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Barriers to and facilitators of implementation of isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe

Dzavakwa, Nyasha Veronica

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Faculty of Health Sciences
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BARRIERS TO AND FACILITATORS OF IMPLEMENTATION OF ISONIAZID PREVENTIVE THERAPY GUIDELINES FOR UNDER-FIVE CHILDREN THAT ARE HOUSEHOLD CONTACTS OF TB CASES BY HEALTHCARE PROVIDERS IN HARARE, ZIMBABWE

Name: Nyasha Veronica Dzavakwa

Student Number: 2185595

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology-Implementation Science

Supervisor: Professor Latifat Ibisomi, University of the Witwatersrand
Co-supervisors: Dr. Oludoyinmola Ojifinni, University of the Witwatersrand
Professor Mutsawashe Bwakura-Dangarembizi, University of Zimbabwe

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Declaration

I Nyasha Veronica Dzavakwa declare that this Research Report is my own, unaided work. It is being submitted in partial fulfilment of the requirements for the Degree of Master of Science in Epidemiology- Implementation Science at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Full names: Nyasha Veronica Dzavakwa

Dzavakwa NV

(Signature of candidate)

18th day of December 2020 in Harare

Dedication

This study is dedicated to my late father. Although you never got to physically experience the end of my undergraduate and this graduate school journey with me your advice, life lessons and encouragement have pushed me to always reach for the moon.

Continue to rest in peace

Aaron Sylvester Dzavakwa

1962 -2009

Abstract

Background

Tuberculosis (TB) is a global public health problem in children under-five years. Majority of children under-five with TB infection are household contacts of bacteriologically confirmed TB cases. The World Health Organization has recommended that children under-five that are household contacts of TB cases, be given isoniazid preventive therapy (IPT) at 10 mg/kg for 6 months. This recommendation has been adopted by the Zimbabwe National TB Programme. IPT is an efficacious chemoprophylaxis that reduces incidence of TB disease in children under-five years however, implementation of the IPT guidelines by healthcare providers in Zimbabwe has been reported to be suboptimal. Studies conducted in other countries have reported many operational challenges encountered by healthcare providers in implementing IPT guidelines for under-five child contacts of TB cases. However, there is sparse literature available that has explored factors influencing implementation of IPT guidelines for under-five children by health care providers in the Zimbabwean context. The purpose of this study was to explore the barriers to and facilitators of implementation of IPT guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe.

Methods

A qualitative study was conducted at four health facilities offering TB services in Harare, Zimbabwe. A total of 18 interviews were carried out amongst healthcare providers working in TB outpatient departments. A semi-structured interview guide patterned along the constructs of the Consolidated Framework for Implementation Research (CFIR) was used for data collection. The study used Framework analysis described by Ritchie and Spencer for data analysis.

Results

The main barriers to and facilitators of implementation of the IPT guidelines for under-five child contacts of TB cases by healthcare providers were categorized into themes. The qualitative themes which emerged were role of opinion leaders, providers' attitude towards IPT, experiences with caregivers, facility factors influencing implementation of the IPT guidelines and use of shorter TB preventive therapy regimens.

Conclusion

The primary factors influencing implementation of IPT guidelines for under-five child contacts of TB cases amongst healthcare providers were related to implementation practices within the health facilities. More barriers to implementation of the IPT guidelines were identified than facilitators. This highlights the implementation challenges that need to be addressed by the Zimbabwe NTP before IPT uptake in under-five children can be optimized. It is important for policy makers to capacitate health facilities with adequate resources for the childhood IPT as well as ensuring that clinicians are sufficiently trained about the guidelines.

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Table of Contents Page

Declaration i
Dedication ii
Abstract iii
Acknowledgements v
List of Figures ix
List of Tables x
Abbreviations and Acronyms xi
Operational definitions xii
Chapter 1: Introduction 1
1.1 Background 1
1.2 Problem Statement 2
1.3 Research Question 4
1.3.1 Aim 4
1.3.2 Objectives 4
1.4 Justification 4
1.5 Literature Review 5
1.5.1 Overview of childhood TB 5
1.5.2 Isoniazid Preventive Therapy (IPT) 6
1.5.3 Barriers to implementation of IPT guidelines 6
1.5.4 Facilitators of implementation of IPT guidelines 9
1.5.5 Use of the shorter TB preventive therapy regimens 10
1.5.6 Consolidated Framework for Implementation Research (CFIR) 10
Chapter 2: Methodology 13
2.1 Study Design 13
2.2 Study sites 13
2.2.1 Beatrice Road and Wilkins Infectious Diseases Hospitals 13
2.2.2 Edith Opperman and Kuwadzana Polyclinics 14
2.3 Study population 14
2.4 Participants Selection 15
2.5 Data collection 16
2.6 Data management 16
2.7 Data analysis 17
2.8 Ethical considerations 19

2.9 Researcher reflexivity 20
Chapter 3: Results 21
3.1 Participant Characteristics 21
3.2 Facility performances with regards to IPT initiation 22
3.3 Emerging themes 22
3.4 Barriers to implementation of IPT guidelines 23
3.4.1 Role of peer opinion leaders 23
3.4.2 Providers' attitude towards IPT 24
3.4.3 Experiences with caregivers 26
3.3.4 Facility factors influencing implementation of the IPT guidelines 28
3.5 Facilitators of implementation of IPT guidelines 32
3.5.1 Role of opinion leaders 32
3.5.2 Providers' attitude towards IPT 33
3.5.3 Experiences with caregivers 34
3.5.4 Facility factors influencing implementation of the IPT guidelines 35
3.6 Use of the shorter TB preventive therapy regimens 36
Chapter 4: Discussion 39
4.1 Barriers to implementation of IPT guidelines 39
4.1.1 Role of peer opinion leaders 39
4.1.2 Providers' attitude towards IPT 39
4.1.3 Experiences with caregivers 40
4.1.4 Facility factors influencing implementation 40
4.2 Facilitators of implementation of IPT guidelines 42
4.2.1 Role of peer opinion leaders 42
4.2.2 Providers' attitudes towards IPT 42
4.2.3 Experiences with caregivers 42
4.2.4 Facility factors influencing implementation 43
4.3 Use of the shorter TB preventive therapy regimens 43
4.4 Limitations 44
4.5 Strengths 45
Chapter 5: Conclusion and Recommendations 46
5.1 Conclusion 46
5.2 Recommendations 47
5.2.1 Policy related 47

5.2.2 Service delivery related....47
5.2.3 Research implications....48
5.3 Funding....48
5.4 Conflict of interest....48
References....49
Appendices....60
Appendix 1: Plagiarism Declaration....60
Appendix 2: Turnitin Report....61
Appendix 3: The original CFIR framework....67
Appendix 4: Definition of the CFIR domains....68
Appendix 5: Screenshot example of charting....69
Appendix 6: Study information sheet....70
Appendix 6: Consent forms....73
Appendix 7: Interview guide....76
Appendix 8: Wits HREC ethics certificate....79
Appendix 9: Zimbabwe Medical Research Council (MRCZ) ethics certificate....80
Appendix 10: Permission letter from Harare City Health Department....81

List of Figures Page

Figure 1: The Consolidated Framework for Implementation Research.....12
Figure 2: Original CFIR framework from Damschroder et al. 2009 67

List of Tables Page

Table 2.1: Number of staff members interviewed in each role per facility 16
Table 3.1: Participant characteristics 21
Table 3.2:Participant roles as used in the results section.....22
Table 3.3:Emerging themes and the associated CFIR domains.....23

Abbreviations and Acronyms

AIDS	Acquired immunodeficiency syndrome
ARI	Acute respiratory infections
BRIDH	Beatrice Road Infectious Diseases Hospital
CFIR	Consolidated Framework for Implementation Research
EHT	Environmental health technician
HIV	Human immunodeficiency virus
INH	Isoniazid
IPT	Isoniazid preventive therapy
LTBI	Latent tuberculosis infection
MDGs	Millennium Development Goals
m-health	Mobile health
MNCH	Maternal, Neonatal and Child Health
NTBMG	National tuberculosis management guidelines
NTP	National TB Programme
PCs	Primary caregivers
SDGs	Sustainable Development Goals
TB	Tuberculosis
UN	United Nations
WHO	World Health Organisation
WIDH	Wilkins Infectious Diseases Hospital

Operational definitions

Active TB/ TB disease: the disease state due to *Mycobacterium tuberculosis* infection

Burden of disease: a non-specific concept used to describe death and loss of health due to a health problem or illness (1). In this study, the term refers to tuberculosis (TB) disease in children.

Childhood tuberculosis: refers to an infection with *Mycobacterium tuberculosis* in children 0 to 14 years.

Healthcare providers: staff members at the health facilities involved in implementing isoniazid preventive therapy guidelines for children under five years.

High TB burden country: "A country with a WHO estimated incidence rate of TB of greater than or equal to 100/100 000 population,"(2).

Household contact: a child less than five years, "who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime periods during the 3 months before the start of the current treatment episode," (2).

Latent TB infection: a state of continued immune response to the *Mycobacterium tuberculosis* pathogens with no evidence of clinically active TB disease (2). In this study it is when a child under five years has TB infection but not active TB disease.

Morbidity: the state of having a disease or having symptoms of the disease

Mortality: death

Miliary TB: a type of widespread dissemination of *Mycobacterium tuberculosis* throughout the whole body

Peer Opinion Leader: outspoken and influential individuals within an organisation who assume informal leadership roles, and can influence their colleagues' attitudes and behaviour with respect to implementing an intervention (3). In this study, this term does not include supervisors and clinic managers.

Chapter 1: Introduction

1.1 Background

Tuberculosis (TB) is one of the leading communicable diseases causing significant morbidity and mortality after HIV/AIDS (4,5). The World Health Organization (WHO) in its 2019 global TB report stated that of the 10 million new cases of TB in 2018, 1.1 million cases (~11%) occurred in children 0-14 years and of these 205 000 died (6,7). The exact number of under-five children who had TB disease is not known (6,8,9). However, in 2014 Dodd et al estimated that globally 51.4% of all paediatric cases (0 -14 years) of TB occurred in under-five children (8,10) with 80% of TB deaths occurring in the same age group (5). Zimbabwe is amongst the top 30 TB endemic countries with an estimated prevalence of childhood TB of 9.1%, of whom 51% are children younger than five years (11). Majority of under-five children with TB are household contacts of bacteriologically confirmed TB cases (12).

Childhood TB continues to be neglected in Sub-Saharan Africa as most children remain undiagnosed and untreated (13). This is primarily because of challenges with diagnosing young children and the lower priority given to childhood TB programmes compared to adult TB programmes and HIV (14). TB progresses rapidly from latent infection to active disease in children less than five years of age (15). The time lag from infection to disease state in infants can be as short as a few weeks. Children under-five years are also at high risk of severe disseminated disease and death (7).

With TB causing significant morbidity and mortality amongst children, prevention of TB disease is of utmost importance. The WHO as part of the End TB strategy which focuses on reducing TB incidence by 90% by 2035 has recommended that, “Children <5 years of age who are household or close contacts of people with TB and who, after an appropriate clinical evaluation, are found not to have active TB disease should be given 6 months of Isoniazid preventive therapy (IPT) at 10 mg/kg per day, range 7–15 mg/kg, maximum dose 300 mg/day,” (15,16). The END TB strategy is a global TB care and control strategy developed by the WHO. It is aligned with the Sustainable Development Goals (SDGs) which target to reduce the global TB epidemic by 2035. It was preceded by the STOP TB strategy which intended to attain global TB control targets by 2015 and was based on the Millennium Development Goals (MDGs) (6,17)

Isoniazid is an efficacious TB chemoprophylactic drug which has been shown to decrease incidence of tuberculosis in children by more than 60% for a period up to three years if taken regularly for six months (18). Despite the universal recognition of the value of IPT amongst children exposed to TB, very few National TB Programs in high TB burden and low to middle income countries implement these guidelines at the health facility level (19). Globally in 2018, approximately 1.3 million children under-five years were household contacts of bacteriologically confirmed pulmonary TB cases. However, only 27% were commenced on TB preventive treatment. This is below the WHO 4 million target to provide TB preventive treatment to under-five children who are household contacts of TB cases during the years of 2018-2022 (6) – a commitment made by member states at the United Nations (UN) high-level meeting on TB which took place in September 2018 (6). In 2018, the Zimbabwe National TB Programme (NTP) reported initiating 30% of all eligible children under-five on IPT. This is despite the NTP adopting the WHO END TB strategy recommendation into the 2015 National TB management guidelines (17,20).

There is sparse literature available that has sought to identify facilitators of implementation of IPT guidelines for under-five children that are household contacts of TB cases in TB endemic areas (21,22). Existing literature has identified lack of knowledge of the benefits of IPT among healthcare providers, stock outs of paediatric formulations, lack of TB screening tools, poor support and supervision of childhood TB programmes and non-prioritization of TB in children as some of the barriers to implementation of IPT guidelines (22) by healthcare providers. The purpose of this study is to explore the barriers to and facilitators of implementation of isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe.

1.2 Problem Statement

Worldwide children account for 1.1 million of all the tuberculosis cases with a mortality of close to 25% (7,8). Dodd et al. estimated that 80% of paediatric TB-related deaths occurred in children under-five (5). The true extent to which TB is an underlying cause of morbidity and mortality in under-five children is not known due to overlap in symptomatology with other infections, challenges with making a definitive diagnosis of TB in children and the under reporting of childhood TB cases (8,9). Majority of TB related deaths in children under-

five, are often misclassified as acute respiratory infections (ARI), pneumonia, meningitis, HIV/AIDS, or malnutrition (9,23). Childhood TB is thus, a global public health emergency requiring safe and effective strategies to prevent unnecessary under-five morbidity and mortality (21).

