

**Factors associated with uptake of Isoniazid  
Preventive Therapy among Human  
Immunodeficiency Virus-infected clients in  
Zimbabwe.**

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A minithesis submitted in partial fulfilment of the requirements for the degree of Master of Public Health at the School of Public Health, University of the Western Cape.

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**UNIVERSITY of the  
WESTERN CAPE**  
November 2017

## DECLARATION

I declare that Factors associated with uptake of Isoniazid Preventive Therapy among Human Immunodeficiency Virus-infected clients in Zimbabwe is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

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**Signed:**



## ACKNOWLEDGEMENT

I would like to extend my gratitude and profound appreciation to my supervisor, Dr Lucia Knight for her invaluable input and expertise, as well as rapid turnaround time of all my draft submissions to her.

Special mention to all my MPH course convenors for their enthusiasm throughout.

I am also especially grateful to the Ministry of Health and Child Care as my employer and ultimate authority of the ePMS for granting me the time to study as well permission to use the ePMS data for my study.

I would like to thank my wife, Audrey for her love and support throughout the course, my son Ayden, parents, siblings, extended family and friends.

I cannot overstate the role that coffee played towards completion of this course.



## ABBREVIATIONS

3Is- Intensified case finding (ICF), Isoniazid preventive therapy (IPT), Infection control for tuberculosis (IC)

AIDS- Acquired Immunodeficiency Syndrome

ART- Anti-Retroviral Therapy

ATP- HIV/AIDS and TB Programme

EPMS- Electronic Patient Monitoring System

HIV- Human Immunodeficiency Virus

INH- Isoniazid

IPT- Isoniazid Preventive Therapy

MOHCC- Ministry of Health and Child Care

OI- Opportunistic Infections

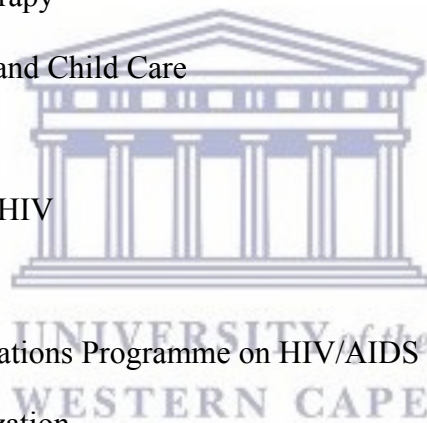
PLWHIV- People living with HIV

TB- Tuberculosis

UNAIDS- The Joint United Nations Programme on HIV/AIDS

WHO – World Health Organization

ZIMPHIA – Zimbabwe Population-based HIV Impact Assessment

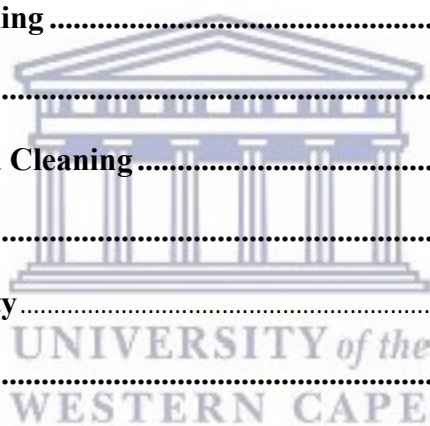




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## ABSTRACT

**Background:** HIV continues to be the single greatest risk factor for developing Tuberculosis (TB) both globally and in sub-Saharan Africa. Zimbabwe is a country that has featured prominently on lists developed by the World Health Organisation (WHO) of countries with a high burden of HIV, of TB, and of TB among people living with HIV. The WHO has developed normative guidance for helping to reduce the burden of TB among people living with HIV, including Isoniazid Preventive Therapy (IPT). Zimbabwe adopted this policy in 2013 as a pilot that has since been rapidly rolled out nationally.

**Methodology:** This study is based on an analytical cross-sectional study done as a secondary analysis of the electronic Patient Monitoring System (ePMS) data for HIV services currently operational in selected facilities in the country. The overall aim of the study was to establish the uptake of the IPT policy among IPT-eligible PLHIV at facilities with the ePMS. The specific objectives were to establish the uptake of IPT among eligible PLHIV in Zimbabwe; to identify patient factors associated with implementation of IPT; and to identify facility factors associated with implementation of IPT. Data on 345,414 people living with HIV from 205 public health facilities across the country providing HIV services were extracted from the ePMS to establish the uptake of IPT among eligible PLHIV. Bivariate analysis, followed by simple binary and multivariable logistic regression analyses were used to identify both patient and facility factors associated with uptake of IPT.

**Results:** This study showed that uptake of IPT, across all of the 205 facilities implementing IPT was 0.4%, due to the study being carried out soon after a rapid rollout of the programme. The following patient factors were associated with uptake of IPT- age of 0- 14 years (AOR 0.16; 95% CI: 0.06-0.44); age 15- 19 years (AOR 0.23; 95% CI: 0.08- 0.63); age 20- 29 years (AOR 0.62; 95% CI: 0.46-0.82); Not pregnant (AOR 2.50; 95% CI: 1.54- 4.00); WHO Clinical Stage 1 and 2 (AOR 1.14; 95% CI:1.05-1.23); clients between 4 – 7 years since enrolment into HIV care (AOR 1.21; 95% CI: 1.12-1.30); and clients that have been at least eight years since enrolment into HIV care (AOR 1.32; 95% CI: 1.16-1.50). Facility factors that were associated with IPT uptake, referral facility- secondary level or higher-(AOR 0.46; 95% CI: 0.43-0.51); facilities with HIV caseloads of less than 1000 patients in care (AOR 0.49; 95% CI: 0.44-0.54); facilities in Harare province (AOR 0.30; 95% CI: 0.26-0.34); Manicaland (AOR 0.52; 95% CI: 0.43-0.63); Mashonaland Central (AOR 0.13; 95% CI: 0.10-0.18); Mashonaland East (AOR 0.71; 95% CI: 0.58-0.87); Masvingo (AOR 0.06; 95%

CI: 0.04-0.08); Matabeleland South (AOR 0.07; 95% CI: 0.05-0.10); Midlands (AOR 0.68; 95% CI : 0.56-0.81); urban setting (AOR 1.66; 95% CI: 1.47-1.87)

**Conclusion:** Uptake of IPT is very low, partly due to inclusion of facilities that had only recently begun implementing the IPT policy due to a phased approach to the rollout. In spite of this, patient and facility factors identified in this study need to be used to target interventions aimed at reducing the huge burden of TB on people living with HIV. Another evaluation of this nature is recommended in future to assess the impact of any targeted interventions identified through this study on IPT uptake.



# Chapter 1- Background

## 1.1 Chapter synopsis

This chapter will explore the current global picture of HIV, along with the burden of TB among PLHIV before briefly focusing on the Zimbabwean context of this TB/HIV crisis. It will conclude with the problem statement and purpose of the study.

## 1.2 Introduction

The Human Immunodeficiency Virus (HIV) has, and continues to be, a global public health challenge. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 36.7 million adults and children worldwide were living with HIV in 2016, with 1.8 million of these being new infections. The same UNAIDS report also estimates that 19.5 million of these were accessing antiretroviral therapy (ART) in 2016. In spite of the advances and investments made with the development of drugs to manage and treat HIV, one million people died from AIDS-related causes in 2016, a third of these being attributable to tuberculosis (TB) (UNAIDS, 2016).

TB in people living with HIV is a major public health concern, with the World Health Organisation (WHO) noting that HIV is the single strongest risk factor for developing TB among individuals with either latent TB infection and/or new infection (WHO, 2014). For example, in countries with a very high prevalence of HIV, like Zimbabwe, the notification rate of TB cases rose more than three-fold when comparing the late 1980s to the late 1990s (Raviglione, Harries, Msiska, Wilkinson, & Nunn, 1997). This was the same time when Zimbabwe identified its first HIV case and the HIV burden was picking up momentum in terms of incidence and death rates. The risk of TB among individuals living with HIV is said to be 20 to 37 times more among PLHIV compared to their non-infected peers. This risk remains relatively high even after clients have been put on lifelong ART (Getahun, Gunneberg, Granich, & Nunn, 2010). Additionally, TB is responsible for more than a quarter of deaths among people living with HIV (Getahun, Gunneberg, Granich, & Nunn, 2010).

To address this substantial burden of TB on PLHIV, the WHO developed guidance on how to manage this public health concern. Amongst other measures was provision of ART; as well as the Three Is for HIV/TB namely *Intensified Case Finding*, *Infection Control of TB*, as well as *Isoniazid Preventive Therapy* (WHO, 2012).



Isoniazid Preventive Therapy is a form of chemoprophylaxis that, according to the WHO, is supposed to be offered to all clients living with HIV after having had active TB disease ruled out through asking a series of screening questions (WHO, 2014). If a respondent has even one response that is positive, they might already have active TB disease, and are therefore not put on IPT but rather undergo appropriate investigations for active TB disease. If, after these investigations of the presumptive TB case, PLHIV is found to have active TB, they are put on full TB treatment. If investigations turn out to be negative for presumptive TB, they are also put on IPT for six months like their counterparts that were screened but responded negatively to all screening questions. Similarly, the WHO also recommends, although provisionally, that IPT should be given for a 36 month duration in high TB transmission areas like Zimbabwe.

Zimbabwe is geographically located in sub-Saharan Africa, a region noted for bearing a disproportionate proportion, over 50%, of the global HIV burden while at the same time comprising only 6.2% of the total global population (AVERT, 2016). A recent household-based national survey estimates that 14.6% of the 15-64 year age group are living with HIV (ZIMPHIA, 2016). The peak prevalence is just under 30% for certain demographics, like females aged 40-44 years old and males in the 45-49 year age group. As regards incidence, the same study estimated it at 0.48% for the 15-49 year olds, a high figure, but nonetheless demonstrating a notable improvement compared to a peak national incidence noted in 1993 of over 5.5% (Humphrey et al., 2006).

Similarly to the HIV picture, the country is also one of the 14 countries identified as having a high burden of TB; TB/HIV; as well as a high burden of the drug resistant form of the disease (DR-TB). To put things into context, it should be noted that according to this classification, countries in the top thirty in each of the three categories bear 85-90% of the total global burden. This means Zimbabwe is consistently part of the lists of countries bearing the majority of the TB, TB/HIV and DR-TB burden worldwide (WHO, 2015). According to preliminary data from a national prevalence study, the country has an estimated prevalence of 343.7 cases of bacteriologically positive cases of TB per 100,000 population (Sandy, Mutsvangwa, & Matambo, 2015). Many scholars, including McKeown et.al. have established the link between poor socioeconomic development and a higher prevalence of TB. Studying population trends and diseases like TB in 18<sup>th</sup> century England, he established that improved living conditions led to a decline in TB long before the medical therapeutic interventions were introduced (Colgrove, 2002; Mckeown, 2016; McKeown & Record, 1962; van Helden, 2003). A case can then be made to explain this burden of TB in Zimbabwe, at least partially,

to the poor socioeconomic conditions currently affecting the country described in subsequent sections of this paper.

