation (Interview 2, project manager). They noted how this organisational characteristic would made it possible for the lower tiers of the organisational hierarchy to accept and adapt the mental health integration in existing TB services (Interview 2, project manager). However, these remarks described a hypothetical scenario in which the respondent highlighted the most important facilitator for implementation, in their opinion. Thus, the actual conditions of Learning Centeredness in the implementation sites and their influence on implementation were undetermined.

Individuals

The findings for this domain show that most of the impact that the individuals had as facilitators or barriers was the same in both cases, private and public. The only difference was in the role of Mid-level leaders, for which they acted as a facilitator for private facilities and had mixed impact for implementation in public facilities. The roles of **Implementation facilitators, Implementation leads, Implementation team members, and Innovation deliverers** were facilitators for implementation for both cases. The role of **Other implementation support,** and the **Capability** and **Motivation** of all the implementation team was also a facilitator for implementation across facility types. Most interviews had positive comments about the implementing organisation, the implementation team, and their experience delivering the intervention. Referring to the **Implementation leads** and **Implementation facilitators,** an interviewee said: "*…our management is very*

cooperative…the toughness was usually faced from the outside hospitals…We had really good relationship with our management… they supported us a lot.". (Interview 3, mental health lay counsellor trainee)**.** The **Implementation team members** were the **Implementation leads** and the **Innovation deliverers**. They all contributed towards the implementation of the intervention positively. *"…I helped establish that relationship with the doctors and … push for the trickle down of that…my part was more in developing the more formal relationships or at least making that push for integration and team building to come from their line management whereas the counsellors and field supervisors and the other people did the more informal relationship-building…"*(Interview 12, project manager). The **Innovation deliverers** (i.e., the mental health lay counsellor trainees) interviewed for this study had positive experiences during their participation in the intervention. They believed they were doing something good, they believed they were helping people with TB, and they believed they were growing professionally because of their participation in this programme and their collaboration with the implementing organisation (Interview 3 to Interview 8, mental health lay counsellor trainees). Although some report that there were difficulties in accessing all the sites, as the 6 implementation sites were distributed across the city of Karachi, and traffic and long-distances would affect their travel significantly, their recount of their experience is overwhelmingly positive (Interview 7, mental health lay counsellor trainee). *"It was really good experience. Counselling is a good thing so we had good vibes about it."* (Interview 3, mental health lay counsellor trainee).

The implementing organisation had access to in-house expertise on different topic areas relevant to the intervention such as programmatic TB management in Pakistan, implementation of mental health interventions, global public health, grant writing, research methodology, epidemiology, and program management. I coded this to **Other implementation support** as this expertise and their reputation helped to design, implement, and secure funding for the intervention. *"Ok, so, at that point we were working a lot of things … we were already doing this work programmatically… within* [the implementing organisation]*, since we are a research-based organisations, we have that expertise within* [the implementing organisation]*… And then through that, we started writing the actual proposal itself, the application itself, to* [international funding body]*."* (Interview 11, principal investigator). This expertise can also relate to the **Capability** of the implementation team, including implementation leaders and counsellors. All of them reported having the required abilities to fulfil their roles. The implementation leaders and other members of the implementation team had these acquired these skills before the intervention through their professional life; the trainings delivered as part of the intervention helped the mental health lay counsellors acquire and improve the abilities needed to fulfil the role. *"I can say that is*

my own achievement. I have to say that a big world has been (the implementing organisation) *in my journey because they have provided me with the confidence that allowed me to take a lot of changes in my life and allowed me to be where I am.*" (Interview 6, mental health lay counsellor trainee).

For the construct of **Motivation**, I coded all the data in which participants involved in the design and/or delivery of the intervention expressed their commitment to the delivery of the intervention. For example, all the counsellors interviewed in this study described their participation as a beneficial influence in their personal and professional life. *"… [the counsellor] says that his time in* [the implementing organisation]*, he still remembers it. And he says that the work there was so nice, and everybody works so committedly, that you yourself would want to work harder… the environment was such that it motivated you… seeing everyone else work that hard, I wanted to work that hard as well".* (Interview 7, mental health lay counsellor trainee). Although the TB doctors at the implementation site were not motivated about the intervention at first, this reluctance was gradually overcome by the implementation team (Interview 12, project manager).