IPT is an evidence-based intervention, which reduces progression to TB disease by 60 -90% in children (21,24). Without IPT, 5-10% of children infected with TB will develop active disease within a year. The risk is significantly increased in children under-five, particularly those who are two years and below (21,25). Despite the proven efficacy of IPT in reducing incidence of TB disease in at-risk children under-five years, implementation of IPT guidelines in this age group has not been prioritized in TB endemic countries including Zimbabwe (19,26).

Zimbabwe is amongst the high TB burden countries in the world (4). The high transmission rate of TB among under-five children in Zimbabwe is attributable to them being household contacts of TB cases (9). In 2018, Zimbabwe reported initiating only 30% of eligible children under-five years on IPT far below their 100% target (6,27). This low uptake of IPT in Zimbabwe has been attributed to inadequate integration of TB preventive treatment services for under-five children into other Maternal, Neonatal and Child Health (MNCH) programmes (20). Most health facilities in Zimbabwe provide childhood TB preventive treatment services as a separate entity to other child health programmes and this has significantly contributed to the low IPT uptake in under-five children (17,20,27). Furthermore, healthcare providers in some health facilities particularly in peripheral health centres in Zimbabwe have not received training on diagnosis and management of childhood TB (17,20).

With Zimbabwe failing to optimise the administration of IPT in under-five children and the impact TB has on morbidity and mortality in this age group; there is an urgent need to identify and mitigate barriers in the implementation of IPT guidelines for under-five children. However, very little is known about factors influencing implementation of IPT guidelines for under-five child contacts of TB cases by health care providers in Zimbabwe.

1.3 Research Question

What are the barriers to and facilitators of implementation of IPT guidelines in children under-five that are household contacts of TB cases by health care providers in Harare, Zimbabwe?

1.3.1 Aim

To explore the barriers to and facilitators of implementation of IPT guidelines in children under-five that are household contacts of TB cases by health care providers in Harare, Zimbabwe**.**

1.3.2 Objectives

1. To explore the barriers to implementation of IPT guidelines by health care providers in children under-five that are household contacts of TB cases in Harare, Zimbabwe.
2. To explore the facilitators of implementation of IPT guidelines by health care providers in children under-five that are household contacts of TB cases in Harare, Zimbabwe.
3. To explore healthcare providers opinions on the use of the shorter TB preventive therapy regimens.

1.4 Justification

The purpose of this study is to explore the barriers to and facilitators of implementation of IPT guidelines for children under-five years that are household contacts of TB cases by health care providers. In Zimbabwe the majority of children eligible for IPT do not receive the treatment and this puts them at a high risk of developing TB disease and its associated complications (26). This is despite evidence showing the efficacy of IPT in treatment of latent TB infection (LTBI) in children (2,21,28) and the incorporation of childhood IPT guidelines into the Zimbabwe National TB Management Guidelines (NTBMG) (17,20). It is therefore crucial to explore the factors influencing implementation of IPT guidelines for under-five children by healthcare providers in a Zimbabwean context, as this will help identify why differences exist between current and expected practices in the implementation process and help close the gap between IPT policy and implementation.

It will also be beneficial to healthcare providers working in TB units, as it will allow them to know the quality of implementation as well as, quality of care that they offer to children under-five. In addition, the study findings will help TB programme managers, staff within facilities and other stakeholders to come up with effective implementation strategies that can be used to increase the administration of IPT to eligible children under-five residing in their catchment areas. Apart from contributing to the existing body of literature on implementation research, this study will also serve as a benchmark to inform future research that will evaluate implementation outcomes of the IPT programme in Zimbabwe.

1.5 Literature Review

1.5.1 Overview of childhood TB

Tuberculosis is an airborne and infectious lower respiratory tract infection caused by the organism *Mycobacterium tuberculosis*. The true international burden of TB disease in children is not known (7). This is mainly due to challenges in making a definitive diagnosis as a result of high frequency of extrapulmonary TB disease in children under-five years, an overlap in symptomatology with other childhood illnesses, absence of a standard case definition, unavailability of epidemiological data for children from TB endemic countries and low public health priority afforded to childhood TB in comparison to adult TB programmes (8,29).

In 2018, children less than 15 years contributed to 11% of all incident TB cases with 205 000 deaths reported (~13,8% of all TB deaths). It has been estimated that children under-five years contribute to 51.4% of all childhood TB cases with more than 80% of deaths occurring in the same age group (5). Clinical studies have shown that TB is a common finding in children with severe pneumonia (30–32). Pneumonia is one of the top three causes of under-five mortality in the whole world. Approximately 921 000 children under-five years died from pneumonia in 2015, majority of these deaths occurred in TB endemic regions (23). Zimbabwe which is amongst the 30 high TB burden countries has a childhood TB prevalence rate of 9.1% with 51% being children under-five years (11).

Children under-five years are a significant demographic group to understanding TB epidemiology. Most children are usually infected by household contacts with active TB disease (7). In TB endemic regions children constitute about 40% of the caseload (33). TB

usually advances rapidly from latent infection to active disease with a significant risk of severe disseminated disease such as meningitis or miliary TB. The highest risk of developing TB disease after an infection occurs in infants and young children, who progress from latent infection to active TB disease after only a few weeks of infection (25). Children therefore, serve as sentinel cases which indicate new and ongoing TB transmission in a community (7).

1.5.2 Isoniazid Preventive Therapy (IPT)

TB in children continues to be a neglected global public health problem (26). Majority of childhood TB-related deaths represent a missed opportunity for prevention (5). As a result, the WHO has recommended that, "Children <5 years of age who are household or close contacts of people with TB and who, after an appropriate clinical evaluation, are found not to have active TB should be given 6 months of isoniazid preventive therapy (IPT) at 10 mg/kg per day," (16,17,20). This intervention is part of the END TB strategy which aims to reduce TB incidence by 90% by year 2035. The same recommendation has also been adopted into the Zimbabwe NTP.

Isoniazid (INH) is an evidence based and efficacious tuberculosis chemoprophylactic drug that is known to reduce incidence of active TB disease by approximately 60-90% in children younger than 15 years when taken daily for six months (21). It prevents progression of TB infection from latent to active disease (26). Latent TB, "is a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB" (2). In this study, latent TB is when a child under-five has TB infection but not active TB disease.

1.5.3 Barriers to implementation of IPT guidelines

Majority of TB-related deaths in children under-five are as a result of them being household contacts of bacteriologically confirmed TB cases and not having received chemoprophylaxis. This reflects a missed opportunity by healthcare providers to implement the IPT guidelines (5). In most TB endemic countries, implementation of the IPT guidelines for under-five children that are household contacts of TB cases by healthcare providers has been suboptimal(26,34,35).

For a program to be successfully implemented in a health facility, the healthcare providers must be educated and familiar with the medications and services they are offering (26). A significant number of studies highlighted that gaps exist in health-care worker understanding of the benefits of IPT in children under-five years (26,34,36,37). A study conducted in India reported inadequate knowledge among healthcare providers about which under-five children were eligible for IPT as a barrier to implementing the guidelines (34). Most providers were not convinced that benefits of treating LTBI outweigh the risks (19,36) as they strongly believed that initiating a child on IPT would promote antibiotic resistance to INH, one of the primary drugs used in TB treatment (26,36,37).

Lack of prioritisation of childhood IPT by National TB Programmes of many low to middle income countries has also been cited as a reason for failure of health care providers to implement IPT guidelines for under-five children. Many TB endemic countries give precedence to management of childhood TB disease, adult TB programmes and HIV (19,38). Very little to no resources are allocated to household contact management. The Zimbabwe NTP also reported the poor implementation and integration of IPT guidelines for under-five children into other Maternal, Neonatal and Child Health (MNCH) programmes (20). Similarly, another study conducted in Zimbabwe identified that staff shortages resulted in healthcare providers failing to prioritise implementation of the IPT guidelines as they had to give more attention and time to activities of other programmes running within the facilities (39).

The WHO has reported challenges faced by healthcare providers in distinguishing between latent TB infection, sub-clinical TB and active TB disease in children under five as a barrier to implementation of the guidelines. They have also identified that some of the WHO approved diagnostic tests required to screen under-five children are not readily available in most high TB endemic countries (16). Healthcare providers in resource-limited settings are concerned by challenges they face in definitively excluding TB disease due to the cumbersome screening tests (36). In Botswana, health care providers reported TB diagnosis in children to be complicated. The reasons mentioned included the overlap of TB symptoms with other respiratory tract infections, challenges with collecting samples for testing and the absence of reliable testing strategies (35). Likewise, another study done in India also reported that the screening process was time-consuming such that, some clinicians would end up not following the guidelines accurately (34).

Some studies have also indicated the laborious process involved in preparing paediatric doses as well as supply chain difficulties in acquiring child-friendly dispersible formulations from Global Fund as a sticking point for clinicians to deliver IPT to children (34). In other studies, the providers mentioned long periods of stock out of INH as a major challenge. They reported that this discouraged them from screening the eligible children under-five for TB as they would not have anything to offer them after screening (18,34). Another challenge highlighted was the delay in getting test results back from the laboratories as well as, loss of the test results which would then result in providers failing to implement the guidelines (40).

Peer opinion leaders have been identified to play a crucial role in negatively influencing implementation of healthcare interventions (41–44). This is because most healthcare providers work in peer groups that share common beliefs and norms and this can greatly influence a clinician's attitude and behaviour towards a particular intervention (44,45). Peer opinion leaders are defined as outspoken and influential individuals within an organisation who assume informal leadership roles, and are capable of influencing their colleagues' attitudes and behaviour with respect to implementing an intervention (3,44,46). In this study peer opinion leaders are defined as influential healthcare providers or peers within the health facilities who everyone in the TB unit looks up to and who can influence other providers' decisions to implement the IPT guidelines. The term did not include supervisors and clinic managers.

A study conducted in South Africa identified that some healthcare professionals were reluctant to recommend IPT in children because of the influence from some peer opinion leaders who openly disputed the benefits of IPT (41). Likewise, doctors in England described the negative influence that their peer opinion leaders had on their prescribing behaviour (47). The doctors reported that their discomfort with prescribing was due to the fear of looking incompetent in front of their peers or violating an agreed management policy with their peers (47). Another study in Tanzania identified that malaria over-diagnosis by healthcare providers was greatly influenced by peer opinion leaders and that most malaria diagnostic decisions were made as a group rather than as individuals (43).

A substantial number of studies have also revealed that most providers fail to implement the guidelines because of the primary caregivers' (PCs) attitude and beliefs towards IPT for their

under-five children (18,26,48). It has been reported that most caregivers are reluctant for their under-five children to undergo a long period of treatment for, “an asymptomatic condition” that may never progress to active TB disease. Issues to do with access to the health facilities resulting in high transport burden on the caregivers as they try to bring the eligible child for initiation of treatment and clinic reviews have also recurred throughout different studies as a barrier to implementing the guidelines (26,36). This has resulted in most caregivers feeling disheartened with committing their under-five children to the preventive treatment process (36).

1.5.4 Facilitators of implementation of IPT guidelines

There are limited studies that seek to identify facilitators of implementing IPT guidelines specifically in under-five children. However, some literature is available on factors that have promoted implementation of other TB management guidelines.

A study done in Cape Town, South Africa found that health care providers’ commitment to reducing incidence of TB in children was important in promoting implementation of IPT (49). The staff providing IPT at the health facilities were determined to always operate at their best service despite health system problems with implementation of IPT (49). Another study conducted in Eastern Cape South Africa reported nurses’ unwavering commitment and effort in managing TB patients as a facilitator for continued use of the National TB Management Guidelines (50).

Regular TB meetings which were held in the facilities by TB nurses, managers and programme coordinators provided an environment for support, problem solving, information sharing as well as, building morale for continued implementation of the guideline (50) to providers who were working in TB units. A study conducted in Zimbabwe also found that availability of TB screening algorithm tools in health facilities was an important driver of implementation of the IPT guidelines (27). These TB screening tools provided health workers in the facilities with important information on eligibility criteria for TB preventive therapy (27,51).

Caregivers of under-five children also play an important role in facilitating implementation of the IPT guidelines by healthcare providers. There are studies that have shown that caregivers’

acceptance of IPT, recognition of the importance of IPT in TB prevention and the need to spare their children from the same disease experiences they had with TB as some of the facilitators to implementation of the guidelines (49,52). For some caregivers the health facilities were a safe haven for their children on IPT as they felt supported by the clinicians offering TB services to their children (49).

1.5.5 Use of the shorter TB preventive therapy regimens

The WHO as part of its strategy to scale up LTBI treatment in high TB burden countries has introduced a three months short course of isoniazid and rifapentine (3HP) to replace the 6 month course of isoniazid monotherapy (4). 3HP is a 12-week course of weekly Isoniazid and Rifapentine which has been shown to be efficacious in the treatment of LTBI in children (53,54). The Zimbabwe Ministry of Health and Child Care has also adopted this recommendation and is planning to roll out 3HP in health facilities offering TB services in order to scale up treatment of LTBI. This study will explore whether healthcare providers perceive use of shorter TB regimens as an implementation driver or barrier to implementing TB preventive treatment guidelines for under-five children.

Previous studies have shown that 3HP is safe in children, has higher treatment completion rates than isoniazid monotherapy (54–56). Furthermore, 3HP is popular amongst young children and healthcare providers as it comes in paediatric-friendly and dispersible formulations which are easy to dispense and administer (57). This has resulted in a significant increase in the implementation of IPT guidelines for under-five children by healthcare providers as well as scale up of LBTI treatment (57,58). Although, use of 3HP has significantly improved implementation of TB preventive therapy guidelines in low TB endemic regions, there is still lack of substantial evidence to determine whether similar results will be reported in high TB endemic regions (57). Use of 3HP will require healthcare providers in high TB endemic regions to be trained on the drug side effects and potential drug to drug interaction with other medicines which may result in unacceptability of the drug by healthcare providers and subsequent implementation failure (56,57).