In addition to poor socioeconomic conditions contributing to the TB burden in Zimbabwe, HIV is another major driver of TB. In their treatise on HIV-associated TB, Getahun et al. (2010) demonstrated the intricate links between the two diseases- showing that PLHIV were at up to 20 times at risk of developing TB than their non-infected counterparts- while also historically tracing the resurgence of TB with the emergence of HIV. For example, they show how, from the late 1980s, TB notifications rose three-fold, mirroring the increase in HIV prevalence albeit with a four to seven year delay. The same paper estimates that in 2007, 80% of the global HIV/TB burden to have been in sub-Saharan Africa. Finally, they conclude by noting the slow uptake of, and the need to accelerate, TB/HIV collaborative activities that include the *3Is* of HIV/TB (Getahun et al., 2010).

Following this, in efforts to ameliorate this very high burden of TB on PLHIV, Zimbabwe, in line with WHO guidance, began pursuing the possibility of giving PLHIV without active TB disease IPT as early as 2011 (MOHCC, 2011). However, due to some logistical and other challenges that both the TB and the ART programmes were experiencing at the time, they could not recommend rolling out of IPT throughout the public health sector (MOHCC, 2013). This meant that IPT could not be implemented as a public health approach to managing this burden of TB on PLHIV. In 2013 however, with the launch of the IPT guidelines, the programme really took off in earnest in a few pilot sites with plans for a rollout once the pilot was completed. However since this pilot began, it still remains to be seen how the uptake of the IPT programme has been in the public sector, becoming the basis for this study.

### 1.3 Problem Statement

As noted in the introduction above, HIV and TB are epidemic infections in Zimbabwe, with the HIV epidemic credited for the resurgence of TB. The Ministry of Health, in an effort to ameliorate this scourge, adopted the IPT guidelines in 2013. This followed active resource mobilization as well as extensive planning to ensure smooth implementation of this policy to address concerns that had delayed earlier implementation. These concerns included staff capacity to implement IPT, staff hesitancy to take on more work, logistical issues affecting steady supply of the Isoniazid for this programme, as well as coordination issues between the two departments (TB and HIV).

With all these concerns that led to delays in launching and implementation of the IPT policy

addressed, it goes without saying then that there is a need to carry out some evaluative work to reflect on implementation thus far and to quantify the extent of uptake of IPT among implementing facilities. In addition to assessing level of uptake it will be important to identify what aspects have facilitated uptake and which aspects have impeded progress. In addition, such an exercise will help to identify demographics, if any, whose uptake has been lower than others so that the programme can implement initiatives to focus on these demographics to also improve their outcomes as regards this scourge of TB on PLHIV.

It is worth noting that the Zimbabwean Ministry of Health and Child Care- HIV Treatment and Care preliminary 2015 Annual Progress Report recognizes that implementation of IPT has been slow across the board (MOHCC, 2016). It further speculates that this could be due to, among other issues, inadequate capacity among health workers and possibly inadequate buy-in from the sub-national level manager. The same report notes that only 39,264 PLWHIV received IPT, out of 879,271 PLHIV that were on treatment at the time in the country (MOHCC, 2016). Granted, some of these 879,271 PLHIV could be already on treatment for TB, and another portion not eligible, but the figure noted in the report falls far short of expectation. This is a cause for concern that warrants further investigation to elucidate the issues/factors contributing to this. Save for an evaluation done in Shurugwi district (Makoni et al., 2015), and a cohort study of IPT completion rates in seven pilot sites (Takarinda, et al., 2017), very little work has been done at national level to both quantify IPT uptake systematically, as well as to identify factors associated with uptake of the IPT policy. This study aims to address this knowledge gap.

## 1.4 Purpose

The purpose of this study to assess the uptake of the IPT policy among implementing facilities in the Zimbabwean public health sector using coverage as a proxy. In addition, the study intends to identify any determinants associated with implementation, both facilitatory and inhibitory factors, of the IPT policy. Identification of these factors can then be used to optimize policy implementation through elimination of inhibitors, as well as wider implementation of facilitators.

In an endeavor to do this, the next sections of this mini-thesis will carry out an extensive literature review, explain the methodology used to achieve this purpose, share the results, discuss the same results as well as giving appropriate recommendations stemming from the findings.

Specifically, the following chapter will carry out an extensive literature review, identify current gaps in knowledge on IPT uptake before setting out the aim and objectives of the minithesis.



# Chapter 2- Literature Review

## 2.1 Chapter synopsis

In this chapter, a general overview of the country will be given including its global status on general development indicators. The overall health system structure and performance will be described in some detail as the study will investigate the effect of the health system on IPT uptake. The history of TB and HIV in the country will be explored up to the current trends to appreciate the synergistic effect these two conditions have on each other. The effect of ART on TB incidence, as well as that of TB chemoprophylaxis, will be explored before looking at contemporary knowledge on uptake of IPT as well as completion rates of IPT. The chapter will be concluded by identifying knowledge gaps and finally outlining the aims and objectives of the study.

## 2.2 Zimbabwe

### 2.2.1 Country profile

Zimbabwe is a landlocked sovereign republic located in southern Africa covering an area that is 390,757 square kilometres, bordered by Zambia to the north, South Africa to the south, Mozambique to the east, and Botswana and Namibia to the west. Administratively, it is divided into ten provinces, eight rural and two metropolitan; 62 administrative districts; as well as 31 urban authorities. There are 16 official languages including sign language (UN, 2015).

There is an estimated population of 13.1 million, 52% of this being females. The predominant population is fairly young with 41% of it being 15 years and below. The majority of the population is rural, comprising about 67% of the total population (ZIMSTATS, 2012).

The country attained its independence from British rule on the 18<sup>th</sup> April 1980, inheriting the 1979 Lancaster House constitution in the process. The country promulgated a new constitution on the 22<sup>nd</sup> May 2013, after a consultative process which guarantees, among other rights- the right to healthcare (Constitution, 2014; COPAC, 2013).

Economically, the country is emerging from an economic crisis between 2000 and 2008 that was characterised by high levels of poverty, with the World Bank estimating that 72% of the population lived below the poverty line, and a fifth in extreme poverty (World Bank, 2016).

The highest official inflation rate was noted to be 231 million in July 2008, when capacity utilisation in industry was less than 10% (UN, 2015). At this point, the country's ranking using the Human Development Index (HDI) fell to 173<sup>rd</sup> out of the 187 countries, worse than some countries that were in conflict at the time. Currently, the World Bank estimates the 2016 Gross Domestic Product (GDP) for the country to have been at USD 16.289 billion, while Gross National Income (GNI) per capita was USD 940 in 2016 (World Bank, 2017). Government has since introduced the 2013-2018 Zimbabwe Agenda for Sustainable Socio-Economic Transformation (ZIMASSET) as the "blueprint and turnaround plan" for improving the economic prospects of the country in line with its development priorities. Life expectancy at birth is estimated to be 59 years for males and 62 years for females (WHO, 2017). The Human Development Index (HDI) for the country is currently at 0.397 (UNDP, 2013).

### 2.2.2 Other Aspects of Development

According to the 2015 ZDHS report, 22% of men and 26% women had no formal education, while 11% men and 7% women had more than secondary education (ZIMSTAT, 2016). However, notwithstanding the above, the 2012 Census report put the literacy rate for the country at 96%- a very commendable figure both in the region and globally (ZIMSTATS, 2012).

With regards to individual economic activity, the same Census report notes that 67% of those above 15 years of age were in the labour force, with the remainder either being students, "homemakers" as well as the retired. Of those in the labour force, 11% were not employed. A more worrisome finding was the fact that three percent of children below 15 years were economically active. An estimated 83% of the 15 years and above that were not in the labour force were either students or homemakers. Agriculture was the predominant sector of employment (ZIMSTATS, 2012).

The status of housing in Zimbabwe is a mixed picture. While 59% of dwellers stayed in their own housing, either as owners or purchasers, only 56% of these houses have access to electricity. Of the citizenry, 75% have access to clean water- with only 38% of these clean water sources being located within the premises. Further, of these households, only 24% had a toilet- with the figure being as high as 56% in some provinces like Matabeleland North, with the attendant risks that go with this low coverage. Similarly, having 63% of the population use wood as the main type of cooking fuel (ZIMSTATS, 2012). This has several



documented ill effects, among them pneumonia, heart problems, chronic obstructive pulmonary disease (COPD) as well as lung cancer itself (WHO, 2016).

Finally, the same 2012 Census report notes that the fertility rate, using the direct method, was 3.8 children per woman (ZIMSTATS, 2012). The World Bank estimated it at 3.9 children per woman in 2015- which is high by global averages but relatively low when compared to its regional peers in sub-Saharan Africa and other low income countries (World Bank, 2017). This fertility rate, coupled with a crude mortality rate of 10.2 per 1000 as well as a life expectancy of 38years translates to a healthy net increase of the population of 2.2 per 1000 (ZIMSTATS, 2012).

### 2.2.3 The Health System Strategy

In line with the rights enshrined in the constitution referred to earlier, and the ZIMASSET outlined above, the health system is guided by “The National Health Strategy (2016-2020) - Equity and Quality in Health: Leaving No One Behind” (MOHCC, 2016). In this blueprint, the vision, mission, priority areas, as well as the service delivery platforms and entities are outlined. The national strategy has three main goals- to strengthen priority health programmes; to improve service delivery platforms or entities; as well as to improve the enabling environment for service delivery. Notably, both HIV and TB are priority programmes identified under the priority health programmes to be strengthened- as per the first goal. Specifically, enhancement of HIV/TB collaborative activities is singled out under “Objective 5.2” under the first goal.

In essence, the strategy embraces the Primary Health Care approach, the approach used by government since independence in 1980. Operationally, funding is from three sources- government expenditure on health, foreign funding, as well as out-of-pocket. Notably, out-of-pocket remains unacceptably high at 49%; while, since 2009 the highest contribution to health by government reached a peak in 2012 at 8% of total government expenditure (MOHCC, 2016). It is noteworthy that this peak still falls far short of the Abuja Declaration target of 15%, of which the government of Zimbabwe is signatory (WHO, 2016).

### 2.2.4 Health System Structure

The national public health system is a four tier system reflecting the sophistication of services offered. The most basic services are offered in the clinics (both rural and urban) termed primary level. These basic services, being nurse-driven, are essentially preventive services, as

well as diagnosis and management of clinical conditions that does not require sophisticated equipment or a physician. The next level is the secondary level comprising of mission hospitals, rural hospitals and district hospitals. These are manned by medical doctors offer slightly more sophisticated services including caesarean sections and X-rays. The provincial hospitals is the next level of sophistication, offering more specialised services, with an establishment with medical specialties like surgery, obstetrics, gynaecology, internists and paediatrics. Finally, the highest level is the quaternary level. This is the highest level of sophistication offering only referral support to the lower levels, with clients that require this level of sophisticated care being referred to these facilities. These are also the training institutions. This level would have additional specialised services like oncology, neurosurgery, and other less common specialties. These are only found in the two major cities- Harare and Bulawayo. In terms of numbers, the whole health system is built around its 1848 health facilities- both private and public- divided into 1634 primary level facilities; as well as 214 referral-level facilities that are divided into secondary, tertiary and quaternary level facilities as explained above (MOHCC, 2016).