A barrier shared across cases was the role of **Opinion leaders**. The beliefs and attitudes of TB programme managers at the highest levels and donors was described as a barrier for the programmatic integration of mental health in TB programmes, possibly as a result of the historical vertical design of TB programmes in Pakistan. *"… you have to understand that TB has been run as a siloed program and the doctors, they see TB the do not see anything else… Integrating mental health into TB was a challenge because the team had been functioning in this siloed approach for a very long time. And that's not just for this particular study, I think that's across the entire TB program. We see this from the donor perspective as well, that there's not a lot of donors buy in in to integrate it."* (Interview 2, project manager).

There was only one **High-level leader** interview included in this study and their impact on implementation of the intervention, or on the integration of mental health in TB programmes, is unclear. When asked what was being done to promote the delivery of mental health support, or counselling, to people with TB, they said it was very important and a core element of management (Interview 20, Senior TB programme officer NTP). Their answer, however, defined counselling as the provision of TB-related health education to the patient, not as psychological intervention that could address the mental health needs of people with TB. Although they mention how important mental health is for people with TB, and there is a verbal commitment at the high-level leadership for the provision of mental health for people with TB, in reality there is some reluctance when it comes to the integration of services or implementation of interventions.

Implementation process

There were no differences between cases in this domain. This can mean that the implementation process was the same in both public and private settings, and most differences in the intervention's implementation can be attributed to the facilities' **Inner Setting** characteristics.

The implementation team had created protocols for the design and implementation of this intervention in advance and developed professional collaborations with the implementation sites/organisations before commencing implementation activities for this intervention (Interview 11, principal investigator). I coded this to **Planning**. The planning and decision making was done at the higher executive level, involving the leaders of the implementing organisation, some of the implementation sites, and some of the donors. *"…there were, at various points discussions, with our donors…about the methodology, how we are doing...* [who] *are the people involved. It depends on the kind of decision-making, like at what level. That would determine the cadre of people that were involved, and the conversation, whether it's me and the PI, whether it's the PI and other director..."* (Interview 12, project manager). This is also evidence of positive impact of their activities towards **Assessing context.** For most facilities, the implementing organisation had a deep understanding of the characteristics of the facilities and the TB service where they implemented the intervention. For this, they carried out scoping assessments of the staff, roles, and workflow of the facilities where they had no previous experience of collaboration (Interview 11, principal investigator). The people involved in the design of the intervention had experience working in the public sector in Karachi in different programs adjacent to TB services (Interview 10, principal investigator).

The beneficial impact of these activities is reflected in the **Tailoring strategies** construct. The implementation team chose the implementation strategies based on their experience of working within these facilities.*"… we knew them well enough to know where the sites were, the three sites that we wanted to implement at, we made site visits, we already had the letter of approvals. And you know make it sure that in the process flow of those sites, we knew when and where the counsellor would be seated. And where they would be screening. And then of course, ensuring that the rest of the staff knew what was going on and what we were trying to do. So that if any referrals were required, it would be sent to us, in a timely manner."* (Interview 11, principal investigator). This is similar to the data coded to **Adapting.** The quotes coded to this domain reflect how the intervention was adapted by the implementation

team to fit in with the different workflows and characteristics of the facilities. *"… within* [implementation site]*, that had to be a lot more relationships, … because we were trying to deal with multiple exit points. It did kind of varied by facility and varied by the dynamics of that hospital and varied by the algorithm that the patient's kind of followed."* (Interview 12, project manager).

The innovation deliverers, the counsellors were content for participating in this intervention and being associated with the implementing organisation. I coded this to **Engaging – Innovation deliverers**, as their satisfaction was expressed in the context of working, or being associated, with the implementing organisation. *"The interviewee also expresses his gratitude for* [project manager], *for* [principal investigator]*. And* [the interviewee] *says that they always remembered the* [the implementing organisation] *training and their time in* (the implementing organisation] *in good words".* (Interview 6, mental health lay counsellor trainee).