1.5.6 Consolidated Framework for Implementation Research (CFIR)

The Consolidated Framework for Implementation Research (CFIR) is “a theoretical framework developed to guide systematic assessment of multilevel implementation contexts

to identify factors that might influence implementation of interventions" (59). Studies have shown that the CFIR is a flexible conceptual framework that allows researchers to adapt it to a specific intervention and context (60). It also allows researchers to carry out formative evaluations that assess implementation effectiveness in a particular setting and translation of the findings to another different context (59,61). It has been used widely in implementation research to identify factors influencing or deterring successful implementation of an intervention, such as the case in this study (62).

The CFIR is a collection of 39 constructs grouped into five interrelated domains that influence implementation of interventions (59,62) (See Appendix 3). The CFIR domains were used to guide the exploration of the barriers to and facilitators of implementation of IPT guidelines for under-five child contacts of TB cases in this study. These are intervention characteristics, inner setting, outer setting, individuals involved and implementation process (59,61). Intervention characteristics describe the main features of an intervention that can influence its implementation whilst, outer setting refers to the political and socio-economic environment within which the implementing organisation is set up. Inner setting refers to the structural, political and cultural contexts within a facility that influence implementation of an intervention. Characteristics of the individuals describes the knowledge, attitudes and beliefs of the people involved in the implementation of the intervention and implementation process describes the various processes and strategies incorporated by an organisation in order to promote implementation (59,61,63).

In this study intervention characteristics explored the complexity of the IPT guidelines and the steps involved in implementing the guidelines. Intervention characteristics further explored healthcare providers' perceptions on the use of shorter TB preventive therapy regimens with respect to implementation of the guidelines. Outer setting looked at how socioeconomic status, religious beliefs and IPT knowledge perception of primary caregivers of under-five children influenced healthcare providers to use the IPT guidelines. Inner setting explored practices within facilities that acted as enablers or impediments to implementation. Characteristics of individuals looked at healthcare providers' knowledge, attitudes and beliefs whilst, implementation process explored the influence opinion leaders had on other clinicians' decision to use the IPT guidelines. The application of the CFIR domains to this study was informed by previous researches that have used the CFIR to explore barriers and facilitators to implementation of complex health interventions (60,62,64). (See Appendix 2

for full definitions of the CFIR as used in this study). Figure 1 shows the CFIR framework and how it was applied to this study.

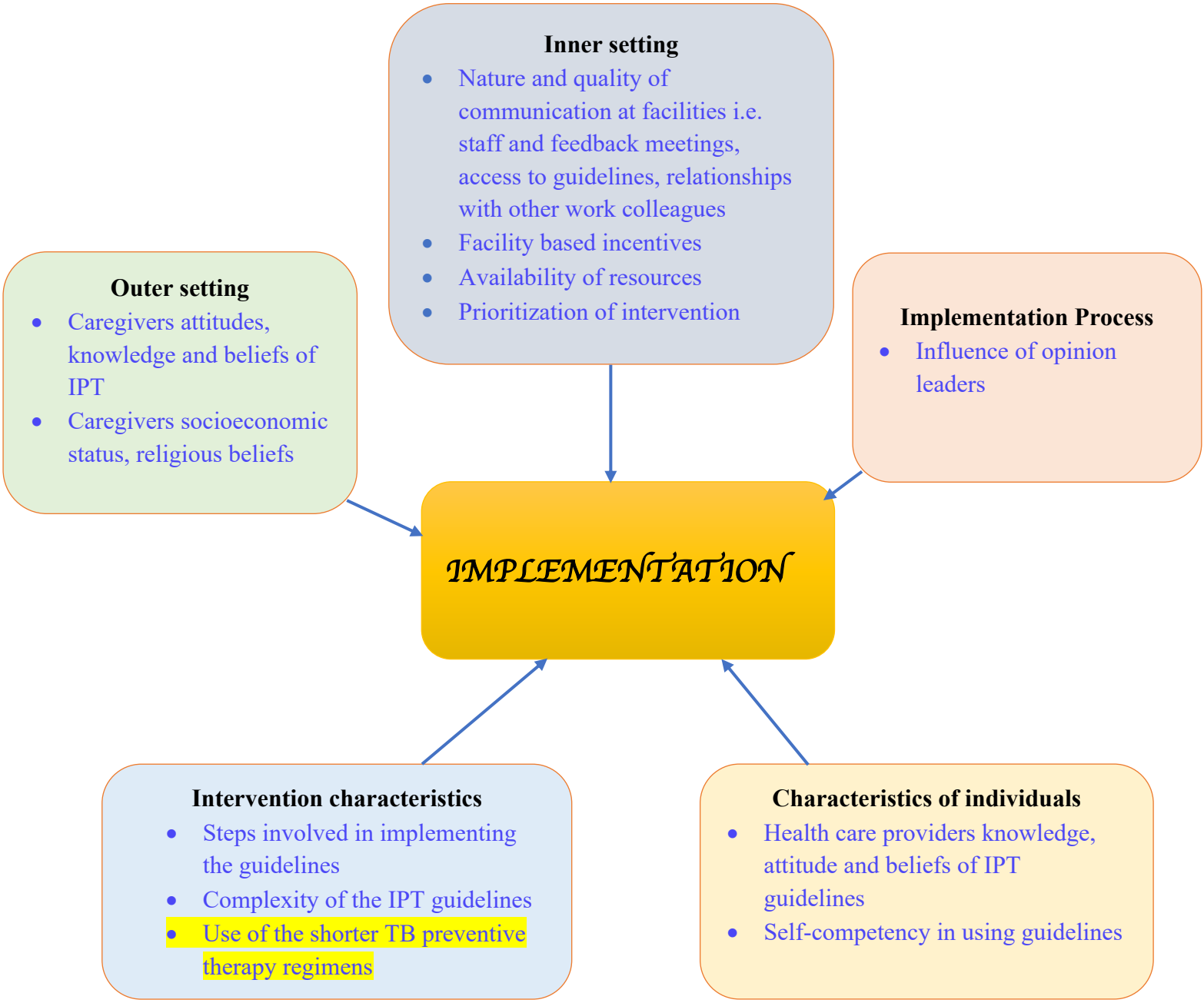


Figure 1: ***The Consolidated Framework for Implementation Research***

Chapter 2: Methodology

2.1 Study Design

This study was purely qualitative. Enquiries were made on the barriers to and facilitators of implementation of IPT guidelines for under-five child contacts of TB cases by health care providers in Harare, Zimbabwe.

2.2 Study sites

The study was conducted in four healthcare facilities. These were Beatrice Road (BRIDH) and Wilkins (WIDH) Infectious Diseases Hospitals as well as, Edith Opperman and Kuwadzana Polyclinics. All the facilities were purposefully chosen because they are high volume centres with dedicated TB units. The healthcare centres are all located in the capital city of Zimbabwe, Harare.

2.2.1 Beatrice Road and Wilkins Infectious Diseases Hospitals

Beatrice Road and Wilkins infectious diseases hospitals are tertiary facilities that are run by the City Health department a subsidiary of Harare City Council. They are located in Harare metropolitan province. As part of Harare City Council's strategy to increase access to healthcare, the facilities have decentralised their childhood TB services to local clinics (51, Unpublished) They both now run as diagnostic and referral centres for complicated TB cases. Both facilities diagnose over 90% of TB cases in Harare and surrounding areas (20).

BRIDH is a 150 bedded hospital that provides isolation services to patients being treated for infectious diseases (51, Unpublished). It is located in the high density suburbs of Harare. BRIDH is the main TB centre for all the city council healthcare facilities. It also houses the main pharmacy department involved in procuring TB drugs for all the Harare City Council clinics. For this reason, majority of the study participants where from this facility. The TB outpatient department (OPD) at BRIDH is run by one nurse manager, TB counsellors and four registered general nurses, one of them who was selected as a TB focal person by the partner organisations supporting the facility. In addition, there are two doctors who are Harare City Council employees who alternate coming to the clinic weekly to see complicated cases.

WIDH is a 35 bedded hospital located in the low density suburbs of Harare. Unlike BRIDH, Wilkins infectious diseases hospital has completely decentralised it's TB services to local clinics (51, Unpublished). According to the providers at the hospital, the TB outpatient clinic had not managed any children under-five years in a very long time. The facility was currently operating as a referral and diagnostic centre managing, only complicated TB cases and conducting screening tests not available at the local clinics. After being seen by a doctor these patients were sent back to their primary care facilities for registration and continued TB care. However, the clinicians at WIDH would advise and recommend the TB patients seen in the clinic to take their under-five eligible children for screening and IPT initiation at their nearest local clinic.

2.2.2 Edith Opperman and Kuwadzana Polyclinics

Edith Opperman and Kuwadzana polyclinics are healthcare facilities also run by the City Health department. A polyclinic is a health care facility that offers both general and specialist treatments for a variety of diseases to outpatients. It usually operates independently of a hospital. The Harare City council polyclinics mainly provide specialist services such as maternity, primary care clinic and family health services (51, Unpublished).

Kuwadzana polyclinic is located in the western region of Harare, and it's main referral tertiary centre is WIDH. Edith Opperman polyclinic is located in the southern region of Harare and its main referral centre is BRIDH. Both facilities have TB outpatient clinics which are currently being run by one TB-trained registered general nurse who also serves as the TB focal person.

2.3 Study population

The study participants were healthcare providers involved in childhood TB care and isoniazid (INH) provision in the four facilities. For this study healthcare providers were defined as, “anyone involved in implementing isoniazid preventive therapy guidelines for children <5years with regards to giving recommendations to screen the child, prescribing, dispensing and disseminating information about IPT” (66,67). These included the nurse managers of each facility, doctors, nurses working in the TB and HIV OPDs, pharmacists, TB counsellors, environmental health technicians (EHTs) and TB programme managers. Some of the nurses also worked as TB focal persons in the facilities. A TB focal person is a nurse or EHT who is

responsible for coordinating TB control programme activities, ensuring regular update of TB registers and quarterly reports and oversees implementation of TB services in the facility (68).

2.4 Participants Selection

Eighteen participants were purposively selected to participate in this study. All participants in the study had been managing TB in children under-five for at least three months prior to onset of the study. Most of the facilities had one nurse working in the TB unit, as such it was difficult to interview two participants for each role. In addition, some participants refused to participate in the study whilst others, were not available due to ill health or workshop attendances. Most study participants were from BRIDH, the main TB tertiary facility under Harare City Health Department. At BRIDH, two participants were selected from each role where possible. Table 2.1 shows the number of participants who were interviewed for each role in each of the four facilities.

The nurse manager at each facility assisted with introducing the researcher to the healthcare providers offering paediatric TB services as well as, orienting her to the unit. The selected participants were approached to discuss logistics of the interviews such as date, time and a suitable venue within the facility. Most interviews were conducted in the morning before start of clinic activities. The participants preferred to be interviewed at their workstations which was usually a consulting room or office in the clinic. The participants from the four health facilities had adopted the flexible hour system (flexi-hours). The flexi-hours system was an initiative adopted by many health facilities in Zimbabwe to curb the high transport costs incurred by healthcare personnel while travelling to work. Clinicians therefore came to work twice or thrice per week according to a predetermined schedule. Logistical arrangements for interview times with the participants were therefore crucial for the study.

Table 2.1: Number of staff members interviewed in each role per facility

Facility Name	Participant role	Number of staff members interviewed
BRIDH	TB programme manager	1
	Nurse manager	1
	Medical doctor	2
	Pharmacist	2
	TB nurse	2
	TB counsellor	1
WIDH	Medical doctor	1
	TB nurse	1
Edith Opperman Polyclinic	Nurse manager	1
	TB nurse	2
	TB counsellor	1
	Environmental health technician	1
Kuwadzana Polyclinic	Nurse manager	1
	TB nurse	1

2.5 Data collection

A semi-structured interview guide was used for data collection (See Appendix 5). The interview guide was patterned along the CFIR framework domains: the characteristics of the intervention, inner setting, outer setting, provider characteristics and implementation process (3). The researcher pretested the interview guide on healthcare providers offering IPT in under-five children at a different health facility from the study sites. Post pretesting the interview guide, a few grammatical corrections were made, and some interview questions were refined for clarity. Interviews were conducted from January to March 2020. All interviews were conducted by the researcher and were approximately 30 to 35 minutes long. The interviews were all conducted in English and were digitally recorded using a portable audio recorder as well as the researcher's cellphone for backup. Field notes of observations made at the facilities were taken during and after the interviews. The field notes were useful for consolidating information collected during the interviews.

2.6 Data management

Interviews were transcribed verbatim by the researcher. The researcher checked the data for accuracy and completeness by going over the transcripts and listening to the audio recordings

multiple times. This was done to identify and resolve any variations between the transcripts and what the participants actually said during the interviews. The transcripts were then imported into MAXQDA2020, a qualitative software for analysis.

2.7 Data analysis

Data analysis was an iterative process, which began after completion of the first interview and proceeded concurrently with data collection. Framework analysis described by Ritchie and Spencer (69) was used for data analysis. Framework analysis is defined as a "comprehensive approach to qualitative data analysis that offers a systematic structure to manage, analyze and identify themes" in a study (70). It enabled the researcher to identify barriers to and facilitators of implementation of IPT guidelines by health care providers (71). Framework analysis follows a five-step process: 1) familiarisation, 2) identifying a thematic framework, 3) indexing, 4) charting and 5) mapping/interpretation (69,72).

Multiple reviews of audio recordings, transcripts and field notes were carried out by the researcher to familiarise herself with the data. During this stage, the researcher listened to all the audio recordings and read through all transcripts and field notes. Memos were used to document emerging themes during this process. The CFIR was used as an apriori framework to generate a codebook based on the five CFIR domains and some of the CFIR constructs that were deemed relevant to the study. Emerging themes that were noted during familiarization were reviewed to see where they fit in the CFIR framework. Some of the emerging themes fit into more than one CFIR domain.