For the human resource aspect to provide services at these facilities, a recent service readiness assessment found that the overall density of the core health workers (physicians, non-physician clinicians, nurses, and midwives) is eight core health workers per 10 000 population, that is, about a third of the recommended target of 23 per 10 000 population by WHO. This has implications on not only the quality of health service delivery, but also the experience of seeking services at these institutions related to, for example, waiting times. (ZSARA, 2015).

### 2.2.5 Health System Performance

Childhood mortality rates are considered, globally, as very sensitive indicators of a country's socio-economic level and its citizens' quality of life. This is because the childhood mortality levels are influenced by a myriad of factors such as poverty, level of education of mothers; by the availability, accessibility and quality of health services; as well as by environmental risks including access to safe water and sanitation; and nutrition (You et al., 2015). In 2015 the under-five mortality was estimated at 69 deaths per 100 000 live births (ZDHS, 2016), the lowest it has ever been since the ZDHS was ever measured in Zimbabwe in 1988. It is interesting to note that this indicator peaked at 102 deaths per 100 000 live births in 1999 (ZIMSTAT, 2016).



The maternal mortality ratio, an indicator of access to health services, was at 651 deaths per 100,000 live births. Although a great improvement from the previous ZDHS done in 2010-11 in which maternal mortality ratio was at 960 deaths per 100,000 live births, it is still worrisome. This is especially so when it is acknowledged that the same indicator was as low as 283 deaths per 100,000 live births in 1993- a period in which many countries had just committed to reducing their maternal mortality ratios by 75% by the year 2015. This means that the 2015 target for Zimbabwe was in the region of 70 deaths per 100,000 live births- meaning that Zimbabwe failed to attain its Millennium Development Goal Number Six (UN, 2014; Rosato et al., 2008; UN, 2015; ZIMSTAT, 2016). As a matter of fact, instead of reducing the figure as per MDG targets, Zimbabwe more than doubled it. For context, it is also important to note that 10% of married women have an unmet need for family planning, down from 59% in 2011. Also, 72% of women are reported to have delivered at a health facility, up from 65%; while 78% attended to by a health professional, a notable increase from 66% in 2011 (ZIMSTAT, 2016).



### 2.2.6 HIV and TB in Zimbabwe

Zimbabwe had its first case of HIV in Hurungwe district in 1986 (Denhe et al., 1992). In 2004 the country began to offer HIV treatment and care services on the public system in a systematic manner (NAC, 2012), in line with the HIV policy set out in 1999 (MOHCW, 1999). Monitoring of HIV trends since then until 2004 was based on modelling from projections based on sentinel surveillance in antenatal clinics through anonymous unlinked HIV testing there. When the Epidemic Projection Package (EPP) and the Spectrum software were run in 2010, they projected that the epidemic had peaked at 26.5% prevalence among adults aged 15-49 years of age during 1997 (UN, 2008; NAC, 2012). Through a well-coordinated multi-sectoral response, tremendous progress has been made towards halting and reversing the effects of HIV (WHO, 2015). The 2015-2016 national population-based HIV impact assessment (ZIMPHIA) noted that the prevalence of HIV among the 15-49 year demographic had declined from that peak in 1997 of 26.5% to 14.0% (ZIMPHIA, 2016). This is at least partly due to changes in sexual behaviour, most notably a drop in the number of sexual partners; improved condom use; and mortality from AIDS as at this point there was a lack of access to lifesaving treatment (NAC, 2012). The ZIMPHIA is discussed in more detail in later sections.

A 2011 modes of transmission study done by Fraser et al. (2011) noted that HIV was very homogenous, driven primarily by heterosexual sex- accounting for over 90% of new transmissions (NAC, 2012).

As referenced earlier, albeit briefly, the Zimbabwe Population-Based HIV Impact Assessment (ZIMPHIA) - a household-based national survey designed to measure the status of Zimbabwe's national HIV response- showed that prevalence of HIV among adults 15-49 years was down to 14% from a 26.5% peak in 1997. Granted there was a difference across sexes, with females in that age demographic having a prevalence of 16.6% while for their male peers the prevalence was only 11.2% (ZIMSTAT, 2016). However noting that this is almost half of the peak prevalence speaks volumes about the progress made. The same ZIMPHIA noted that 74.2% of PLHIV ages 15 to 64 years reported knowing their HIV status, still short of UNAIDS target of having 90% of PLHIV knowing about their HIV status by 2020. Although below target, it is a marked improvement on the 2015 ZDHS in which only 49% of women 15-49 age group and 36% men of the same age having been tested and received a result in the preceding 12 months. For those that know their status and are on self-report being on treatment, the ZIMPHIA noted that 86.5% of these people aged between 15-64 years were virally suppressed- almost reaching the 90% target set for 2020 set by UNAIDS a few years before its due (UNAIDS, 2017; ZIMSTAT, 2016).

This progress is due, in no small part, to the multi-sectoral approach to HIV coordinated by the National AIDS Council, set up by an act of parliament after adoption of the national policy on HIV and AIDS in 1999 (MOHCW, 1999; NAC, 2012). The policy was swiftly complemented by the National HIV and AIDS Strategic Framework of 2000-2004, and then subsequently by a series of Zimbabwe National HIV/AIDS Strategic Plans (ZINASPs). Among other achievements set out in these documents was a 3% AIDS levy on payee and corporate income to supplement the HIV response; as well as the prohibition of employers from discriminating based on an individual's HIV status (NAC, 1999).

As a result of this policy framework, the Zimbabwe Service Availability and Readiness Assessment (ZSARA) carried out in 2015 at 275 facilities noted several issues related to HIV service delivery. HIV counselling and testing services (HTS) are the entry point to HIV services (WHO, 2016). These HTS and TB services were offered in nine out of ten health facilities surveyed- speaking to how decentralised these services were; similarly, readiness to provided HIV-related services such as HIV counselling and testing was high at 92%. PMTCT Readiness was at 90%; while readiness to provide care and support services was at 79%. Also

notable was that 90% of facilities had at least one clinical staff member trained in the management of HIV and TB co-infection. As noted earlier, the overall density of the core health workers was found to be eight core health workers per 10 000 population, that is, about a third of the recommended target of 23 per 10 000 population by WHO. Among other notable findings- 95% of facilities had guidelines available for HIV/AIDS; 90% of facilities had at least one staff member trained on clinical management of HIV/AIDS; 68% availability of guidelines on TB/HIV coinfection; 87% had a system for diagnosis of HIV among TB clients (ZSARA, 2015).

### 2.3 TB in HIV

In their review of the global HIV infection-associated TB, Getahun et al. (2009) note that just under a third of PLWHIV had TB infection, although the bulk of it was the latent variety rather than active TB disease. In the same paper, they estimate that 80% of these cases of HIV-associated TB are in sub-Saharan Africa. They further assert that TB is responsible for more than 25% of deaths among PLWH. They conclude by noting that implementation of TB/HIV collaborative activities, the *3Is* to be specific, amongst which one is IPT, has been slow and that there is a need to accelerate this aspect in countries like Zimbabwe that have a generalized epidemic. Several other scholars independently corroborate this implementation gap (Corbett et al., 2003; Getahun et al., 2010; van Halsema et al., 2010).

It is also worth noting that the reverse is also true, that there is also a substantial HIV burden among patients with TB, especially in sub-Saharan Africa. In a 2014 national TB cohort in Zimbabwe, a total of 28,556 TB cases were reported through the national reporting structures, and of these 94% (26,916) cases were screened for HIV, attesting to a high uptake of HIV testing among TB patients. More worryingly, on further analysis of this national data it turned out that of these 26,916 TB patients that were tested for HIV, 84% turned out to be co-infected with HIV (MOHCC, 2016). This speaks to the synergistic effect of the two infections (Pawlowski, Jansson, Sköld, Rottenberg, & Källenius, 2012; The Lancet Infectious Diseases, 2010).

### 2.4 ART and TB incidence

With the evidence demonstrating the massive burden of TB on PLWHIV shown above, the next logical step would be to identify interventions grounded in scientific proof that can address this burden. The most logical of these programmatically is initiating ART, which has been

corroborated by a systematic review and meta-analysis carried out by Suthar et al. (2012) which demonstrated that ART was protective of TB among PLHIV in spite of level of CD4. While this is convincing proof of the effect of ART on preventing TB among PLHIV, it is also worth noting that this protective effect does not totally eliminate the risk of TB imposed by HIV. PLHIV are still at substantially higher risk of TB than their non-infected peers even after sustained periods on ART with high CD4 count rates (Gupta, Wood, Kaplan, Bekker, & Lawn, 2012).

## 2.5 TB Chemoprophylaxis and Its Effect on TB Incidence and Mortality

Several studies have previously demonstrated the effects of using chemoprophylaxis among adults and children without HIV to reduce the burden of TB on them. However this chemoprophylaxis had several issues identified contributing to a low efficacy including a high drop-out rate among those on nine month of Isoniazid as well as higher toxicities among shorter multidrug regimens (Finnell, Christenson, & Downs, 2009; Greinert & Zabel, 2003; Lobue & Menzies, 2010; Parekh & Schluger, 2013; Person & Sterling, 2012; Volmink & Woldehanna, 2004).

Chemoprophylaxis among PLWH was demonstrated to reduce incidence of active TB disease by as much as 32% (CI- 15-46%) in a systematic review of 12 trials involving more than 8500 clients (Akolo, Adetifa, Shepperd, & Volmink, 2010). An earlier meta-analysis in 2004 by Woldehanna and Volmink (2004) found a slightly higher protective effect of 36% among the eleven trials that were eligible. An even earlier meta-analysis done in 1998 had demonstrated a similar effect, albeit with the protective effect being more exaggerated at 42% for the seven trials used then (Bucher et al., 1999). It is worth noting that, in a high TB burden country like Zimbabwe where the burden of TB is high as noted in the [introduction](#), that the bulk of the population will be tuberculin test positive. This is an important issue to note as all three meta-analyses demonstrated that in this tuberculin test positive group of PLWH, the protective effect of chemoprophylaxis is even more exaggerated- with Akolo et al. (2010) arriving at a figure of 62% (CI- 43-75%). This enhanced protective effect of 62% among tuberculin test positive PLHIV improves its appeal to managers of TB and HIV programmes. Even more-so is the fact that this effect was sustained no matter what form of chemoprophylaxis they were on and of whatever duration (Akolo et al., 2010; Bucher et al., 1999; Volmink & Woldehanna, 2004). In addition to the exaggerated protective effect of chemoprophylaxis on development of active

TB disease noted above among the tuberculin positive PLWH, the additional effect on this demographic of reducing mortality is notable, especially for those studies that used Isoniazid as the chemoprophylaxis (Akolo et al., 2010). However, the other two meta-analyses failed to duplicate this effect- finding no statistically significant association between chemoprophylaxis and reduced mortality (Bucher et al., 1999; Volmink & Woldehanna, 2004). The lack of replication of the findings on reducing mortality notwithstanding, the findings noted make chemoprophylaxis especially suited for the Zimbabwean context of TB and HIV described in



earlier sections.