Throughout the intervention, the implementation team collected quantitative data to assess the success of the intervention, which aligned with the definition of the **Reflecting and evaluating – Innovation** construct. They had a dedicated role, the research assistant, within the implementation team to collect, analyse, present, and ensure the quality of the data (Interview 9, research associate). This person would collect data on TB outcomes and the intervention's outcomes. This helped with the data collection, particularly in difficult facilities. *"I think public facilities, … maybe the credibility of the data … was more questionable, in terms of how they maintained their TB outcomes data, which is something that we needed for our study. So that is something that was observed… But when it came to other private facilities, the data was more organized. … TB treatment outcome data."* (Interview 9). Also, it was reported that all relevant data was collected and evaluated according to their protocols (Pasha *et al.,* 2021).

The collaboration between staff from the implementation organisation and staff from the implementation sites was complex and had a mixed impact on implementation. I coded the statements about such collaboration as **Teaming**. Some of the implementation's team perspective was that collaboration was open and easy. *"I think the acceptability and the collaboration was there at each facility. So even if there was even if there was any challenge the counsellors were accommodated"* (Interview 9, research associate). However, from the mental health lay counsellors' perspective, the working relationship with the staff at the implementation sites was difficult and unreliable. "*… there was a problem of cooperation at* [implementation site]*. We were outsiders… we were partners… not insiders".* (Interview 3,

mental health lay counsellor trainee). TB doctors at the implementation site expressed hesitancy in sending people to the counselling units after the privacy and confidentiality of one of the people with TB was compromised. *"We were told that these are the qualified persons who are going to advise people. I think people got benefitted… Sometimes they created problems for us too…Sometimes they've called and phone them to visit them for counselling, and patient are directly telling us, '*you are who called us on phone*', '*why did you call us?'*. Because this disease, tuberculosis... Many people do not want to even* (let this) *know to their family members."* (Interview 15, head of TB department, public facility).

There were unmet needs of people with TB receiving counselling, which I coded as a barrier for both implementation sites under **Assessing needs – Innovation recipients.** It is unclear whether the implementation team consulted with innovation recipients (people with TB) before the design of the intervention. The mental health lay counsellors expressed the language and cultural barriers they experienced when interacting with people. "*Language was the biggest barrier. While I am in well versed in Sindhi and Saraiki I helped those people out but Pashto became one of the biggest barriers in terms of language and we were not able to explain stuff to Pashto speaking people"* (Interview 5, mental health lay counsellor trainee). The privacy and confidentiality needs of people were also compromised in the pursue of providing counselling to all eligible people (Interview 15, head of TB department, public facility). Additionally, the barriers expressed in other codes such as negative attitudes towards mental health amongst people, the need for private spaces, and gender dynamics between counsellors and people seems to indicate that the needs of people were not thoroughly assessed before or during implementation.

The interviewees made references to the adaptations they made to circumvent obstacles and challenges during the implementation process. For example, they referred to early implementation challenges as inconsistency in data collection which the implementation leads considered solved at the time I interviewed them. However, the responses of other interviewees and the intervention documents showed that such challenges persisted throughout the implementation process until the end of the intervention. I coded this as unclear impact as barrier or facilitator under **Doing**. For example, the forms "Data extraction forms – Mental health screening data format (Documentary source, implementing organisation private documents) " and "Data extraction forms – patient file symptomatic (Documentary source, implementing organisation private documents)" show inconsistency in the data collected from people at the facilities. The difficulty in maintaining the quality of data collection was also described by mental health lay counsellors. *"So within that increased flow of patient a lot of things were going on. I was providing counselling, the paperwork was*

going on, I had to fill out the forms, and the clinic closed at 8 and that was the time when we would … there with the files. So it got pretty difficult and there was no time for me to check, and set the right form to the right file." (Interview 8, mental health lay counsellor). Additionally, there were pervasive challenges in day-to-day implementation activities in larger private and public facilities, compared to smaller private facilities. *"A smaller facility was always more streamlined, …there are subsequently also less problems, there are also less people that you are dealing with. It's easier when it's smaller to actually to deal with all. … the amount of time that it took us to streamline within a smaller facility versus a larger facility."* (Interview 12, project manager)