Coding of the transcripts was done in MAXQDA2020. Both deductive and inductive coding methods were used to identify key messages and patterns in the transcripts. Deductive coding was based on the themes from the CFIR framework and inductive coding was based on the new emergent themes identified during indexing. The CFIR framework was modified to fit the themes that were identified during inductive coding. Definitions of the CFIR domains were modified to suit the emergent themes from the study (See Appendix 4). The researcher ensured that the original definitions of the domains were not lost during this process. No new domains or constructs were added to the conceptual framework. Memos were used to define codes and make comments on any patterns or relationships identified in the data. Intercoder agreement was achieved by asking a colleague to code four transcripts (22%) and these were compared to the ones the researcher had coded. Queries and variations in coding were resolved by discussion

between the researcher and the colleague. A major issue noted during intercoder agreement was the differences in starting or end point of highlighting the texts to be coded such that MAXQDA2020 picked it up as different coding, yet the texts were indexed under the same code. Some codes were redefined during this process so that they would be easier to understand.

After coding, the researcher began the process of charting in MAXQDA2020. The process involved summarizing sections of the coded segments for each of the identified themes and presenting the summaries in a table format. The researcher went through each of the codes and summarized all the data that had been coded in that category for each participant. The participants words were paraphrased during writing of the summaries. To avoid losing meaning of the participants' words and, or interpreting what the participants said, the researcher ensured that the summaries were elaborate. MAXQDA2020 also allows one to view the original text and the summaries on one interface so that the abstraction process can be assessed. In cases were the participants' words were concise, the participants' words were quoted as is. The words were highlighted by putting them in quotation marks. The result was a table where the interviews were summarised and organised according to themes and to what the participant said for each theme (See Appendix 5). This enabled the researcher to read the summaries across for within-case analysis or downwards for a particular theme for between-case analysis.

After all the coded data had been summarised and charted according to themes, the researcher went through all the summaries to identify key characteristics of the data as well as, to map and interpret the whole data set. Although, there were some associations and patterns that had been observed during familiarisation, indexing and charting, the systematic identification of associations in the data only began at this stage. To ensure that associations identified were relevant to the study, the researcher based the mapping and interpretation process on the research question and objectives. The identified themes were reviewed, and some themes were merged together if they were noted to speak of similar issues, other codes were renamed, and some codes were left out if they did not answer the research question.

The researcher ensured that themes selected for interpretation were reflective of the participants' opinions. It was during this process that the researcher realised that some of the emergent themes fit into more than one CFIR domain. A final codebook was prepared and

shared with the supervisors for review. During the process the researcher was aware of the objectives of qualitative analysis describe by Ritchie and Spencer which are, “defining concepts, mapping range and nature of phenomena, creating typologies, finding associations, providing explanations, and developing strategies” (69,71)

A feedback session to share initial findings and check for accuracy in interpretation of the findings was supposed to be done with healthcare workers overseeing the TB programme at Harare City Health Department and some of the study participants. However, due to the current restrictions on gatherings put up by the Government of Zimbabwe as a measure to mitigate spread of the Covid-19 virus the feedback session was not held. A virtual meeting could not be set up because of challenges with access to internet as some of the facilities do not have internet access. The Harare City Health Department has planned for a feedback session at their earliest convenience in 2021. In addition, a copy of the research report and any publication from the study will be shared with the Medical Research Council of Zimbabwe.

2.8 Ethical considerations

Permission to conduct the study was obtained from the Human Research Ethics Committee (Medical) from the University of the Witwatersrand (ethics clearance number: M191060) and the Medical Research Council in Harare, Zimbabwe (ethics clearance number: MRCZ/B/1840) (See Appendices 8 and 9). Local permission to conduct the study at the four facilities was obtained from the Harare City Health Department (See Appendix 10). All participants were provided with information sheets of the study and they signed a written informed consent for partaking in the study and for audio recording of the interviews. Pseudonyms were used for the facilities and the participants; other personal identifiers were removed from the interviews. All study material, audio recordings, transcripts and field notes were stored in a password protected computer that was only accessible to the researcher. The research material will be kept for two years after the study is completed if a scientific publication arises from the study and six years if there is no publication. Thereafter, the research material will be deleted.

2.9 Researcher reflexivity

The author of this research report is a medical doctor in Zimbabwe. She is currently studying towards a Master of Science in Epidemiology in the field of Implementation Science at the University of the Witwatersrand. For this study the researcher has assumed an insider position. The researcher's prior experience working in the paediatric section of a government tertiary institution influenced the choice of the research topic, questions, and the study design. The researcher was cognisant that she had to set aside her own views and opinions with regards to implementation of the IPT guidelines by healthcare providers. She therefore tried to remain neutral whilst interviewing the study participants. It was difficult however, in some instances to remain objective as some of the issues raised resonated with the researcher's personal experiences having worked in a paediatric TB and HIV setting. Having had no prior affiliation with the study participants and sites, the researcher's chances of directly influencing participants responses was minimal.

Chapter 3: Results

3.1 Participant Characteristics

A total of 18 healthcare providers were interviewed from the four health facilities. The sample included six nurses, two TB counsellors, three nurse managers, three doctors, two pharmacists, one EHT and one TB programme manager. There were more females (n=13) than males (n=5) who participated in this study. The mean age of the participants was 42 years; age range 40-49 years. Nine participants had been working in their current role for more than five years. The participants' characteristics are presented in Table 3.1. For the results section, nurse managers and doctors were identified as clinical supervisors whilst, nurses and counsellors were identified as family care practitioners, and pharmacists, TB programme managers and EHTs were identified as other healthcare providers. The clinical supervisors, family care practitioners and other healthcare providers who participated in the study were abbreviated as "CS," "FCP," and "OHP" under their respective quotes (see Table 3.2).

Table 3.1: Participant characteristics

Variable	Category	Frequency (n=18)
Age	0-29	1
	30-39	6
	40-49	6
	50+	5
Sex	Male	5
	Female	13
Number of years in current role	0-5 years	9
	>5 years	9
Role in implementation of IPT guidelines	Nurses	6
	TB counsellors	2
	Nurse Mangers	3
	Medical Doctors	3
	Pharmacists	2
	TB programme manager	1
	Environmental health technician	1

Table 3.2:Participant roles as used in the results section

Participant	Identifying role	Abbreviation
TB nurses	Family care practitioners	FCP
TB counsellors	Family care practitioners	FCP
Nurse managers	Clinical supervisors	CS
Medical doctors	Clinical supervisors	CS
Environmental health technicians	Other healthcare providers	OHP
Pharmacists	Other healthcare providers	OHP
TB programme managers	Other healthcare providers	OHP

3.2 Facility performances with regards to IPT initiation

According to the DHIS Zimbabwe 2019 data, in the last quarter of 2019 BRIDH had 9 out of 13 children under-five initiated on IPT. Reports from healthcare providers at Edith Opperman and Kuwadzana polyclinics showed that both facilities had not been performing well with regards to implementation of the IPT guidelines in 2019. This was attributed to the industrial action which had resulted in disruption of normal clinic services. In 2019, 1645 children under-five years were treated for severe pneumonia (ARI) at Edith Opperman polyclinic however, only one child was initiated on IPT. Kuwadzana polyclinic reported 3187 children under-five treated for severe pneumonia (ARI) and only nine children initiated on IPT.

3.3 Emerging themes

Five themes were identified as barriers to and facilitators of implementation of the isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe. Elements of the first four themes were found to be both barriers and facilitators of implementation of the IPT guidelines in this study. The themes which emerged from the study were; role of opinion leaders, providers' attitude towards IPT, experiences with caregivers, facility factors influencing implementation of IPT guidelines and use of shorter TB preventive therapy regimens. Table 3.3 shows the identified themes, sub themes and the associated CFIR domains.

Table 3.3:Emerging themes and the associated CFIR domains

Theme	Sub themes		CFIR domain
	Barriers	**Facilitators**	
1. Role of opinion leaders	• Negative influence	• Positive influence	• Implementation process
2. Providers' attitude towards IPT	• Providers' lack of knowledge and fear of side effects • Other negative personal attributes	• Providers' commitment to use IPT guidelines • Guidelines easy to follow	• Characteristics of individuals • Intervention characteristics
3. Experiences with caregivers	• Caregivers' reluctance • Challenges with transport and accessing health facilities • Religious beliefs	• Caregivers' willingness	• Outer setting
4. Facility factors influencing implementation of IPT guidelines	• No access to hard copies of guidelines • Intervention not prioritised • Lack of screening tools • Challenges with screening children under-five • Staff shortages • Poor follow up and monitoring of children initiated on IPT	• Access to meetings and training workshops on childhood TB • Availability of drugs • Role of partner organisations	• Inner setting • Characteristics of individuals • Implementation process
5. Use of shorter TB preventive therapy regimens	• Disadvantages of a shorter TB preventive therapy regimen	• Advantages of a shorter TB preventive therapy regimen	• Characteristics of individuals • Intervention characteristics • Inner setting • Outer setting

3.4 Barriers to implementation of IPT guidelines

3.4.1 Role of peer opinion leaders

Under this theme the researcher sought to identify whether there were any influential peers or work colleagues within the health facilities who had an effect on the healthcare providers' decision to implement the IPT guidelines. Peer opinion leaders were defined in this study as influential healthcare providers or peers within health facilities who everyone in the TB unit

looked up to and could influence other providers' decisions to use or not use the IPT guidelines. The term did not include supervisors and clinic managers.

Negative influence

Healthcare providers indicated that opinion leaders at the facilities were at times the barriers to implementation of the IPT guidelines. These opinion leaders would discourage other healthcare providers dedicated to implementing the guidelines by making them feel like they were wasting their time and effort. The participants also expressed that some opinion leaders would openly question the benefits of IPT in children and this had a negative impact on the implementation of the IPT guidelines by the other providers.

"So you find out that one is committed to give IPT to the under-five children but you find their peers (opinion leaders) telling them that they are working hard for nothing and it demotivates this other one…" [CS, Facility A]

"But there are those other nurses who are influential and do not like to give IPT to children because of their attitude or follow what the supervisors will have said with regards to TB. And it becomes a problem because they influence their peers to do the same. It's a problem." [FCP, Facility D]

"… the opinion leaders I am referring to are usually healthcare providers at facility level. If one says INH does not work or causes side effects, and the word spreads around [uhum] then it becomes so difficult to influence other healthcare personnel to use the guideline… because once the opinion leaders are negative especially at clinic level then the zeal of other clinicians to use the guidelines and everything else will be negatively affected…" [OHP, Facility A]

3.4.2 Providers' attitude towards IPT

Under this theme the researcher explored healthcare providers' perception to implementation of the IPT guidelines. This encompassed the providers' lack of knowledge, misconceptions about IPT, fear of side effects and their other negative personal attributes (personality traits) that affected implementation of the guidelines.

Providers' lack of knowledge and fear of side effects

The healthcare providers expressed that some clinicians were afraid of the drug side effects and they would discourage primary caregivers of under-five children from giving them INH. The clinicians also stated that at times the under-five children would be turned away because providers on duty were not knowledgeable and confident enough to use the IPT guidelines. In addition, some facilities would hire locum (stand-in) staff to assist in the facilities who would fail to implement the guidelines because of lack of knowledge.

"One thing that I have seen, most providers have a negative attitude towards INH because they are afraid of the side effects. They are very sceptical of the side effects and it's going to be very difficult for the IPT programme, to go on. Some of the providers actually tell parents that if your child takes INH they will end up with peripheral neuropathy… also if the staff are not knowledgeable about IPT [uhum] it's obviously going to affect the IPT programme in a negative way. The clinicians are not going to dispense the IPT once they don't know why they are giving it." [CS, Facility B]

"Usually when these children come when I'm not here they are not given this IPT [uhum] they are told come when your nurse is here because the other clinicians are not confident and knowledgeable about the guidelines [okay]and yes some of them (other clinicians) are not confident, they are afraid of the side effects" [FCP, Facility C]

"… we often hire locum nurses. Some of them are newly qualified nurses or have not been trained in TB so they have no knowledge of how to use the guidelines." [CS, Facility D]

Other negative personal attributes

The participants highlighted that at times a clinician's general personality trait towards a patient could act as a barrier to implementation of the guidelines. It was indicated that providers who were anti-social faced challenges with implementing the guidelines. Some participants also mentioned that most healthcare personnel were not motivated to use the guidelines because of the current incapacitation.

"…but you find those who are anti-social who don't have time to talk to people they hardly ask about children at home i.e. "How are your children doing at home?" then those people have challenges implementing the guidelines." [CS, Facility A]

"With this staff incapacitation and apathy it's very difficult to motivate the staff. The morale is very low and nobody is willing to follow up on those children who need IPT…" [CS, Facility C]

3.4.3 Experiences with caregivers

This theme explored the extent to which primary caregivers of children under-five eligible for IPT influenced implementation of the IPT guidelines by healthcare providers. The issues identified included caregivers' reluctance to have their children on IPT, issues pertaining to high transport costs and access to health facilities and religious beliefs.

Caregivers reluctance

Healthcare providers indicated that most primary caregivers of children under-five were not willing to have their children on preventive therapy making it difficult for them to implement the guidelines. The providers brought up issues to do with caregivers' misconceptions about a child receiving TB preventive treatment; particularly with regards to treatment of an asymptomatic child with a drug known to treat active TB disease. They went on to add that some primary caregivers were convinced that TB was a disease that only affected the adult population. In addition to this, some caregivers were said to be afraid of IPT side effects.

"At times the parents of the child are not willing because the child is not even sick. Most caregivers know that INH treats TB so they don't want their child to be treated for TB when they don't have TB. To them it's like you are treating TB in a child who does not have TB so they are not willing, they are not forthcoming to have their child on IPT." [CS, Facility C]

"Usually the caregivers are a bit adamant because they feel children don't get TB like that, maybe because of knowledge deficit you find that when we are giving treatment they assume TB is for adults only. So, with children they will just think, children are babies who won't get infected with TB… they don't consider that they are at high risk because of their age…" [FCP, Facility B]

"…but some parents are very reluctant to give IPT to their children. I don't know maybe there are myths around the side effects of TB preventive treatment. So, some are really sceptical about those ones…" [FCP, Facility D]

Challenges with transport costs and accessing health facilities

The providers mentioned that some caregivers failed to bring their children or would present late with their eligible children because of issues to do with transport costs. The healthcare providers mentioned that some of their patients were from low socioeconomic backgrounds and some lived far from the health facilities and did not have enough money to make multiple trips to the facilities with their eligible children for IPT screening and initiation.