## 2.6 IPT as the Drug of Choice for TB Chemoprophylaxis

The landmark studies on TB chemoprophylaxis in both PLWH and HIV negative individuals were mostly with nine months of Isoniazid (Lobue & Menzies, 2010; Parekh & Schluger, 2013). By virtue of the long duration, nine months, there was a high drop-out rate before completion of the Isoniazid which made the intervention effective but not efficacious (Lobue & Menzies, 2010). Several subsequent studies, some still ongoing, into using multidrug chemoprophylaxis have since been undertaken. These multidrug chemoprophylactic regimens afforded the opportunity to administer shorter duration chemoprophylaxis to address the issue of high drop-out rates. While this is a novel solution to the problem of high drop-out rates on Isoniazid mono-prophylaxis, they encountered a problem of a somewhat different nature but unique only to these novel approaches. Clients on these multi-drug chemoprophylaxis experienced a higher rate of adverse reactions, meaning they ended up having to be terminated from continuing on these regimens of chemoprophylaxis prematurely (Greinert & Zabel, 2003; Lobue & Menzies, 2010). So instead of experiencing high drop-out rates because of the long duration on IPT, the high drop-out rates became those caused by adverse effects instead. Additionally, the more complex supply chain, increased cost, adherence and logistic arrangements necessary to sustain these approaches makes them somewhat less appealing to managers of national TB and HIV programmes (Akolo et al., 2010). Hence, Isoniazid still maintains its status as the drug of choice for chemoprophylaxis, at least for the time being (Akolo et al., 2010; Greinert & Zabel, 2003; Lobue & Menzies, 2010; Parekh & Schluger, 2013).

In conclusion of this section, it is also important to emphasize, especially in the current context of making ART available to all PLHIV, that the effects of IPT augment the effects of ART on reducing the incidence of TB (Golub et al., 2009; WHO, 2014).

## 2.7 Uptake of IPT

TB screening remains the entry point to IPT (Burgess et al., 2001; Getahun et al., 2010). It stands to reason that a low uptake of TB screening would have a consequent effect of reducing IPT coverage among eligible populations as these people would not have been identified effectively and efficiently. Initiating IPT without screening for active disease increases likelihood of undertreating actual cases with active TB with Isoniazid monotherapy



leading to higher risk of developing Isoniazid resistance- a concern raised by health workers in several studies as a barrier to their implementing IPT (Moolphate et al., 2013; Teklay, Teklu, Legesse, Tedla, & Klinkenberg, 2016). With proper screening, these concerns are unfounded (Balcells, Thomas, Godfrey-Faussett, & Grant, 2006; van Halsema et al., 2010). Nationally, according to the 2016 progress report on the Treatment and Care program, uptake of TB screening ranged by province from a low of 81% of PLHIV screened for TB in Matabeleland South, to a peak of 98% in Harare metropolitan province (MOHCC, 2017). A cautionary note here on using the symptom screening tool to rule out TB is that Wood et al. (2007) have found that as much as 5% of PLHIV will be identified as not having active TB when they do actually have TB. This means that the use of the screening tool on its own before initiating IPT will result in 5% of people with actual TB being put on IPT instead of being rightfully being on a full treatment regimen rather than IPT chemoprophylaxis. However Getahun et al. (2010) noted that the additional logistics of using chest x-rays, for example, to improve the positive predictive value by a small margin would be far outweighed by the cost implications of these additional measures.

Globally, few countries were reporting on IPT implementation progress in 2008, among the few that did, their coverage among PLHIV screened for TB was less than one percent- an obvious reason to worry. This is attributed to a myriad of issues among them- leadership and governance issues, service provision barriers, health worker challenges, health information impacting quality of reported data as well as issues related to health financing (Getahun et al., 2010).

Predictably, evaluations to assess uptake of IPT in public health settings show a variable picture depending on context both geography and health system settings. Moolphate et al. (2013) in northern Thailand found that only 20% of health facilities that should have been offering IPT actually were providing this service. Among the 80% majority of non-implementers, they further found that the main barriers were the unclear direction of national policy (60%), fear of emerging Isoniazid resistant tuberculosis (52%), as well as fear of poor adherence (30%) once patients were initiated. Among implementers the motivating factors were by the knowledge that IPT can prevent TB (63%), adhering to national guideline (34%), and concern for TB prevention even after the expansion of access to ART (32%) (Moolphate et al., 2013).

In a damning case study of a UMD/ACTION project in Nigeria, Musa et al. (2009) found that amongst 23 of the 60 clinics that were supposed to offer TB/HIV services, only just over six

percent of clients were even screened for TB, a much lower figure than the performance reported nationally in Zimbabwe noted above (MOHCC, 2017). Of those screened, four percent were found to have active TB. More importantly, among those that had TB ruled out, only six percent were subsequently put on IPT (Musa et al., 2009). Bearing in mind the huge burden of TB among PLWH, this is a serious cause for concern.

In northern Ethiopia, one study found the coverage of IPT among eligible PLHIV to be 19.6%. There was a wide variation in uptake, although not statistically significant, when hospitals were compared with other smaller facilities (hospitals had higher uptake); as well as when the authors compared early implementers to the late adopters of IPT. It is also worth noting that for the 19.6% that were initiated on IPT, a third did not complete their course (Teklay et al., 2016).

In a cross-sectional study done at one hospital in Kenya of adults that had been on treatment and care services for at least six months an uptake of IPT of 77% was noted, a very modest figure compared to the northern Ethiopian and Nigerian studies referred to earlier, although somewhat short of the 90% target set by Kenyan programming of TB/HIV. Of clients recruited, it is also notable that 98% of those recruited were already on ART (Omesa et al., 2016) as other studies have identified this as a significant factor associated with uptake and completion of IPT (Ayele, van Mourik, & Bonten, 2016). Finally, three variables were found to independently affect initiation on IPT, these were- fear of acquiring TB, having received IPT-associated health education, as well as having a good relationship with the healthcare worker (HCW) (Omesa et al., 2016).

Closer to Zimbabwe, but much earlier, a clinical trial in Botswana setting out to describe reasons for exclusion from IPT, as well as to describe outcomes of PLWH after six months of IPT, found that 68% of those that had TB excluded via two-stage TB screening process were initiated on IPT. It also found that being on ART was significantly associated with greater adherence to IPT, even after multivariate analysis (Mosimaneotsile et al., 2009). The study being proposed would be an opportunity to investigate this effect, especially in light of the recently introduced policy of putting all PLWH on ART in spite of immune competence and/or clinical symptoms (WHO, 2016).

In one study, to evaluate the implementation of the IPT policy in a district in Zimbabwe, Makoni et al. (2015) noted a 54% coverage of IPT among 5255 eligible PLWHIV on ART in health facilities in Shurugwi. Also notable was a 0.6% drop-out rate credited to Isoniazid



toxicity and a 0.3% drop-out rate due to subsequent development of active TB disease. It is not made clear why the authors chose to focus only on the PLWHIV that were on ART only, leaving out a probably substantial demographic of PLWHIV that were not yet on ART. This is especially worrying because at the time the study was carried out only PLWHIV that had particular criteria like CD4 count below 500 and WHO stage three and four were being put on ART, leaving out a substantial demographic enrolled in care but not yet eligible for ART. This group would also have been at substantial risk of developing TB and therefore eligible for IPT, and should have ideally also have been part of the study. Leaving this subset out would leave a lot of unanswered questions about uptake of IPT among this group of PLWHIV. This aspect is the reason why the author is proposing carrying out this study- which will include PLHIV enrolled into care, but not yet on ART. Additionally, the Makoni et al. (2015) study was focused on only one of 63 districts in Zimbabwe, introducing limitations to external validity. This current study would then fill in this knowledge gap, especially because the program has since grown exponentially over the past year since this study was carried out as elaborated upon in the [methodology](#) section to follow. Another particular weakness of cross-sectional studies, of producing different results depending on “WHEN” they are carried out, is noted in the limitations section, therefore warranting regular execution of studies of this nature to address this gap.

In conclusion of this section, it is worth noting that some scenarios outside of the public health programming found higher rates of IPT initiation. A good example of this is IPT uptake of 82% noted at a workplace HIV prevention and care program for miners in the Free State province of South Africa among eligible PLHIV in the mining setting (Charalambous et al., 2004). How their findings relate to routine public health programming, and what lessons can be learnt from these, remains to be seen.

## 2.8 Adherence to IPT and Rates of Completion of IPT

Uptake of IPT can be thought of as a process indicator for monitoring incidence of TB among PLHIV. Further downstream, indicators such as adherence to IPT, completion rates of IPT among PLHIV initiated on ART, as well as the incidence of TB among PLHIV can also be monitored.

Although beyond the scope of this minithesis, it is worth noting that several authors have already begun studying these very issues that are further downstream from just uptake of IPT,

namely, adherence to IPT, and IPT completion rates- with findings going across the spectrum from very poor to modest ones.

The lowest rates of adherence, for example, were demonstrated by Ayele et al. (2016) who found a 64.2% adherence rate among PLHIV in Ethiopia through a prospective cohort. Those clients on ART and Cotrimoxazole- an antibiotic used to reduce incidence of common opportunistic infections among PLHIV- were significantly associated with better adherence; while conversely, development of opportunistic infections and high stigma were associated with poor adherence. Several other studies corroborate the finding that being on ART improves adherence (Berhe, Demissie, & Tesfaye, 2014; Mosimaneotsile et al., 2010). Other notable factors associated with higher adherence were being at least five months on IPT (c.f. two months or less on IPT) (Berhe et al., 2014), having IPT explained by a health worker, being comfortable taking IPT in front of others, as well as regular clinic attendance (Mindachew, Deribew, Tessema, & Biadgilign, 2011). Lastly, the other authors found substantially higher IPT adherence rates than Ayele et al. (2016), all at least 86%- although due to the study design they utilised one is inclined to lean towards their estimate as the other two studies were cross-sectional studies, while the third was a very tightly controlled randomised control trial with conditions that do not even closely approximate real life scenarios (Ayele et al., 2016; Berhe et al., 2014; Mindachew et al., 2011).

In terms of IPT completion rates, a similarly heterogeneous picture is found. A randomised control trial found a 65% IPT completion rate in Brazil (Durovni et al., 2010). Teklay et al. (2016) found similar rates with a completion rate of 68%. A study by van Griensven et al. (2015) among PLHIV that were ART-naïve at being initiated on IPT found completion rates as high as 78% however. Completion rates seem to be higher among the ART-naïve demographic compared to their counterparts on ART. Further, the authors found that the ART-naïve group that was subsequently put on ART while on IPT had lower completion rates. This is somewhat baffling as being on ART was identified by several authors to have a positive effect on adherence, as noted earlier. Being on ART could however have an adverse effect on treatment completion compared to adherence through a separate mechanism. This remains to be explored and needs to be studied urgently in light of its programmatic implications. To support this, the authors note that the commonest reason for not completing IPT among those that ended up with concomitant ART was drug toxicity, while the commonest reason among those that were ART-naïve until end of IPT was being lost to follow-up (van Griensven et al., 2015).