" It's very difficult for a parent to come with the child. Let's say they are coming from Area 1, to board two buses to town then to this facility for x-rays and screening and then, again for IPT initiation. They won't come, they will say they did not have the bus fare to come… If there was another health facility where there was an x-ray machine which is nearer to them [uhum] then it would be better [okay] than for them to come to this place" [CS, Facility A]

"*Most of our patients are from poor socioeconomic backgrounds and they cannot afford the transport costs. So, the challenge we then run into is the presentation of the child. Sometimes the child comes four months into the treatment of the contact so presentation itself is a challenge they don't present early… "* [OHP, Facility A]

"… distance is an issue. It may not be easy for some of the caregivers to access this facility because some of them might be staying as far as Area 4 (~30km away) and considering transport issues and costs [uhum] they might not come back with the child for IPT initiation because they don't have money for transport… So even if there is a child exposed to TB in the family they won't come to the hospital or clinic because they don't have money." [FCP, Facility B]

Religious beliefs

Healthcare providers also expressed primary caregivers' religious beliefs as a barrier to them implementing IPT guidelines for under-five children. They stated that there were some religious sects that forbid their congregants from seeking medical treatments from health

facilities. This made it difficult for the providers to implement the IPT guidelines as some of the caregivers would only seek treatment for their child when they now had advanced TB disease. The providers also mentioned that at times the caregivers only came to the health facilities to have their child initiated on IPT but would default treatment thereafter.

"Religious beliefs are sometimes a hinderance. Many caregivers from conservative religious sects don't appreciate medication [uhum] until it's rather far too late for the child in terms of having TB disease. Some of the caregivers who attend these churches do not even bring their children for TB screening, or attend health education lessons. They will tell you that we are not allowed to come to the health facility…that is one of the challenges we face here." [FCP, Facility A]

"Some parents from conservative religious groups are not willing for their under-fives to take medications [uhum]. So, at times they just come and you give them the information on TB prevention but then it's so difficult for them to come back. Some they can get the initial doses of IPT but for them to continue [uhum] is very difficult due to religious beliefs."[CS, Facility D]

3.3.4 Facility factors influencing implementation of the IPT guidelines

The researcher explored how current practices at the facilities negatively influence implementation of the IPT guidelines from the healthcare providers' perspective. The practices identified included no access to hard copies of updated guidelines, intervention not prioritized, lack of screening tools and staff shortages. In addition, other issues such as challenges with screening children under-five and poor follow up and monitoring of children initiated on IPT were explored.

No access to hard copies of updated guidelines

Healthcare providers mentioned that they had problems with accessing hard copies of the updated guidelines for use within the facilities. The researcher observed during visits that there were no hard copies of the TB guidelines in consulting rooms of most of the health facilities. In some healthcare facilities, providers were using electronic copies of outdated TB guidelines which they had received on their mobile telephones. Some providers indicated they were not comfortable with using a soft copy of the guidelines because of network and

technical challenges with accessing the electronic copy on their devices. Other providers preferred hardcopies or having the guidelines on wall charts compared to electronic copies, saying they were more easily accessible.

"That's our major challenge for now we don't even have any copies of the latest TB guidelines. As we speak, we don't have TB guidelines [uhum] we were told there has been a change in the guidelines, but even the old ones we don't have them. So, I don't know whether it is the Ministry which is not printing [uhum] or it's our employer… we don't even know where to get the guidelines. I probably have the old TB guidelines on my laptop on softcopy but we are saying why can't you just avail hardcopies when you change the guidelines, avail so that we get information that is up to date." [OHP, Facility D]

"Okay we have had challenges as far as accessing these guidelines are concerned…most of the people are old school and they are not fully vested with technology. So they prefer to have the guidelines printed and distributed… Even if people get the electronic copies to use there is still a challenge because, when you follow-up and ask you find out people never received the electronic copy of the guidelines whilst, others received them on their phone but did not know how to access them. These clinicians prefer hardcopies or charts, or something written on the walls in the consulting room which they can easily refer too." [CS, Facility A]

Intervention not prioritised

Healthcare providers felt that TB in children was not being prioritised as much as other programmes that were running in the facilities. The providers expressed that the bulk of the support and resources at the facilities were channelled to programmes such as HIV.

"Actually TB in under-fives has been neglected. TB programmes are not treated the same as HIV programmes. A lot has been done when it comes to HIV but as for TB I think we are still lagging behind. Although, it's usually a co-infection with HIV, but a lot has been done for HIV and TB has been left behind." [CS, Facility A]

"It seems as if TB has not been prioritised. Maybe it's lack of funding or what. But, people are no longer willing to deal with TB the way they are dealing with HIV like now we don't even have the cell phone [uhum] to make the follow ups, we don't have." [OHP, Facility D]

Lack of screening tools

Providers at the facilities also mentioned they failed to implement the guidelines due to lack of screening tools. They expressed that at times an under-five child eligible for IPT would present at their local clinic but they failed to initiate them on IPT because screening tests and tools used to diagnose TB would be unavailable.

"I would say these steps are quite straight forward. But at one point they are limited by availability of resources [okay] because, when you get an under-five who is exposed to TB you want to do Mantoux skin test to confirm if they have TB but in some cases you don't have the Mantoux test. The implementation is not a problem but the challenge is lack of resources." [CS, Facility A]

"We are not carrying out any investigations at the moment. Because we don't have the Mantoux test and we also don't have an x-ray machine." [FCP, Facility D]

Challenges with screening children under-five

Challenges with screening children under-five years was mentioned by healthcare providers as a barrier to implementing the IPT guidelines. Some providers had challenges with conducting screening tests like, Mantoux test and collecting gastric aspirates. At times it was difficult for the clinicians to rule out active TB disease especially in the very young children who they said they mostly presented with non-specific signs and symptoms. The providers also pointed out the difficulties with collecting specimens in children under-five such that they ended up opting for alternative screening tests that were not diagnostic in children.

"… people are not comfortable dealing with children under six months. The screening itself is a problem. You know you end up with a child presenting with non-specific signs and symptoms that needs probably a paediatrician to try and determine whether it's TB or there is something else that is wrong with the child [uhum]. A child who comes in and not gaining weight for example being a contact of a TB patient, that child presents a challenge if we do a chest x-ray and we don't find any lesions consistent with tuberculosis." [CS, Facility A]

"I think maybe it's because of the difficulty in getting a sputum sample from the kids especially getting gastric washings to send for TB microscopy. It's quite difficult… So

sometimes we end up using a chest x-ray though it's not really diagnostic but that's what we usually have." [CS, Facility B]

Staff shortages

Lack of adequate staff was also raised as a barrier to implementation of the guidelines by the providers. Most healthcare providers stated that their facilities were understaffed or had recently undergone staff reduction. In such circumstances, the facilities would have one or two providers working in multiple departments at the same time resulting in them not spending enough time with the TB patients due to high workload. The researcher also observed that some of the facilities had one TB trained healthcare provider working in the TB unit who was also the TB focal person.

"The staff coverage has been reviewed downwards instead of upwards. If we consider other competing programmes at the facility it's difficult to balance the workload. You can have two nurses working in multiple departments; one will be consulting and the other doing the injections, laboratory tests, wound dressings, TB clinic and dispensary. They both won't have enough time with the TB clients - to collect the sputum, to give the TB health education and to initiate the children on IPT. So, it's a lot of work for them. They won't cope." [CS, Facility C]

"The healthcare providers that we have are not enough. Basically we don't have enough doctors and nurses to diagnose and manage childhood TB cases [okay]. There are a lot of issues, we find that our staff coverage was made long back in the 1980s and the demand for clinicians with TB training is now higher [okay]…" [OHP, Facility A]

Poor follow up and monitoring of children initiated on IPT

Healthcare providers expressed that one of the barriers to implementing the guidelines was poor follow up and monitoring of under-five children on IPT. The providers reported that they hardly receive any feedback from primary caregivers, community health workers and environmental health technicians with regards to adverse drug reactions and tolerability of the drug for the children initiated on IPT compared to adult patients on IPT. The healthcare providers proceeded to highlight that some of the facilities had no transport or functional telephones to contact the caregivers to bring their under-five contacts to the clinics. For those facilities that had cell phones the clinicians reported that the airtime allocation was not

enough to do TB contact tracing and the little they receive is usually reserved for maternity emergencies.

"*…then the challenge with under-fives like I said you really don't get enough information from the clinicians. Maybe because these are kids. We have not received any under-fives' adverse drug reaction reports [okay]. I've only been receiving the adult ones for IPT so, it's difficult to know what will be happening to the children on IPT."* [OHP, Facility A]

"...but we don't even have the phone [okay]. The landline is not working since December 2018 and the cell phone at times we are given ZWL 200 (USD$ 2.00 equivalent) for a month. Most of the time we reserve the airtime for the maternity patients... Sometimes you can just follow the TB patient to come and get their medication, but it will be very difficult to follow them up so that they bring their children." [CS, Facility C]

3.5 Facilitators of implementation of IPT guidelines

The facilitators of implementation of IPT guidelines for under-five children that are household contacts of TB cases were also identified in the same themes. These themes were role of opinion of leaders, providers' attitude towards IPT, experiences with caregivers and facility factors influencing implementation of the IPT guidelines.

3.5.1 Role of opinion leaders

Under this theme the researcher explored how peer opinion leaders influence had a positive impact on healthcare providers' decision to implement the IPT guidelines.

Positive influence

Healthcare providers highlighted that at times opinion leaders positively influenced them to implement the guidelines. They encouraged and supported staff members to use the guidelines as well as, help spread information on the importance of using the IPT guidelines to reduce burden of TB morbidity in children.

"... in this facility the opinion leader is very influential... Most of the times she does encourage her colleagues in a very positive way to use the IPT guidelines [okay]. I have

never had any problems with her influencing other colleagues in a bad way. Every time, it's always in a positive way." [CS, Facility B]

"The opinion leaders play a major role uhm because without them really the programme would fall out of place. So, they usually give influential decisions that help promote the IPT programme… They help with educating us on IPT, getting us TB supplies and organising transport in the event we want to do home visits." [FCP, Facility B]

3.5.2 Providers' attitude towards IPT

The researcher under this theme explored healthcare providers commitment to implement the guidelines and their perception that the guidelines were easy to use.

Providers' commitment to use IPT guidelines

Some healthcare providers mentioned that they were committed to using the IPT guidelines as the intervention had been scientifically proven to be beneficial to under-five children. Some of the providers cited the need to prevent TB disease in children under-five as motivator for them to use the guidelines. Other clinicians expressed that it did not sit well with their conscience to see young children being treated for TB disease.

"I'm quite committed to giving IPT to those below the age of five. It's really not the ideal situation to get an under-five coming in two months later with TB disease when you have diagnosed sputum positive in an adult. It shows that you are not doing your work right [uhum]. So, really I'm quite motivated. I know IPT works and yeah (I am) quite supportive of the programme." [CS, Facility A]

"Okay, you know as a health worker to just send these children without IPT when you know that they are going to benefit and that they are going to be prevented from getting infected with TB, you just feel guilty. Your guilty conscience just kicks in because you just need those children to be helped [uhum]. I think that's the one reason that motivates me. It will be something which is not good [uhum] if they now come back with active TB when they could have benefited from IPT." [FCP, Facility A]

Guidelines easy to use

Healthcare providers in some facilities also stated that they were motivated to use the IPT guidelines because they found the guidelines easy to use. The providers mentioned that the steps involved in implementation of the IPT guidelines were easy to understand and straight forward. However, the researcher observed that the healthcare providers in these facilities were using soft copies of the outdated 2010 Zimbabwe National TB guidelines.

"I don't have any problems with the guidelines. They are quite easy to use [uhum], and straightforward." [FCP, Facility A]

"The guidelines are not very difficult to follow because they are simple, clear and straight forward." [FCP, Facility D]

3.5.3 Experiences with caregivers

Under this theme the researcher explored some of the positive experiences that healthcare providers had with primary caregivers of under-five children that enabled implementation of the guidelines. The theme explored was caregivers' willingness to have their eligible children under-five be initiated on TB preventive treatment.

Caregiver willingness

According to the healthcare providers, some primary caregivers of the under-five children were willing to have their children on IPT. They were very appreciative of the intervention and were determined not to have their child progress to active TB disease. At times some of the parents even took the initiative to ask the providers if their children could be put on TB preventive treatment.

"Aah so far I haven't met any difficulties. Rather the parents are so happy to hear that there is something that can be given to their children, to the young ones to prevent them from getting infected. Yeah, they are so happy..." [CS, Facility A]

"...so, with most mothers on TB treatment. Some of them they come and actually ask you of their close contacts or their young ones [uhum] if there is anything that they can get to

protect them from getting TB. Some of them are proactive in having them get the IPT." [CS, Facility B]

3.5.4 Facility factors influencing implementation of the IPT guidelines

The researcher explored facility practices that enabled implementation of the IPT guidelines by healthcare providers. This included access to meetings and training workshops on childhood TB, availability of drugs and role of partner organizations.

Access to meetings and training workshops on childhood TB

Healthcare providers in some of the facilities indicated that workshops, TB quarterly review meetings, staff meetings as well as, feedback meetings from other work colleagues who had attended TB training workshops provided opportunities for them to receive latest information on the IPT guidelines. This made them stay abreast with changes in the guidelines. In the event of facing difficulties with implementing the guidelines the providers expressed that they were comfortable with consulting their peers and supervisors.