In a retrospective cohort study carried out in seven pilot sites in Zimbabwe, Takarinda et al. (2017) found that 81% of PLHIV on IPT completed their course, a notably high figure. This is potentially confounded by the fact that these pilot sites started IPT implementation much earlier than the other 627 IPT-implementing facilities, and have since matured through any teething issues and therefore do not reflect the performance of the facilities that started to implement more recently. Teklay et al. (2016) noted this effect with respect to IPT uptake, but it could equally affect IPT completion. The Zimbabwean study further noted that over 90% of those that failed to complete IPT were due to three reasons only- being lost to follow up, undocumented reasons, as well as drug toxicity. Finally, the authors note that in the study being currently on ART, and receiving a two month supply of isoniazid at the start of treatment as being associated with a lower risk of not completing IPT; while missing clinic visits prior to starting IPT was associated with a higher risk of non-completion, corroborating findings from Mindachew et al. (2011) that regular clinic attendance improved adherence.

## 2.9 Knowledge Gaps

In conclusion, it becomes apparent from the studies noted above that Zimbabwe is currently burdened by the double epidemic, notably synergistic, of HIV and TB in spite of the tremendous progress made to halt and reverse these two conditions as per the millennium development goals that expired in 2015 (UNAIDS, 2015; WHO, 2016).

The two most notable efforts to address this double burden are the roll-out of both ART and IPT. As noted by Golub et al. (2009) these two act to augment the effect of the other in reducing the burden of TB on PLHIV.

Computing the coverage and uptake of ART has been refined to almost an art form, with these being calculated on an annual basis to a very high degree of accuracy and precision. This is perhaps attributable to the clearly elaborated goals set out by UNAIDS of reaching 90-90-90 targets referred to earlier, that countries and sub-national regions are monitoring annually to assess progress towards these well-known targets (UNAIDS, 2017). The middle 90 refers to a target to, by 2020, to have 90% of PLHIV that know their status being on sustainable ART. However, no similar framework exists to monitor and evaluate IPT programmes.

Makoni et al. (2014) attempted to do this in one district in Zimbabwe, but one oversight of this study was that only PLHIV that were on ART were eligible for this study, leaving out a substantial group of PLHIV that are not on ART from being evaluated when they are actually

eligible for IPT. Their findings would tend to overestimate the coverage of IPT among eligible PLHIV by not counting the PLHIV that are not on ART from the population at risk of TB- when it could be argued that they are actually at an even higher risk of TB than their counterparts on ART, as referred to earlier.

Takarinda et al. (2017) did a well thought out study to evaluate IPT completion and factors associated with it. However, as referred to earlier, it was only done on seven pilot sites, missing out on the other 627 IPT implementing facilities that are bound to be inherently different from the “early adopter” pilot sites- affecting the external validity of the study. Finally, as was also referred to earlier again, IPT adherence, IPT completion and incidence of TB among PLHIV on IPT are all more outcome measures of IPT implementation. They are important and need to be studied. However, at their core, they tend to assume that performance on uptake of IPT is already optimal and therefore seek to understand more downstream factors related to outcomes. This, as findings on IPT uptake from other countries show, may not be true at all. Regions and facilities that began IPT implementation as far back as 2009 seem to have sub-optimal figures of IPT uptake. It could be argued that a country that launched IPT much later in 2012/2013 might very well have even less optimal uptake. This study will attempt to close this knowledge gap to complement the gaps left by the studies noted above.

## 2.10 Aims and Objectives

### 2.10.1 Aim

The aim of the study is to establish the uptake of the IPT policy among IPT-eligible PLHIV at IPT-implementing facilities that have the ePMS in the Zimbabwean public health sector, and identify factors associated with its uptake.

### 2.10.2 Objectives

The objectives are thus to-

- Establish the uptake of IPT among eligible PLHIV in Zimbabwe
- Identify patient factors associated with implementation of IPT
- Identify facility factors associated with implementation of IPT.

## 2.11 Conclusion of chapter

In this chapter a review of literature was done with respect to Zimbabwe both in terms socio-economic development but also in terms of the structure of the health system and its current performance in the context of the current socioeconomic status. Literature was reviewed in terms of HIV, TB and TB/HIV collaborations in Zimbabwe. The role of ART on TB incidence was described, as well as that of different forms of chemoprophylaxis. The global, regional and local academic discourse on IPT uptake, adherence and completion rates was presented. Current knowledge gaps on IPT were identified and the study aims and objectives were framed in line with these knowledge gaps.



# Chapter 3- Methodology

## 3.1 Chapter Synopsis

This chapter will describe the ePMS- the data source for the study, including its historical background. It will subsequently justify the selection of facilities for the study; describe and justify the epidemiological study design used, and then discuss the reliability, internal and external validity of the study; analysis plan; discuss the study limitations; before concluding with ethical considerations.

## 3.2 The Electronic Patient Monitoring System

As alluded to earlier, in 1986 Zimbabwe identified its first case of HIV (Denhe et al., 1992). In April 2004, the country adopted a public health approach to HIV treatment and care in which treatment for HIV would be availed through the public health system beginning with the five quaternary-level hospitals (UNAIDS, 2012). The numbers of facilities providing treatment and care for PLHIV, as well as the actual number of clients receiving treatment has since grown exponentially- to a total of 1566 facilities providing services and a corresponding 975,667 PLHIV accessing care at these facilities (MOHCC, 2017). This was at least partially aided by the rapid decentralisation of HIV services recently (UNAIDS, 2015).

The level of effort and coordination required to plan, provide, and administer quality HIV services to keep up with this stratospheric increase in numbers of people on antiretroviral therapy (ART) is gargantuan, by any standards. Effective and efficient execution of this requires a robust, accurate, complete, and valid health information system providing real-time data. With the exponential growth in numbers of facilities providing HIV services and patients on treatment described earlier, the HIV health record system that was there before 2012 was proving inadequate to cater to the data demands of the programme. This was partly due to being entirely paper-based at the time, contributing to a labour-intensive as well as a time-consuming process of data collection, collation, processing and analysis of both individual client records as well as aggregated totals (UNDP, 2014).

With these challenges in mind, a working group was set up to assess Zimbabwe's needs as regards a new health information system for HIV to address these concerns. Among the needs identified the new system had to enable frontline health workers to make common patient registrations, capture demographic details, be able to store patients' past medical histories,



enable documentation of follow-up visits, capture laboratory investigations, as well as to document prescription and dispensing of drugs. In 2012, a “roadmap” was finalised, culminating in the identification of three systems to be piloted in line with the needs for a new health information system. Of the three piloted systems the system developed by the University of Dar es Salaam, Tanzania was selected and rolled out to three facilities in 2012- a quaternary, a provincial, as well as at a district hospital. In 2013, it was rolled out to 85 facilities throughout the country that had the highest caseloads of HIV patients, by volume of clients on ART (UNDP, 2014). By the end of 2016, the same system was at 583 high-volume HIV clinics, representing 37% of the 1566 facilities providing HIV services at the end of 2016 (MOHCC, 2017). However, it is important to note that although the ePMS is operational at just 37% of HIV facilities, due its rollout that targeted high volume facilities, clients on the ePMS represent a disproportionately higher 72% of the total clients in care- 700,000 clients on the ePMS out of a total of 975,667 in absolute figures (MOHCC, 2017). This current arrangement lends itself well to the purpose of the study- to ascertain uptake of Isoniazid Preventive Therapy (IPT) at the highest volume HIV facilities in the country.

Currently, the process of data collection on this system is such that clinicians update records on a paper-based record dubbed “the chronic care booklet” and less formally the “green booklet” as they attend to a patient; it is then sent to a data entry officer who then updates the system with the same information. The ePMS is essentially a duplicate of this “green booklet”. Plans are to eventually do away with these paper-based green booklets and then proceed to use the ePMS directly at the point of care, as a client is being attended to, in a process dubbed “de-commissioning”.

None of the 583 facilities are virtually connected to the central database managed from head office, although plans are at an advanced stage to get these facilities connected through a “Local Area Network” to enable real time submission of reports at the end of each month. Currently, once the data entry of a particular review period, usually a month, is complete at the facility the data is exported into a more up-to-date backup of the data that is then submitted to the next reporting level through use of flash drives. At this next level, management delete the previous backup for this particular facility and replace it with the more recent version. A similar process takes place at the next level, and ultimately at central level- with a new backup each month. This national level database will be the data source for this study.

Regarding information contained on the ePMS, there is a myriad of data points including, but not limited to,

- Health system- province, district, facility level, HIV caseload,
- Patient level- age, sex, address, education level attained, clinical history (WHO clinical stage at enrolment), date of enrolment, clinical issues at presentation, whether on ART or not, whether screened for TB or not, and whether on IPT or not,

This readily-available wealth of data is amenable to manipulation and analysis to identify, if any, factors that are a barrier or facilitator of IPT implementation. This explains why this platform was selected to carry out this exercise.

### 3.3 Study Design

Through a secondary data analysis of the electronic patient monitoring system (ePMS), an analytical cross-sectional study was carried out in order to establish the coverage of IPT among clients that are eligible for it. Detels et al. (2009) identify one of the foci of cross-sectional studies in the community as being that of monitoring of programme activities, like the IPT programme, and the surveillance of changes within such programmes, leading to an evaluation of their effectiveness. In the same chapter they identify cross-sectional studies as being able to provide information that will contribute to the planning and coordination of services, like IPT; to the effective implementation of care, for example for that provided for PLHIV; as well as to decision-making on the continuation and modification of those services depending on findings of the same studies (Detels et al., 2009).

This kind of study has the additional advantage of enabling the identification of certain demographics of the population that are not being adequately covered by the IPT programme through sub-analysis of IPT coverage among the eligible population after having disaggregated by sex, age, geographical region, and type of facility (Goldberg, McManus, & Allison, 2013). This would be necessary as a recent population-based HIV impact assessment demonstrated inequity of uptake of HIV services across the whole cascade with males having lower uptake of testing, treatment and viral suppression; while younger age groups, for example, demonstrated lower levels of viral suppression (ICAP Zimbabwe, 2016). In addition, similar differences were noted across the different provinces of the country- emphasising the need to identify these demographics to enable intentional targeting of these marginalised groups with interventions to improve uptake of IPT (ZIMSTAT, 2016). As a



corollary to the above, this kind of study will also enable the identification of any factors, if any, associated with higher uptake of IPT. The intention then would be to use the findings from the study to make appropriate recommendations to address any inequities identified associated with IPT uptake.

Variables studied to establish associations with uptake of IPT are summarised in Table 1 below.