"Usually we go for workshops [okay] yes that is where we are taught about the new guidelines." [FCP, Facility C]

"Sometimes we go for workshops to get acclimatised with the latest IPT standards that are prevailing. We also have feedback meetings as well. Those of us who have attended some refresher courses inform the other staff members…" [FCP, Facility A]

Availability of drugs

Healthcare providers highlighted that it was easy for them to implement the IPT guidelines in their facilities as the drugs were always available. The providers mentioned that INH was given for free to the eligible children and that, they always ensured that they had enough stock before commencing a child on IPT to avoid interrupting treatment.

"In terms of drugs, the IPT is always available. TB drugs are always available and TB treatment is free so patients can always come in." [CS, Facility B]

"…we have tried to make sure that as soon as someone is started on IPT the nurses have the full six months stock separately reserved for the patient [okay] so that, we don't interrupt their treatment." [OHP, Facility A]

Role of partner organizations

Partner organizations were mentioned by healthcare providers to have played a significant role in promoting implementation of the IPT guidelines for under-five children. The partner organizations were said to have assisted the facilities by training staff members to conduct TB screening tests in children, accessing information on the updates of the IPT guidelines through workshops, providing support and supervision and offering incentives to continue motivating the healthcare providers.

"Recently I am glad that we have some partners and organisations like Elizabeth Glassier Paediatric Foundation (EGPAF). They took it up to strictly monitor the under-fives so that we screen them. Most of us health care workers, we didn't know how to screen these children. However, from their intervention and from the workshops they have held I think it has come to our sense now that we have to be vigilant with the children because we were treating most of them as ARI (acute respiratory infections) yet it's actually TB. The support we have had from the workshops hosted by the partners, I think health care workers are aware now to screen every eligible child under-five." [CS, Facility A]

"I can say that this facility is also supported by a partner organisation. The organisation supports uuh maternal and child health care. So when they come they also incorporate childhood TB management. They motivate us because they give us some incentives. After an assessment, they look at our quality of care and they will give us an incentive of 25% of what we get from the whole assessment." [CS, Facility D]

3.6 Use of the shorter TB preventive therapy regimens

Under this theme the researcher explored healthcare providers perception towards the use of a shorter TB preventive therapy regimen. The aim was to explore the impact that a three months short course of Isoniazid and Rifapentine (3HP) would have on implementation of the IPT guidelines for under-five children by the healthcare providers. 3HP is a 12-week course of weekly Isoniazid and Rifapentine which has been shown to be efficacious in the treatment

of latent TB infection (53,73). The Zimbabwe Ministry of Health and Child care is planning on conducting a national roll-out of 3HP soon in health facilities offering TB services. The advantages and disadvantages of a using a shorter TB preventive therapy regimen with regards to implementation of the IPT guidelines were explored.

Advantages of a shorter TB preventive therapy regimen

Most providers said they would be happy to use a shorter TB preventive therapy regimen. They mentioned that it would improve adherence, reduce duration of treatment and pill burden. A shorter regimen would be most favoured by both primary caregivers, their under-five children as well as the providers as it would reduce the number of clinic visits of the child on preventive treatment and also reduce the clinicians' workload.

"I think this is quite a good move because we are saying 6 months of prophylaxis is quite long. There are issues to do with adherence. You know with children giving them medication it can be quite a headache. So, reducing it to 3 months will actually improve compliance and adherence..." [CS, Facility A]

"...it's okay since we were giving the children a review date of three months. So, it will be only a once-off thing now which is quite good for us the clinicians in terms of workload… Suspension is good [uhum] especially for the young ones. You know the tablet is difficult to give the child. That's what I was also saying about the pill burden but, if we have got a suspension [uhum] I think it will be good for the children." [FCP, Facility D]

Disadvantages of a shorter TB preventive therapy regimen

Some providers were worried about facility readiness to implement a shorter TB preventive therapy regimen. They cited that the problems encountered with use of INH such as lack of adequate information on paediatric TB guidelines and having adequate drug stocks to supply every eligible child may still be experienced by clinicians when the shorter TB preventive therapy was introduced.

"...right now we might be saying let's move to the 3HP but I don't know if that decision to move to 3HP is informed by any reports because if we don't have any reports then there is no need for us to move to 3HP unless there are other reasons. Why? because when it comes to

cost benefit analysis that's really not, not a good idea. If we are going to have the best effect out of the minimum that we have then we would rather maintain the current regimen unless there are other reports that we don't really know off. From my end based on the current paediatric guidelines we still need to do more when it comes to the paeds before we can change the regimen." [OHP, Facility A]

"The only disadvantage that we might face [uhum] I'm not sure if we are ready as a country, [uhum] if we have enough stock for rifapentine... The issue of drug availability. Is it going to be available widely [uhum] such that, we don't have interruptions in treatment to say this month it's available and next month it's not there so, that's the main challenge we might face and that's our fear." [CS, Facility B]

"*Changing the regimen is okay but, we may continue having these same shortfalls like underperformance and poor coverage of TB preventive treatment if we don't address these issues first."* [OHP, Facility D]

Chapter 4: Discussion

The purpose of this study was to explore the barriers to and facilitators of implementation of isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe. The emergent themes in this study were: role of opinion leaders, providers' attitude towards IPT, experiences with caregivers, facility factors influencing implementation of IPT guidelines and use of shorter TB preventive therapy regimens. The CFIR guided the exploration of the barriers to and facilitators of implementation of IPT guidelines for under-five child contacts of TB cases in this study. The definitions of the CFIR domains were modified to suit the context of the study and its findings (63,74). Previous studies have supported the flexible nature of the CFIR and how it can be tailored to suit design and context of specific health interventions (3,59,63).

4.1 Barriers to implementation of IPT guidelines

4.1.1 Role of peer opinion leaders

In this study, peer opinion leaders were found to negatively influence other healthcare providers from implementing the IPT guidelines for under-five children because they were doubtful of the benefits of IPT in children. This is similar to the findings of a study conducted in South Africa, which reported that hostility of opinion leaders to the use of IPT in children had a significant negative impact on other providers who became resistant and reluctant to implement the guidelines (41). Negative actions from influential peers have also been reported in malaria over-diagnosis by healthcare workers in Malawi (43).

4.1.2 Providers' attitude towards IPT

Consistent with findings of other studies (26,41,75), our study identified that some providers had a negative attitude towards implementing the IPT guidelines because of IPT knowledge deficit and fear of side effects. This is despite previous studies showing a negligible side effect profile in children on IPT (76–78). Lack of knowledge of the IPT guidelines and fear of being blamed for causing unnecessary adverse events to under-five children on IPT has also been reported by healthcare providers in India (75). In contrast to studies that have found healthcare providers' pleasant personality as a facilitator of implementation of health interventions (67,79), our study found that a clinicians' negative personality trait could deter implementation of the IPT guidelines. This is because the providers had challenges with

establishing effective communication with TB patients resulting in them failing to enquire about the patients' household circumstances with regards to having children under-five years.

4.1.3 Experiences with caregivers

In this study, primary caregivers of under-five children were reported by healthcare providers to be unwilling to have their children on IPT because of fear of side effects, drug resistance as well as, misconception of the benefits of treatment of LTBI in children. Previous studies have reported that most caregivers believe that if their child is given monotherapy for perceived, "TB" it may induce side effects and drug resistance (26,28,33,38). Furthermore, many caregivers have a strong belief that, "no symptoms suggests, no treatment" (26,80) because of the low-risk perception of progression of TB disease in children (26,81,82).

Our study found that IPT services for under-five children were primarily facility based, this created a transport cost burden on caregivers who had to travel long distances with their children for screening and IPT initiation. This created an implementation challenge to healthcare providers as most caregivers did not have the financial capacity to access healthcare facilities. Similar findings have been reported in Malawi and Timor-Leste, were low uptake of IPT in children was attributed to high transport cost incurred by caregivers in trying to get their children to the facilities for screening and IPT initiation (82,83).

The finding that some conservative religious groups forbid their congregants from seeking formal healthcare for their under-five children, replicates findings from studies that have reported that some conventional denominations use church doctrine to forbid their members from seeking medical treatment for their children who may be at risk of developing life threatening illnesses (84,85). Likewise, under-five mortality in Zimbabwe has been reported to be significantly higher amongst children belonging to conservative faith groups compared to those from liberal religions (85).

4.1.4 Facility factors influencing implementation

In this study, it emerged that healthcare providers failed to implement the IPT guidelines because they had no access to hardcopies of the guidelines and faced challenges with accessing electronic copies on their mobile devices. This is similar to a report from the WHO

that identified lack of guidelines as a barrier to IPT delivery in under-five children (51). Lack of access to TB guidelines has also been reported by healthcare providers in India (75).

Most NTPs, Zimbabwe included prioritise IPT in adults and people living with HIV compared to under-five children (6,11). Likewise, our study identified that IPT in under-five children was not prioritised and had been surpassed by other competing programmes being implemented within the facilities like TB in adults and HIV. Non-prioritization of childhood IPT has resulted in some facilities failing to access the WHO recommended TB screening tools (41). This is consistent with our study findings that providers failed to implement the guidelines because of lack of screening tools required to exclude active TB disease. Health workers in Malawi have also reported of the challenges they face with ruling out TB disease in under-five children because of lack of screening tools such as Mantoux test and chest x-ray (83). In comparison, studies in India and Botswana have reported challenges with ruling out TB diagnosis in the very young children because of overlap in symptomatology with other childhood infections (34,81). Challenges with ruling out TB disease in infants because of the non-specific signs and symptoms were also highlighted by healthcare providers in this study.

Healthcare facilities in this study were found to be under-staffed, this resulted in the providers failing to screen and initiate children under-five on IPT because of time constraints and increased workload. This is identical to studies that have reported time constraints and increased workload due to staff shortages as a barrier to healthcare providers initiating under-five children on IPT (34,41).

Our study identified that poor transport and communication infrastructure resulted in inadequate feedback reports and poor follow up and monitoring of under-five children initiated on IPT. This resulted in poor implementation of the guidelines as the providers neither had means of contact tracing the children nor information to determine how the children on IPT were faring. There are some low income countries with poor network and communication infrastructure that have successfully adopted and implemented mobile-health (m-health) as a means of improving communication to people in need of health services (86–89). However, Zimbabwe has been reported to be in its very early stages of developing m-health services. M-health is an electronic health component that is cost-effective and allows healthcare providers to offer health services and information via mobile technologies such as mobile phones, tablets and computers (89). Successful m-health implementation initiatives

have been reported in Chivi District in Zimbabwe an area with poor network infrastructure. This has served to highlight the feasibility of using m-health services to improve healthcare in Zimbabwe (87,90) .

4.2 Facilitators of implementation of IPT guidelines

4.2.1 Role of peer opinion leaders

Similar to other studies, our study also found a few implementation drivers of IPT guidelines for under-five child contacts of TB cases (40,50,79). Consistent with studies that have reported that peer opinion leaders can positively influence the behaviours and attitudes of other staff members to implement health interventions (43,91). Our study found that in some facilities, peer opinion leaders promoted implementation of IPT guidelines because of the encouragement and support they gave to providers working in TB units. Positive influencing opinion leaders have been used as change agents in Malawi and London to help change the attitudes and behaviours of other health workers (43,91).

4.2.2 Providers' attitudes towards IPT

This study identified that healthcare providers were committed to using the IPT guidelines because they wanted to help reduce TB burden in under-five children and they also found the guidelines easy to use. This is similar to a South African study that reported high level of commitment to end TB morbidity amongst healthcare professionals offering TB services despite the health system challenges they faced (79). Healthcare providers in Ethiopia have also reported that guidelines that were easy to understand were an implementation driver of a programme aimed at reducing HIV-related stigma in healthcare facilities (92).

4.2.3 Experiences with caregivers

Previous studies in Sub-Saharan Africa have reported caregivers' willingness and commitment to have their under-five children on TB preventive treatment, a solid foundation for successful implementation of IPT guidelines (79,93). Similarly in our study, some caregivers facilitated implementation of the guidelines because they were willing to have their under-five children initiated on IPT to prevent them from developing active TB disease. A strong association between successful implementation of IPT guidelines and caregivers' commitment to have their children treated for LTBI has also been identified in Rwanda and Indonesia (15,94,95).

4.2.4 Facility factors influencing implementation

In this study, healthcare providers in some facilities were implementing IPT guidelines because they were up to date with changes in the guidelines and had opportunities to discuss and solve problems encountered in implementing the guidelines from the regular workshops they attended. Regular meetings have been reported to be an important communication platform for problem-solving, making decisions, coordinating information and morale building (50). Whereas previous studies have reported drug shortages as a barrier to implementation of IPT guidelines (9,26,34,35), our study found that INH was readily available in the facilities and was offered free of charge.

Partner organisations were found to play a significant role in supporting some facilities with implementation of the IPT guidelines in this study. The partner organisations trained providers to screen children and provided financial support to help facilities sustain childhood TB programmes. The WHO has emphasized on the importance of health facilities collaborating with partner organizations to help with scale up and sustainability of health programmes (96,97). Partner organisations have been reported to be catalysts for change that would otherwise not have happened in implementation of health interventions by offering technical support and ensuring fidelity of health interventions (97–99).

4.3 Use of the shorter TB preventive therapy regimens

Our study also explored healthcare providers' perceptions towards the use of a shorter TB preventive therapy regimen. The purpose was to find out if providers considered use of three months short course of Isoniazid and Rifapentine (3HP) in under-five children a barrier or facilitator to implementation of the IPT guidelines. Some providers perceived the use of 3HP a barrier to implementation of the IPT guidelines because of unavailability of information on childhood TB to inform the change of regimen as well as, non-readiness of facilities to switch to 3HP due to non-resolution of current implementation challenges. Our findings are similar to studies conducted in TB endemic regions that have reported lack of substantial evidence to determine whether use of a shorter TB preventive therapy regimens will result in improved implementation of TB preventive therapy guidelines (56,57). Furthermore, National TB programmes of TB endemic countries have been urged to resolve implementation challenges in current TB preventive therapy regimes before introducing new treatments (56,100).

Consistent with our study findings, a shorter TB preventive therapy regimen has been reported to be popular with caregivers and children because of its shorter duration and the fact that it comes in a child-friendly fixed dose formulation (57,101). In this study, use of 3HP was perceived to be an implementation driver of the IPT guidelines because it would be favoured by health workers, primary caregivers and their children under-five years. Similar studies by Marais (9,102) have reported that shorter TB preventive therapy regimens provide an excellent opportunity to revive TB preventive therapy programmes and help enhance adherence.

4.4 Limitations

The findings of this study may not be generalizable to other healthcare providers implementing IPT guidelines for under-five child contacts of TB cases in private, government or rural institutions as well as, caregivers of under-five children. This study was conducted on healthcare workers working at the main TB facilities in Harare the capital city of Zimbabwe. It is possible that some issues raised by the participants may only be unique to their contexts and not be similar to what other healthcare providers in the former settings were experiencing. However, the study findings will be relevant for use by the Zimbabwe MOHCC, Zimbabwe NTP, IPT programme managers and facilities to come up with strategies to promote successful implementation of the IPT guidelines.

This study did not include caregivers of under-five children who were eligible for IPT. The views reported under the theme experiences with caregivers were based on the healthcare providers interactions with caregivers of the under-five children. The researcher acknowledges the possibility of bias as the reported experiences may be subjective or not be representative of all the opinions of caregivers of under-five children. However, for this study healthcare providers were selected as they provided an expert perspective based on their multiple experiences and interactions with the caregivers. A qualitative study that explores the opinions of both providers and end users with respect to implementation of IPT guidelines needs to be conducted in Zimbabwe.

4.5 Strengths

This study is one of the few qualitative implementation research studies conducted in Zimbabwe that has sought to explore factors influencing implementation of IPT guidelines of under-five child contacts of TB cases from the perspective of healthcare providers. Most studies have either explored factors influencing the implementation of IPT guidelines from the end users perspective or used quantitative methods. In addition, qualitative study methods have been shown to be essential in exploring implementation practices of healthcare interventions in developed countries (103,104). However, very few such studies have been done in developing countries such as Zimbabwe.

The study was conducted on providers working at the main TB tertiary facilities who were actually involved in the implementation process. This meant the data collected were based on the providers' first-hand experiences. This is in contrast with selecting participants from peripheral health centres where there was a possibility of getting inadequate information. Some of the peripheral facilities where child TB services were decentralised too were not implementing the IPT programme and were still referring children under-five to the tertiary centres. Our study was guided by the CFIR, a conceptual framework which has been used in implementation research to identify factors influencing implementation of innovations (59,62,105). The adaptations made to the CFIR for this study are generalizable to any study assessing implementation of complex healthcare interventions (74). This helped to increase relevance and validity of the study and it's findings as well as, support the feasibility of using and adapting theoretical frameworks in implementation research (106).

Chapter 5: Conclusion and Recommendations

5.1 Conclusion

This study used the CFIR to identify barriers to and facilitators of implementation of IPT guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe. The barriers to implementation included negative influence by peer opinion leaders, providers' lack of knowledge and fear of side effects as well as, their other negative personality traits, caregivers' reluctance to have their children on IPT, challenges with transport costs and access to health facilities and caregivers' religious beliefs. The study also identified facility factors such as: no access to hardcopies of IPT guidelines, non-prioritisation of the intervention, lack of screening tools, staff shortages, challenges with screening children and poor monitoring and follow up of children on IPT. The main barriers to implementation were related to facility practices influencing implementation of IPT guidelines.

Facilitators of implementation identified included positive influence from opinion leaders, commitment of providers to use the guidelines and non-complexity of the guidelines. Caregivers willingness to have their children on IPT, access to training workshops on childhood IPT, availability of INH in health facilities and support from partner organisations were also some of the identified drivers of implementation. Facility factors influencing implementation also emerged as the main facilitators of implementation of the IPT guidelines by healthcare providers. With regards to use of shorter TB preventive therapy regimens, the healthcare providers had mixed opinions with some providers perceiving use of 3HP as a barrier to implementation of IPT guidelines whilst others saw 3HP as a potential implementation driver.

In conclusion, the primary factors influencing implementation of IPT guidelines for under-five child contacts of TB cases amongst healthcare providers were related to practices within the facilities. The study identified more barriers to implementation of IPT guidelines than facilitators. The Zimbabwe NTP is currently faced with multiple implementation challenges with regards to coverage and uptake of childhood IPT. The projected 100% target for childhood IPT coverage may not be achievable if these implementation challenges are not addressed urgently.

5.2 Recommendations

5.2.1 Policy related

Our study identified that religion had a significant impact in influencing caregivers' health seeking behaviour for their children. Caregivers from conservative religious sects were less likely to accept IPT for their under-five children. TB policy makers should engage with leaders of religious groups so that, they get their buy in to promote IPT uptake in children under-five. This study found that childhood TB programmes were not prioritised as much as adult TB and HIV in health facilities, yet children are at an increased risk of severe TB disease and mortality. There is an urgent need for policy makers to prioritise childhood TB by conducting TB refresher training workshops and ensuring that up-to-date guidelines are accessible to the healthcare providers. Our study also found that there was poor contact tracing, follow up and monitoring of children eligible for IPT by healthcare providers because of telecommunication challenges. The Zimbabwe NTP can adopt and implement m-health services in health facilities to enable under-five children eligible for IPT better access to TB services. Partner organisations were identified to be an important driver of implementation of IPT guidelines for children under-five therefore, the Zimbabwe NTP should continue to engage with more partner organisations that can support health facilities offering TB services to increase IPT uptake in children.

5.2.2 Service delivery related

This study found that only the TB nurse was responsible for IPT and in their absence none of the other healthcare providers in the facility would provide the service. Healthcare providers at all levels of care should be trained on the safety and efficacy of IPT in children under-five to demystify IPT misconceptions amongst the providers. Provision of IPT should neither be the sole responsibility of the clinician working in the TB outpatient department nor the TB focal person. Additionally, nurse managers should ensure that the guidelines are put up on wall charts in every department within the facilities so that, they are easily accessible to every provider. We also identified that in some health facilities there were no screening tools to enable providers to rule out active TB disease in children and determine those eligible for IPT. We recommend that such facilities adopt and use the WHO symptom-based screening tool to screen children for TB. Our study also found that caregivers of children under-five were reluctant to have their children on IPT as they were not aware of the severity of LTBI in children. Health facilities should provide more health education programmes to caregivers of

under-five children about severity of TB and the urgent need to treat LTBI in children. This can be done at either facility level by health promoters or in the community-by-community health workers.

Research implications

This study found factors influencing implementation from the perspective of healthcare providers. Our study findings will help inform TB programme managers, staff within facilities and other stakeholders to come up with effective implementation strategies that can be used to scale up IPT uptake in eligible children under-five. However, this study did not explore caregivers' personal opinions with regards to TB preventive treatment for their children. There is an urgent need to conduct research that will explore opinions from both providers and caregivers in order to ensure success in TB programmes. Our study also highlighted the importance of use of shorter TB preventive therapy regimens as a driver to implementation of TB preventive treatment in children under-five. There is need for further studies to explore organisational readiness of the Zimbabwe NTP and health facilities offering TB services to roll out and implement shorter TB preventive therapy regimens

5.3 Funding

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5.4 Conflict of interest

The researcher declares no conflict of interest in this study. The contents of this research report are independent views and opinions of the study participants. They neither reflect the views of the researcher nor those of the funding body WHO-TDR. The funders and Harare City Health Department had no role in design of the study, data collection, analysis and interpretation. This was the sole responsibility of the researcher.

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Appendices

Appendix 1: Plagiarism Declaration

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FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Nyasha Veronica Dzavakwa (Student number: 2185595) am a student registered for the degree of MSc Epidemiology-Implementation Science in the academic year 2019.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
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Appendix 3: The original CFIR framework

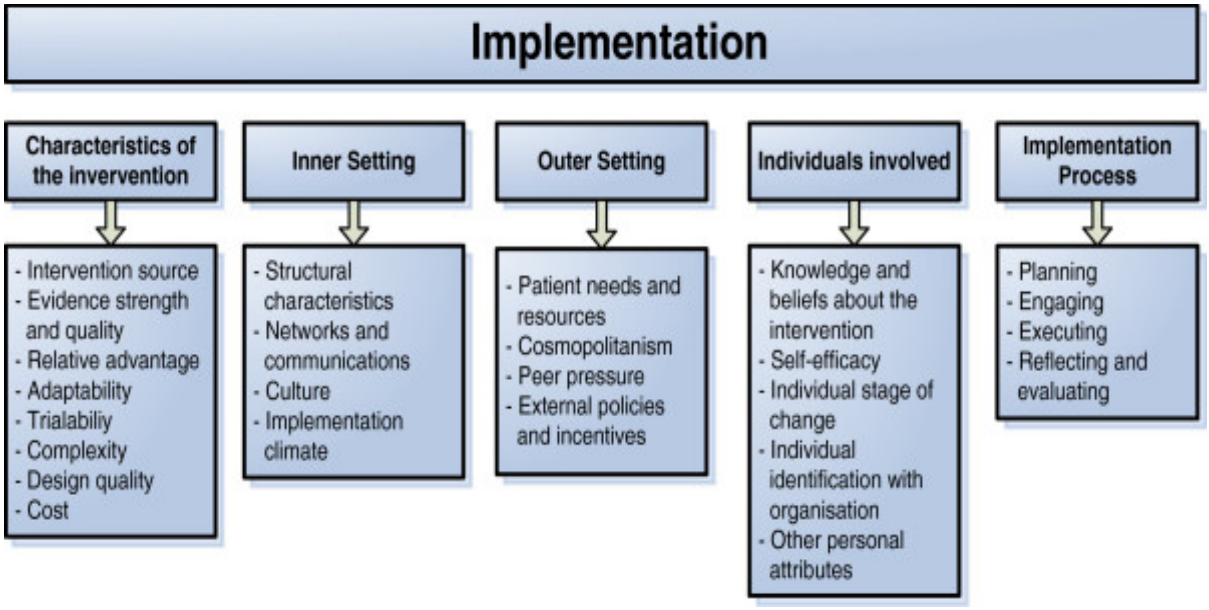


Figure 2: Original CFIR framework from Damschroder et al. 2009

Appendix 4: Definition of the CFIR domains

CFIR Domain	Definition	Application in this study
Intervention Characteristics	Key characteristics of the evidence based intervention that influence its implementation success	Describes the characteristics of IPT guidelines for children under-five years with positive TB contacts with regards to how easy/difficult they are to use. Also explores how healthcare providers perceive the use of shorter TB preventive therapy regimens.
Outer Setting	The economic, political, and social environment within which the implementing organization is set up.	This explores health care providers' experiences with caregivers when they recommend IPT to eligible children under-five. Caregiver's knowledge, attitude, socioeconomic status, cultural and religious beliefs were identified from the providers' perspective.
Inner Setting	Structural, political and cultural contexts within the organization that may influence the implementation process	Practices at the two facilities that deter or enable implementation of IPT guidelines such as learning climate, facility-based incentives and feedback on work performance.
Characteristics of Individuals	Knowledge, attitudes and behaviours of the people involved in implementing the intervention.	Healthcare providers' knowledge and attitudes in implementing the IPT guidelines as well as their perceptions on newer regimens
Implementation Process	Processes and strategies that occur at different levels in the organization that may influence implementation of the intervention.	Explores how peer opinion leaders influence other providers to implement IPT guidelines in the facilities. Peer opinion leaders are healthcare providers or peers who everyone in the TB unit looks up to and is capable of influencing other providers' decisions to implement the IPT guidelines. Supervisors or clinic managers are not included in this definition

Appendix 5: Screenshot example of charting

Documents and variables	Experiences with caregivers	Negative experiences	Positive experiences
Interview transcripts\PS 01 Document name: PS 01 Role in implementation of IPT guidelines : TB focal person Facility name: Facility A		providers do not know how impt IPT is,various beliefs about side effects and that they are actually getting the infection, "Are they knowledgeable enough? Do do do do they [uhum] actually know how important that process is?...here are various myths and misconceptions [okay] about IPT...they actually believe probably they are being given TB, or they will react to the to the to the ...stammers… pre to the medication"	
Interview transcripts\PS 02 Document name: PS 02 Role in implementation of IPT guidelines : Sr in charge Facility name: Facility A		sometimes caregivers report that they failed to access the drug at their local clinics, some do not understand the importance of IPT, "But still some of the caregivers you know they don't understand [uhum] and they don't appreciate the importance of giving their children INH [okay]. They still lack education of why we give it" the duration of treatment is very long, caregivers present late to the facilities with theitr contacts, " because maybe they come after we diagnose a patient for uhm uhm uhm bacteriologically confirmed TB you find contacts after a month or two of which this child will be at risk [uhum} especially the under-five" transport costs, "because yeah we central but if you think of someone coming from Area 2 or somewhere like Area 3 whatever to come here if there was another point where there was an x-ray machine which is nearer to them [uhum] then it would be better [okay] than for them to come to this	caregivers appreciate the intervention; not willing to have their children to get TB disease, "my experience with the caregivers is that uuh they really, really do appreciate if you explain to them and tell them that you are giving your child prophylaxis. They are afraid of their children getting TB so they, really do appreciate and they usually welcome it. I have never had an experience where the mother refuses eeh to have their child put on prophylaxis."

Appendix 6: Study information sheet



STUDY INFORMATION DOCUMENT

Study title: ***Barriers to and Facilitators of implementation of isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe.***

Dear Prospective Participant

My name is Dr. Nyasha Veronica Dzavakwa. I am doing a research to identify factors that influence health care providers at facilities providing tuberculosis (TB) care in Harare, to use Isoniazid preventive therapy guidelines for children under-five years that are household contacts of TB cases (people diagnosed with tuberculosis disease). Research is a process used in finding new knowledge.