TABLE 1: PATIENT AND FACILITY VARIABLES ANALYSED FOR ASSOCIATIONS WITH IPT UPTAKE

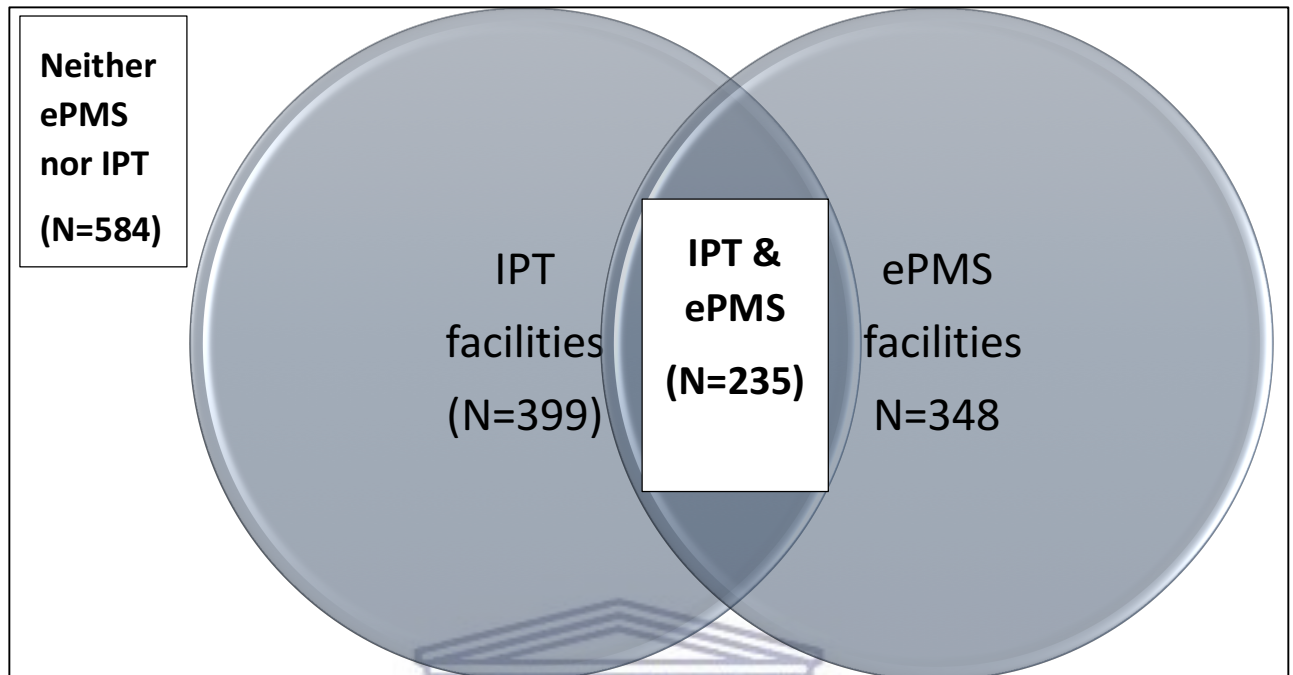
Patient variables	Facility variables
Sex	Level of health facility(primary, secondary, tertiary, quaternary)
Age	HIV caseload
Functional status	Province
WHO clinical stage	Facility distribution (rural or urban)
Pregnancy status among women	
ART status	
Duration since enrolment into chronic HIV care	
Education level	

### 3.4 Population and Sampling

The fact that 72% of the clients on ART and pre-ART in Zimbabwe are on the electronic Patient Monitoring System (ePMS) offers an optimal opportunity for secondary data analysis to establish how effective the implementation of the IPT policy has been among clients enrolled into chronic HIV care.

Two points are worth noting, the first being that, due to logistical challenges, the IPT policy is not being implemented at all facilities that offer HIV services in Zimbabwe. Of the 1566 facilities that offered HIV services in 2016, only 634 of these also additionally offer IPT services, translating to a 40% of facilities. Second, the ePMS is also not available at all facilities that offer HIV services. It is currently available at 583 facilities of the 1566 total facilities that offer HIV services, representing 37% of HIV facilities. The secondary data

analysis will therefore focus on the unique subset of facilities that have both the ePMS as well as offering IPT services (see Figure 1).



**FIGURE 1: SUMMARY OF DISTRIBUTION OF FACILITIES BY ePMS, IPT, AND OVERALL HIV SERVICE PROVISION**

From the ePMS, any records that satisfy the inclusion and exclusion criteria of this study as outlined below were included in the analysis- there was no further sampling from these record. For the descriptive part of the analysis specifically to establish uptake of IPT, the inclusion criteria were,

**Inclusion criteria**

1. Confirmed PLHIV of all ages seen at least once in the selected clinics during review period.
2. Active TB disease ruled out through TB Screening.
3. Seen between the 01<sup>st</sup> July 2016 and the 31<sup>st</sup> December 2016.

**Exclusion criteria**

1. Hypersensitivity/allergy to Isoniazid.
2. Clients with active hepatitis (contraindication to Isoniazid)

3. Chronic alcoholics diagnosed through the CAGE questionnaire (contraindications). The “CAGE” acronym stands for 4 yes/no items constituting the screening test as described below:

- i) Have you ever felt that you ought to **Cut down** on your drinking?
- ii) Have people **Annoyed** you by criticizing your drinking?
- iii) Have you ever felt bad or **Guilty** about your drinking?
- iv) Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (**Eye-opener**)? (Dhalla & Kopec, 2007)

An alcoholic has a higher chance of not only having active liver disease, but also having adherence problems once initiated on IPT (Bruha, Dvorak, & Petrtyl, 2012; WHO, 2010). The ePMS captures a data point called “heavy alcoholism” as one of the reasons for not initiating IPT, clinicians would make this diagnosis using the CAGE questionnaire above and then document on the ePMS whether this was a reason for not initiating.

4. History of convulsions and psychosis. This is because Isoniazid can induce both (Aiwale, Patel, Barvaliya, Jha, & Tripathi, 2015; Alao & Yolles, 1998; Coyer & Nicholson, 1976; Prasad, Garg, & Verma, 2008).
5. Concomitant use of phenytoin, carbamazepine, warfarin, theophylline, disulfiram, SSRIs and ketoconazole. This is because isoniazid interacts with how these medicines are excreted in the liver through the Cytochrome P450, making these medicines reach higher blood and tissue levels when taken at the same time as Isoniazid (Desta, Soukhova, & Flockhart, 2001).

### 3.5 Data Collection

This process began after all the necessary permissions from the Ministry of Health and Child Care, as the sole proprietors of the data had been granted.

As this is a secondary data analysis of already available data, the data collection process involved the running of queries and filters on the ePMS backups of 206 of the 235 facilities with both ePMS and also implementing IPT. The balance of 29 facilities were from one province, Mashonaland West, which did not have backups that covered the period of analysis. The outputs of the queries were exported into Microsoft Excel files with data in Comma

Separated Values (CSV) format with each patient as a row on the spreadsheet. Each of the nine subnational regions that had data, called provinces, ended up with separate Excel spreadsheets with data for facilities and patients falling within their jurisdiction.

### 3.6 Post-Abstraction Data Cleaning

Before the raw data exported from the ePMS was analyzed, it was assessed to ensure that it was of high quality in terms of completeness, and accuracy. Data representing an individual client, in the form of an individual row on the Excel spreadsheets described above was assessed before it was imported into STATA. Specifically, any client data that did not have the unique identifier, the client age, or sex was excluded before analysis. Specific numbers removed are summarised in the flowchart in the Results chapter. Without these very basic individual descriptors it was difficult to identify and eliminate duplicates. The number of files that fit this description and were removed prior to analysis are shown in the first part of the next chapter.

With this process completed, with the data still in the CSV format on Excel, the next stage was identifying duplicates and deleting copies. The only way to do this was to highlight the column with the patients' unique identifiers, then on the "Home tab", selecting "conditional formatting", then "Highlight cell rules", and finally, "Duplicate values". The plan was that once these had been identified, the row with the more complete data points would be kept while the other row would be deleted. No duplicates were identified through this process. Finally, the data was then imported from the Excel sheets onto STATA13.

### 3.7 Analysis

Analysis was carried out over three stages, the first of which was initial descriptive analysis of the participating patients and facilities- median age with interquartile range; sex distribution; pregnancy status; WHO status; distribution of patients and facilities by level of care, by geographical region, by urban/rural location, as well as by HIV caseload of facilities. Before proceeding to further analysis several numerical variables had to be converted to categorical ordinal variables. Age was converted into equal ten-year bands as is routinely reported in the health system. "Duration enrolled in care" and "Duration on ART" were each divided into three categories, those within the first three years, four to seven years, as well as eight years or more. This was based on discussions with the HIV Programme management who felt the need to compare uptake of IPT for the newer to the more mature cohorts and test

whether newer cohorts needed differentiated care especially focusing on them to improve uptake in line with the normative guidance around Differentiated Service Delivery (DSD) models from WHO (WHO, 2016). Similarly, “HIV caseload” was divided into those facilities that attended to up to 1000 PLHIV on ART and those that attended to larger caseloads. This again was based on discussions from the same meeting with HIV Programme management that is now shifting classification of HIV facilities into high and low volume from the previous cut-off of 250 to the 1000 done in this analysis.

Second, addressing objective one of the study, a descriptive analysis to merely establish the uptake of IPT, the primary outcome. This was expressed as a percentage- with eligible clients that received IPT being the numerator, and the total eligible clients for IPT being the denominator (less those on TB treatment, presumptive cases of TB that were being investigated for TB, and those contraindicated to IPT). This can be considered to be the period prevalence of IPT among those “at risk”

Addressing objective two and three of the study, an analytic statistical analysis sought to establish any associations between the IPT coverage and any patient-level factors as well as facility factors. This began by converting all the factors into categorical variables that were subsequently used to calculate “unadjusted odds ratios” with 95% confidence intervals and p-values. These “unadjusted odds ratios” would then be used to approximate prevalence ratios. This process would facilitate simple binary regression to give an indication of the significance of the effect of the variable on IPT uptake before adjusting for potential confounding from other variables.

These “unadjusted odds ratios” described above under simple binary analysis were then inputted into a multivariable logistic regression model using stepwise regression analysis. This ultimately led to the intentional omission of “education level”, “pregnancy status”, as well as “duration on ART” from the final model.

It is also worth reiterating that while odds ratios in cross-sectional studies are inherently intuitive to interpret, they tend to generally overestimate the prevalence ratio and therefore need to be interpreted with caution (Barros & Hiraakata, 2003; Coutinho, Scazufca, & Menezes, 2008). These were used for this study as the uptake of IPT was very low (0.4%) and the effect of overestimation would be at its minimum (Coutinho et al., 2008). Finally, multivariable logistic regression modelling was done using the stepwise approach, with all the variables included in the final model except for “education level”, “duration on ART” and

“pregnancy status”. This was used to identify independent predictors of IPT uptake at the 95% confidence interval and p-value cut-off of 0.05.

### 3.8 Validity and Reliability

With regards to validity, the convenient and ready availability of a massive sample of PLWHIV on the ePMS, representing over half of PLWH enrolled into care in Zimbabwe affords the chance to get not only an accurate measure of IPT coverage but a very precise one as well. Beyond this, by not sampling and using virtually all the patients in care at the facilities concerned to assess uptake of IPT, the likelihood of random chance affecting findings is somewhat eliminated. The high numbers abstracted also additionally enable the computation of IPT coverage for several strata like sex, ART status, WHO status, type of facility, sex, and other variables to a high degree of accuracy even within the strata. A big sample size of 345,414 after removing clients that did not meet the inclusion criteria, boosted the internal validity of the study, especially considering the number of facilities that participated in this study (205).

Clinicians and data entry clerks involved in generating and entry of data into the ePMS went through “Monitoring and Evaluation” trainings in which they were capacitated on how to enter, collate, compile, analyse and report data using the ePMS system. These trainings were facilitated by Strategic Information experts from the Ministry head office, and included in this training was the HIV context in which the monitoring and evaluation is being done, differences between monitoring and evaluation, introduction to data points and indicators, with exercises on data entry, collation, analysis and submission. As a quality assurance measure for the trainings, participants undergo a pre- and post-test to ensure that learning took place during the training. In addition, they are regularly mentored on-the-job. The same group of health workers have job aides, support and supervision, as well as standard operating procedures for performing these ePMS tasks. This meant that very few client records were excluded from analysis due to data incompleteness (1.4%). An argument can be made then based on this finding that, because of this, the data they generate is standardised and therefore reliable to a very high degree to enable this study’s results to be reliable and valid.