In this study I want to learn the barriers and facilitators health care workers face when trying to implement Isoniazid preventive therapy (IPT) guidelines for under-five children who are living with bacteriologically confirmed TB cases. Tuberculosis is amongst the top causes of under-five morbidity and mortality. The 2018 Global TB report revealed that in 2017 1.3 million children under-five years were household contacts of bacteriologically confirmed TB cases and thus eligible for preventive treatment however, only 23% were commenced on TB preventive therapy. In 2017 the Zimbabwe National TB programme reported that 24% of eligible children under five years had been initiated on Isoniazid preventive therapy which was below their 100% target. With TB causing such a significant health burden in children younger than five years and the failure to meet the 100% target with TB preventive therapy. It is of utmost importance to conduct a study such as this one to explore reasons why Isoniazid preventive therapy guidelines aren't being implemented in health facilities. The findings of this study will help inform policy makers and the Zimbabwe National TB Programme to come up with effective implementation strategies that can be used to increase uptake and coverage of Isoniazid preventive therapy.

Invitation to Participate: I would like to invite you to take part in this study:

1. Involve conducting interviews on health care providers working in TB care.
2. Interviews will take place between December 2019 and February 2020.
3. Interviews will be conducted in English and participants will be expected to answer interview questions on factors influencing implementation of IPT guidelines for under-five children that are household contacts of TB cases.

4. Interviews will be conducted at the health facilities the participants are working, they will take approximately 45 to 60 minutes and will be digitally recorded using a portable audio recorder
5. Pseudonyms will be used, and all personal identifiers will be removed during the interviews and analysis. No one will be able to identify you.
6. All study information will be kept in a password protected cloud storage on a password protected computer which will be accessible to the researcher and her supervisors only.
7. All audio recordings will be kept in a password protected cloud storage on a password protected computer for a maximum of 2 years and will be discarded thereafter.
8. Findings of this study will be shared with the study participants

Risks of being involved in the study: **There are no risks to you caused by participating in this study.**

Benefits of being in the study: There is no direct benefit to you as a potential participant. However, the information that you provide will be used to come up with ways of improving health outcomes for children under five years. It will also help to improve your facility's implementation of the IPT guidelines for under-five at risk children.

Participants will be given any relevant or important information on the study while involved in the project and after the results are available.

Participation is voluntary.

Refusal to participate will involve **no** penalty or loss of any benefits to which the participant is otherwise entitled. The study will be explained in more detail during the consent process. However, even if a participant decides to provide consent, they can withdraw this consent at any time if they do not want to continue and the interview will be stopped immediately. Participation will be discontinued without **any** negative consequences, penalty, or loss of any benefits to which the Participant is otherwise entitled. A participant does not have to give a reason for withdrawing from the study. Any information collected will not be used and will be destroyed unless the participant gives consent to use the information.

There is no re-imbursement as no out-of-pocket costs are anticipated for the participant.

Confidentiality: Personal information will be treated in the strictest confidence and will only be available to myself and my Supervisor unless:

- If required by law - Personal information may be disclosed
- the Human Research Ethics Committees of the University may exceptionally require personal data to respond to a formal complaint, or for a compliance audit

All data collected in the course of the study will be securely retained for two (2) years, if a scientific publication arises from the study and six (6) years, if there is no publication. Thereafter it will be destroyed accordingly.

Anonymity: Your name will not be recorded in the interviews, interview transcripts and will not be shared with anyone. All information that could identify you will be removed before the data is analysed.

Contact details of researcher/s: email: nyashadzavakwa@gmail.com cell: +263 773 659 363

Outputs

The expected output of the study is a master's thesis that will compile the information received from the different interviews as well as the analysis of all the data collected. I will share these findings with all participants at a single group feedback session (date to be advised).

Contact details of HREC administrator and chair. Please see the information below to contact the WITS Human Research Ethics Committee if you would like to report any complaints or problems.

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Study Information Sheet.

Appendix 6: Consent forms

WITS UNIVERSITY

PARTICIPANT CONSENT SHEET

Project Title

Barriers to and Facilitators of implementation of isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe.

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached hereto;
2. I was given time to read it, or had it read to me, in the language I best understand;
3. I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory;
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be;
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time;
6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained
7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study I am free to speak to any of these contacts.

Contact details:

Dr Nyasha Veronica Dzavakwa, Principal Investigator, telephone no. +263 773 659 363, or by e-mail at nyashadzavakwa@gmail.com,

Professor Latifat Ibisomi, Supervisor, on telephone no +27 117 172 607, or by e-mail at Latifat.Ibisomi@wits.ac.za

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.
Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____
Date: _____
Place: _____
Signature or mark _____

Witnessed by:
Name of Witness: _____
Signature: _____
Date: _____



CONSENT FORM FOR AUDIO RECORDING OF STUDY PARTICIPATION

Project Title

Barriers to and Facilitators of implementation of isoniazid preventive therapy guidelines of under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe.

I hereby consent to audio recording of the interview[1], or focus group discussion[1], or classroom interaction[1]
.
I understand that:

- The recording will be stored in a secure location (a locked cupboard or password protected computer) with restricted access to the researcher and the research supervisor.
- The recording will be transcribed and any information that could identify me will be removed,
- The recordings will be erased within either (a) two (2) years of the publication of the research findings, or (b) six (6) years, if no publications arise from this research
- Anyone wishing to access this information in the future will first have to obtain the approval of the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg
- Direct quotes from my interview, without any information that could identify me, may be cited in the research report or other write-ups of research.

Name of Participant: _____
Date: _____
Place: _____
Signature or mark _____

Witnessed by:
Name of Witness: _____
Signature: _____
Date: _____

Appendix 7: Interview guide

Participant study number

Age

Sex

Role in implementation of IPT in children under 5 years

Number of months/years in current role

1. Tell me what you know about IPT guidelines for children under-five years who are household contacts of TB cases?

Intervention characteristics

- Can you describe the steps involved when you are managing a child who is a household contact of a TB case?
    - Probe for number of steps involved in the implementation process
    - Complexity or ease of following the guidelines

Outer setting

- Can you describe your experiences with caregivers when you recommend IPT for their under-five at risk children?
    - Probe for:
        - Caregivers knowledge of isoniazid use in children that are household contacts of TB cases
        - Caregivers' attitude towards use of IPT e.g. fear of side effects, pill burden including cultural beliefs
        - Factors influencing health seeking behavior for the child e.g. cultural or religious beliefs, socio economic status

Inner setting

- Describe how you receive information on updates of IPT guidelines in children less than five in this facility?
    - Probe for frequency of staff meetings
    - Relationship with other work colleagues and management
    - Access to guidelines and new information on guidelines
    - Problem solving who is consulted

- Frequency of feedback reports on their work performance

- What motivates your facility to recommend/prescribe/dispense IPT to under-five child contacts of TB cases?
    - Probe for facility-based incentives
    - Supervisor/special recognitions
      Rewards for meeting set targets

- What challenges deter your facility from recommending/ prescribing/ dispensing IPT to under-five child contacts of TB cases?
    - Probe for consequences for not meeting facility set targets
    - Extent of prioritization of the intervention in comparison to other TB programmes running concurrently
    - Availability of TB screening tools for children e.g. Mantoux test, sputum collection, radiology machine
    - Availability of adequate staff

Characteristics of the individuals

- Can you please tell me how you feel about recommending IPT for children under five years who are contacts of TB cases?
    - Probe for confidence/experience with using the guidelines
    - Knowledge of IPT guidelines for children
    - Attitudes/beliefs towards use of IPT in children under-five

- What other treatment options are you aware of (or have you heard of)?
    - Probe for knowledge/awareness of shorter TB preventive therapy regimens such as 3 months short course Isoniazid and Rifapentine (3HP)
    - Probe for any advantages or disadvantages of options mentioned
- What is your opinion on the use of shorter TB preventive therapy regimens such as 3 months short course Isoniazid and Rifapentine (3HP) which will be soon rolled out by the Zimbabwe National TB Programme compared to INH?
  *3HP is a short course TB preventive therapy regimen that is due to be rolled out by the Zimbabwe NTP at the end of 2019 or beginning of 2020. It is a fixed dose

combination that is comprised of two drugs Isoniazid and Rifapentine and taken once daily for 3 months. It is reported that the government is also going to procure palatable paediatric formulations of the drug.*

- Probe for possible/perceived benefits of use of the 3HP over Isoniazid (INH) e.g. being a shorter regimen and a fixed dose combination, reducing staff workload, better adherence by caregivers and children, more palatable formulations
- Perceived disadvantages e.g. drug to drug interactions with some antiretroviral therapy drugs, higher procurement costs compared to INH

For Clinic managers (also add)

- What staff personal characteristics affect implementation of IPT guidelines for children under-five who are contacts of TB cases
    - Probe for positive personal characteristics e.g. self-motivation, competency in using guidelines, dedication to improve child health.
    - Probe for negative personal characteristics e.g. insubordination, demotivation due to lack of resources and health worker fatigue.

Process

To what extent do opinion leaders play a role in influencing your decision to use the IPT guidelines for children? (*an opinion leader is that work colleague who everyone in the unit looks up to and is capable of influencing your decision to use/not use the guidelines*)

Other

- Is there anything else you would like to add about use of IPT guidelines in children under-five who are household contacts of TB cases?

Appendix 8: Wits HREC ethics certificate

UNIVERSITY OF THE WITWATERSRAND

R14/49 Dr NV Dzavakwa

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M191060

NAME: (Principal Investigator)	Dr NV Dzavakwa
DEPARTMENT:	School of Public Health Medical School University
PROJECT TITLE:	Barriers to and facilitators of implementation of Isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe
DATE CONSIDERED:	2019/10/25
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor L Ibisomi
APPROVED BY:	Dr N Naran, Co-Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/01/09

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **October** and will therefore reports and re-certification will be due early in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

16/01/2020
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix 9: Zimbabwe Medical Research Council (MRCZ) ethics certificate

Telephone: 791792/791193
Telefax: (263) - 242 - 790715
E-mail: mrcz@mrcz.org.zw
Website: http://www.mrcz.org.zw

Medical Research Council of Zimbabwe
Josiah Tongogara / Mazowe Street
P. O. Box CY 573
Causeway
Harare

APPROVAL

MRCZ/B/1840 **10 January, 2020**

Dr Nyasha Veronica Dzavakwa
B3371 Gunhill
Chinhoyi

RE: - Barriers to and Facilitators of implementation of isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by healthcare providers in Harare, Zimbabwe

Thank you for the application for review of Research Activity that you submitted to the Medical Research Council of Zimbabwe (MRCZ). Please be advised that the Medical Research Council of Zimbabwe has **reviewed** and **approved** your application to conduct the above titled study.

This approval is based on the review and approval of the following documents that were submitted to MRCZ for review: -

1. Completed MRCZ 101 new application form
2. Study protocol
3. Data collection tools

- **APPROVAL NUMBER : MRCZ/B/1840**

This number should be used on all correspondence, consent forms and documents as appropriate.

- **TYPE OF MEETING : EXPEDITED**
- **APPROVAL DATE : 10 January, 2020**
- **EXPIRATION DATE : 09 January, 2021**

After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the MRCZ offices should be submitted three months before the expiration date for continuing review.

- **SERIOUS ADVERSE EVENT REPORTING**: All serious problems having to do with subject safety must be reported to the Institutional Ethical Review Committee (IERC) as well as the MRCZ within 3 working days using standard forms obtainable from the MRCZ Offices or website.
- **MODIFICATIONS**: Prior MRCZ and IERC approval using standard forms obtainable from the MRCZ Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the MRCZ using standard forms obtainable from the MRCZ Offices or website.
- **QUESTIONS**: Please contact the MRCZ on Telephone No. (0242) 791792, 791193 or by e-mail on mrcz@mrcz.org.zw

Other

- Please be reminded to send in copies of your research results for our records as well as for Health Research Database.
- You're also encouraged to submit electronic copies of your publications in peer-reviewed journals that may emanate from this study.
- In addition to this approval, all clinical trials involving drugs, devices and biologics (including other studies focusing on registered drugs) require approval of Medicines Control Authority of Zimbabwe (MCAZ) before commencement

Yours Faithfully

.....

MRCZ SECRETARIAT
FOR CHAIRPERSON
MEDICAL RESEARCH COUNCIL OF ZIMBABWE

MEDICAL RESEARCH COUNCIL OF ZIMBABWE
2020 -01- 10
APPROVED
P.O. BOX CY 573 CAUSEWAY, HARARE

PROMOTING THE ETHICAL CONDUCT OF HEALTH RESEARCH

Appendix 10: Permission letter from Harare City Health Department

Director of Health Services

DR PROSPER CHONZI
MBChB, MPH, MBA

CITY OF HARARE

All correspondence to be addressed to the
DIRECTOR OF HEALTH SERVICES

DIRECTOR OF HEALTH SERVICES

Rowan Martin Building, Civic Centre,
Pennefather Avenue, Off Rotten Row,
Harare, Zimbabwe.

P.O Box 596
Telephone: +263 (242)753326
753330/1/2
Fax: +263 (242) 752093

Ref: _____

Your Ref: _____

06 February 2020

Nyasha Dzavakwa
University of the Witwatersrand
Johannesburg
SOUTH AFRICA

Dear Sir/Madam

RE: APPLICATION FOR PERMISSION TO CARRY OUT A RESEARCH

I acknowledge receipt of your letter in connection with the above.

Permission is granted for you to conduct a study entitled "***Barriers to and facilitators of implementation of Isoniazid preventive therapy guidelines for under-five children that are household contacts of TB cases by health care providers in Harare, Zimbabwe*** at Kuwadzana Polyclinics, Mt Pleasant, Edith Opperman clinic, Wilkins and Beatrice Infectious Diseases hospitals.

For further assistance please liaise with the matrons at the hospitals and the Sisters In Charge at and the respective clinics

Yours faithfully

DIRECTOR OF HEALTH SERVICES
KPM/rm

c.c.	Matron	-	Beatrice and Wilkins hospitals
c.c.	Sister In Charge	-	Kuwadzana Polyclinics
	Sister In Charge	-	Mt Pleasant
	Sister In Charge	-	Edith Opperman