However, one aspect of the study potentially impacting reliability negatively is the aspect of intra and inter-observer variation in administering the screening question to rule out TB by the clinical staff. In spite of efforts towards capacitating health workers to manage HIV and



implement IPT, it is not inconceivable that one health worker could administer the TB screening questions and classify the client as a presumptive case of TB while another, in that same scenario, would have said the client is not a presumptive case. This is especially so because, in an effort to develop all-round competent clinicians, a policy decision was made to rotate staff within different departments in a facility so they can be exposed to, and subsequently become competent, in different aspects of health service delivery. The unintended consequence of this though is that, at any given time, the HIV departments in which IPT is to be delivered will have staff with less than ideal clinical competencies because they are coming from another department and are yet to be adequately trained to competently work there. This variability in classification of clients in terms of them being a presumptive TB case or not would then lead to a measurement error of making presumptive and non-presumptive cases of TB more homogenous called “non-differential misclassification”. This would tend to cause a “Type 2 Error”- concluding that there is no association when there is an association between variables being analysed for in this study and uptake of IPT.

As mentioned in an earlier section, the ePMS rollout targeted bigger and busier facilities over smaller ones. This would affect the external validity in that the findings of this study could not be reasonably expected to be extrapolated to these smaller facilities as these are bound to be inherently different. Additionally, the study findings would only apply to PLWHIV that know their status and are enrolled into care. It would not be reasonably generalised to PLWHIV that do not know their status and/or are not yet enrolled in care.

### 3.9 Ethics Considerations

The study, being secondary data analysis of the Ministry of Health’s ePMS, did not involve interacting with patients and/or frontline health workers for the purposes of data collection or otherwise. Therefore, there was no participant information sheet used, neither was there a consent form. However, as mentioned earlier, all necessary permissions were requested and approved by the Ministry of Health and Child Care of Zimbabwe- sole proprietors of the data; along with ethical approvals from the Medical Research Council of Zimbabwe as well as the University of Western Cape’s Bio-Medical Research Ethics Committee (BMREC).

Notwithstanding, the study was to be undertaken on a substantial number of clients’ personal level data. Mishandling this data may have been so intrusive as to impact concerned clients’ privacy and confidentiality. This is especially so as it involves a condition, HIV, that still has a lot of stigma in the country, both internal and external (ZNNP+, 2014). The study therefore



undertook to only keep data that could potentially be used to identify a client only up to the data cleaning stage of the study as this would enable de-duplication that could potentially occur during the period under review through formal transfers as described earlier. All data that could be used to identify a client, like the unique identifier used on the ePMS system, were removed before the data was exported onto STATA13. The computer(s) used for the purposes of the data cleaning as well as data analysis were password protected to prevent access by unauthorized individuals. The study also undertook to not report any results that pertain to the condition of a particular individual, but rather, only means and proportions as per original intention.

### 3.10 Summary of Methodology Section

In this chapter the ePMS was described both historically as well as current capabilities in terms of data points and its coverage of facilities. Justification for the use of a cross-sectional epidemiological study design to address the first objective i.e. IPT uptake; as well as identifying any factors associated with uptake in relation to the second and third objectives. The selection of facilities for the study was discussed, as well as for the individual participants. The study's internal and external validity, reliability was discussed. Data collection- from exporting from ePMS into a CSV file on Excel, its cleaning, importation into STATA13 and subsequent analysis was described before finally discussing the study limitations; and ethical considerations.

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# Chapter 4- Results

## 4.1 Chapter Synopsis

In this chapter results of the study will be described, initially with a summary of the process from abstraction to the analysis. Next, background characteristics of the participating PLHIV and facilities will be given. Results of bivariate analysis, using the chi-square, to assess if any variables have an association with IPT uptake will be presented. Similarly, results of simple binary and multivariable logistic regression analysis will be presented, this time using unadjusted and adjusted odds ratios. The level used for statistical significance was the 95% CI and p-value of 0.05. Independent predictors of IPT uptake will be marked in bold. Discussion of the results will be done in a separate chapter.

## 4.2 Abstraction to Analysis

As noted in Figure 2 above, and explained in the Methodology section, not all data was analyzed. Patients that were missing any of the following: unique identifier, sex and TB status, were not included in the analysis. Out of the total of 381,994 records abstracted from the ePMS, 5,493 records were removed due to lacking one or a combination of these critical data points.

Similarly, clients already on TB therapy, and who would therefore not benefit from prevention therapy for TB using IPT were also excluded by virtue of not being “at risk” of TB. These patients were not ineligible for IPT, a total of 7,820 records fit this profile.

The 20,636 (5,6%) clients seen at the facilities but not screened for TB were also not eligible for IPT based on the WHO and national guidelines described in earlier sections (MOHCC, 2013; WHO, 2010). This augurs well when compared to contemporary literature, with Musa et al. (2009) finding that 94% of clients in 60 facilities in Nigeria under a project called UMD/ACTION had not been screened for TB as an example.

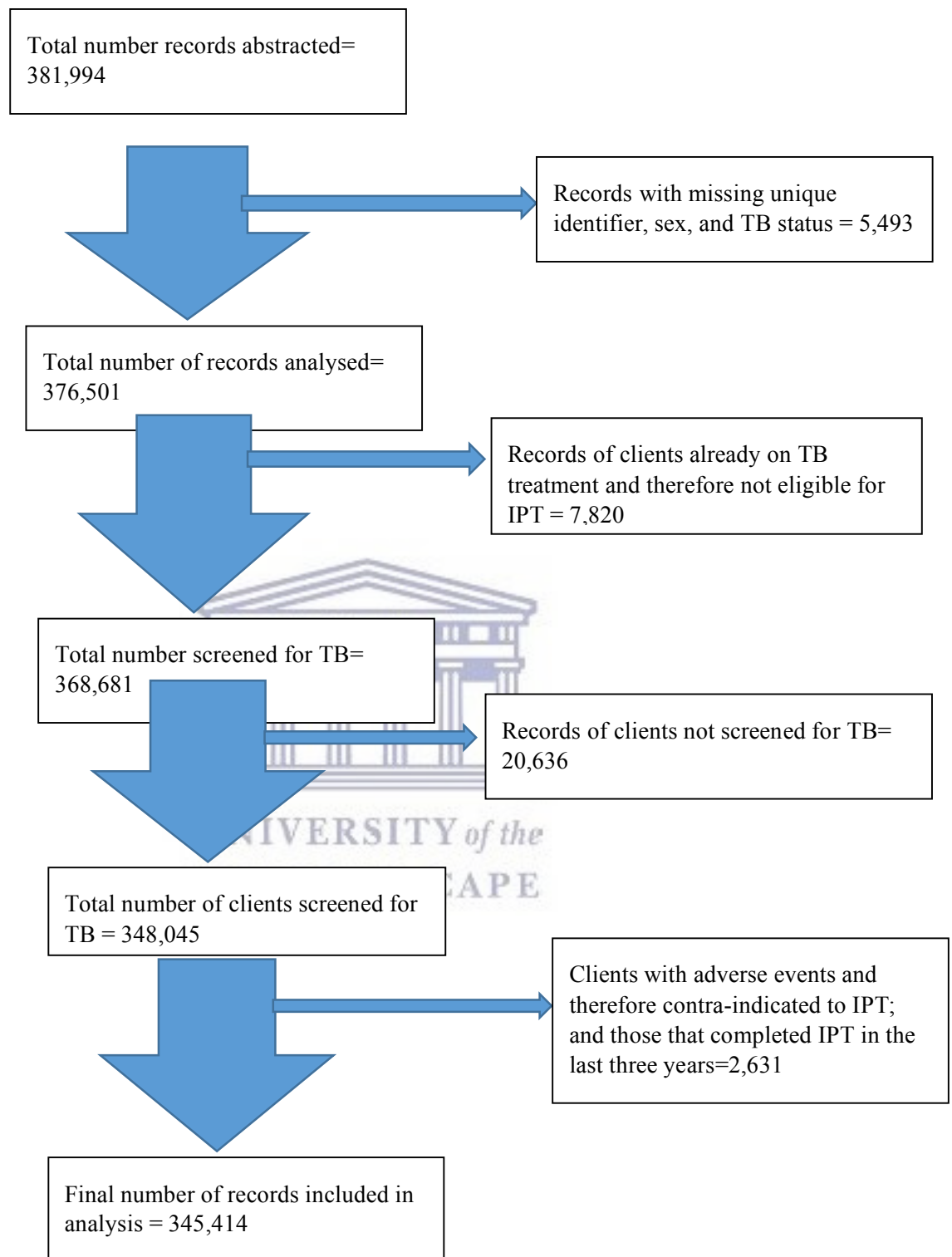
Finally, according to the guidelines described above, and as described under the sampling exclusion criteria, clients eligible for IPT but on other medication that interacts with Isoniazid were also not analyzed. Similarly, clients that completed IPT in the past three years do not need to be initiated on IPT and were also excluded from analysis. Records of clients fitting this criteria that were excluded from subsequent analysis amounted to a total of 2,631.

Notably, IPT data for facilities implementing both IPT and ePMS in one of the ten administrative provinces, Mashonaland West, were not immediately available. Therefore this data were also excluded because all efforts to access this data proved fruitless and would affect the completion of this minithesis. The total number of records that were available for the final analysis- 345,414 –was still substantial enough to enable analysis.



**FIGURE 2: FLOW DIAGRAM SUMMARIZING SELECTION PROCESS OF RECORDS BEFORE**

**ANALYSIS**



### 4.3 Background Characteristics of Clients and Facilities

From Table 2 below, the male to female distribution of clients shows a 36:64 ratio and is heavily distorted towards females, which does not reflect the population distribution in the country as the 2012 Census sex distribution was 48:52 (ZIMSTATS, 2012).

The median age of participants was 40 years (IQR 32-48). This tallies very well with the findings of the ZIMPHIA that also showed that the burden of PLHIV is mostly between 30 and 50 years, although the peak prevalence is earlier in females than for males (ZIMSTATS, 2016).

Amongst females, just over 8% of the records abstracted were pregnant during the period.

In terms of clinical status at enrolment (“WHO status”) the records analyzed show that the distribution is even between those presenting with clinical symptoms of HIV and those without symptoms at enrolment (AVERT, 2017).

About 89% of clients participating in the study are either working or at school, while the ambulant and bedridden comprised just over 10% at the last visit.

Of all the records analyzed, over 94% were of clients that had already been initiated on lifelong ART, with 5.7% on chronic HIV care but ART-naïve, traditionally called pre-ART. Only a miniscule figure had no data on this variable.

Worryingly, 71% of records of those on ART did not have a date for when they were initiated on ART, making the task of calculating their duration on ART difficult. Notwithstanding, for the 29% clients that had this data point, the majority were still relatively new having been on ART for periods less than three years. Those on ART for between 4-7 years constituted a quarter of those three years and less. An even smaller proportion (1.4%) was on ART for periods longer than seven years.

However, when the duration in chronic HIV care since enrolment is used rather than ART duration, the data completeness improves drastically. This variable includes both those on ART and the ART-naïve- as long as they are enrolled in HIV clinics. About 60% are records of clients enrolled less than three years before, with 31% being those of clients enrolled between four and seven years. Nine percent are those of clients enrolled more than seven years ago and a negligible amount without this data point.

Almost half the records did not have a documented education status.

The number of PLHIV seen at facilities beyond the primary health care level were 37%, with the balance being seen at this basic level. All subsequent analyses will therefore not further disaggregate facility level beyond “primary level” and “secondary and above”.

As expected, based on 2012 census data, Harare was the province that contributed the highest number of participants 72,490 (21%) for analysis. However, the three smallest provinces by population- Bulawayo and Matabeleland South and Matabeleland North (in that order)- did not contribute the least records as they coincidentally happen to be the three provinces with the disproportionately highest burden of HIV by prevalence of HIV (ZIMSTAT, 2016; ZIMSTATS, 2012)

The distribution of clients according to whether they receive care at urban or rural facilities was fairly even. It is difficult to unravel as the ZIMPHIA has not further disaggregated HIV burden beyond provincial level. Some rural provinces will have urban clinics in towns within them, making comparisons somewhat more complicated.

TABLE 2: BACKGROUND CHARACTERISTICS OF PLHIV AT THE 205 SITES IMPLEMENTING IPT AND EPMS FROM JUNE-DECEMBER 2016

Variable	Number of clients, n (%)
<b>Patients</b>	345,414 (100)
<b>Sex</b>	
Male	123,514 (35.7)
Female	221,900 (64.2)
<b>Age, (Median (Q1-Q3))</b>	40 (32 – 48)
0- 10 years	7,644 (2.2)
10- 20 years	14,937 (4.3)
20- 30 years	45,554 (13.2)
30- 40 years	103,525 (30.0)
40- 50 years	101,437 (29.4)
50- 60 years	47,476 (13.7)
60+ years	24,831 (7.2)
Missing	10 (0)
<b>Pregnancy status (women only)</b>	
Pregnant	16,890 (8.2)
Not pregnant	188,445 (91.8)
<b>WHO Clinical Stage for HIV</b>	
Stage 1 and 2	180,445 (52.2)

<b>Variable</b>	<b>Number of clients, n (%)</b>
Stage 3 and 4	164,490 (47.6)
Missing	479 (0.1)
<b>Functional status</b>	
Working/school	308,248 (89.2)
Ambulatory	35,607 (10.3)
Bedridden	1,157 (0.3)
<b>ART Status</b>	
Never initiated ART	19,680 (5.7)
Ever initiated ART	325,625 (94.3)
Missing	109 (0)
<b>Duration on ART</b>	
<3 years	75,992 (22.0)
4-7 years	19,666 (5.7)
8+ years	4,684 (1.36)
Missing	245,072 (71.0)
<b>Duration enrolled in care</b>	
<3 years	206,008 (59.6)
4-7 years	107,252 (31.1)
8+ years	32,127 (9.3)
Missing	27 (0.0)
<b>Education level</b>	
None	6,953 (2.0)
Primary level	50,030 (14.5)
Secondary level	115,728 (33.5)
Tertiary	9,079 (2.6)
Missing	163,624 (47.4)
<b>Health facility level</b>	
Quaternary, central	1,840 (0.5)
Tertiary, provincial	15,843 (4.6)
Secondary, district & mission	108,985 (31.6)
Primary, clinics and rural health centres	218,746 (63.3)
<b>HIV caseload at facility</b>	
<1 000 patients in care	73,017 (21.1)
1 000+ patients in care	272,397 (78.9)



Variable	Number of clients, n (%)
<b>Province</b>	
Bulawayo	44,579 (12.9)
Harare	72,490 (21.0)
Manicaland	13,896 (4.0)
Mashonaland Central	25,433 (7.4)
Mashonaland East	31,064 (9.0)
Masvingo	47,042 (13.6)
Matabeleland North	26,428 (7.7)
Matabeleland South	23,362 (6.8)
Midlands	61,120 (17.7)
<b>Facility distribution</b>	
Urban	176,877 (51.2)
Rural	168,537 (48.8)

Table 3 below shows the decentralization of HIV services that took place since 2004, almost 73% of facilities were of the primary level, with the balance of 27% being referral facilities, that is, secondary and above.

When the number of facilities that are busy with caseloads beyond a 1,000 PLHIV are compared to less busy facilities, the distribution is an almost even one, with the busy facilities contributing 53.7% of the total facilities analyzed.

The urban to rural disaggregation of facilities is nearly 1:4 in favour of rural.

**TABLE 3: BACKGROUND CHARACTERISTICS OF THE 205 SITES IMPLEMENTING IPT AND EPMS FROM JUNE-DECEMBER 2016**

Variable	Number of sites, n (%)
<b>Health facility level</b>	
Quaternary	1 (0.5)
Tertiary	5 (2.4)
Secondary	50 (24.4)
Primary	149 (72.7)
<b>HIV caseload at facility</b>	
<1 000 patients in care	95 (46.1)

Variable	Number of sites, n (%)
1 000+ patients in care	111 (53.9)
<b>Province</b>	
Bulawayo	15 (7.3)
Harare	25 (12.1)
Manicaland	10 (4.4)
Mashonaland Central	14 (4.9)
Mashonaland East	24 (11.7)
Masvingo	32 (15.5)
Matabeleland North	22 (10.7)
Matabeleland South	20 (9.7)
Midlands	44 (21.4)
<b>Facility distribution</b>	
Urban	47 (22.8)
Rural	159(77.2)

#### 4.4 Overall Uptake of IPT

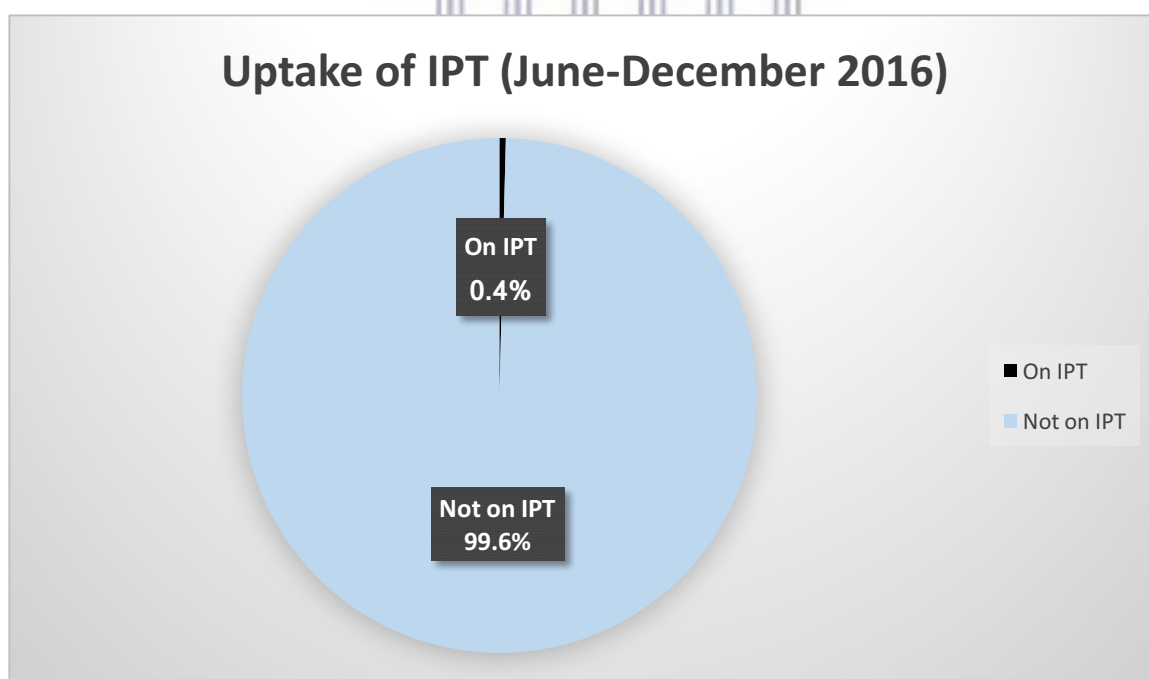


FIGURE 3 : OVERALL UPTAKE OF IPT AMONG PARTICIPATING CLIENTS (JULY-DECEMBER 2016)

Above pie-chart shows the overall level of uptake of IPT among the 345,414 clients whose data was analyzed for.

## 4.5 Bivariate Analysis of Factors Affecting IPT Uptake

As all the variables described under univariate analysis are categorical, including the outcome itself, bivariate analysis was carried out using the chi-square analysis to identify variables that are associated with uptake of IPT. All the variables were analyzed for except “duration on ART”- data for this variable was available for only 29% of clients analyzed.

As can be seen on Table 4, sex is a significant variable affecting uptake of IPT before the effect of other variables is adjusted for. When age is considered, the extremely low p-value shows that there is, in fact, a statistically significant association between age and uptake of IPT. When considering women only, IPT uptake is significantly associated with whether that woman is pregnant or not as shown by the near-zero value for this variable. The clinical status of clients at presentation, “WHO clinical stage” does not seem to be associated with uptake of IPT. Uptake of IPT was also strongly associated with clients’ ART status (whether ART-naïve or not), functional status (whether fully functional; or bedridden or ambulant), duration since being enrolled into care, as well as the highest educational level attained by the same clients as evidenced by p-values well below the 0.05 cut-off.

There were also significant associations with IPT uptake depending on whether clients were seen at a facility in a particular region of the country, how busy these facilities were with respect to HIV caseloads, as well as whether these facilities were urban or rural.

TABLE 4: BIVARIATE ANALYSIS BETWEEN STUDY VARIABLES AND UPTAKE OF IPT USING THE CHI-SQUARE METHOD (SIGNIFICANT ASSOCIATIONS IN BOLD)

Characteristic	On IPT	Not on IPT	Chi-square	Degrees of freedom	p-value
<b>Sex</b>					
Female	954	220,946	4.72	1	<b>0.03</b>
Male	470	123,044			
<b>Age</b>					
0- 14 years	8	13,979	126,90	6	<b>0.02</b>
15- 19years	10	8,584			
20- 29years	113	45,441			
30- 39years	424	103,101			
40- 50years	490	100,947			
50- 59years	258	47,218			
60+years	121	24,710			
<b>Pregnancy status (women only)</b>					
Pregnant	19	16,871	57.89	1	<b>&lt;0.001</b>
Not pregnant	927	187,518			
<b>WHO Clinical Stage</b>					
Stage 1 and 2	764	179,681	1.09	1	0.30
Stage 3 and 4	659	163,831			
<b>Functional status</b>					
Working/school	1,213	307,035	35.09	1	<b>&lt;0.001</b>
Ambulatory and bedridden	211	34,411			
<b>ART Status</b>					
Never initiated ART	26	19,654	39.92	1	<b>&lt;0.001</b>
Ever initiated ART	1398	324,227			
<b>Duration enrolled in care</b>					
<3 years	469	205,539	434.64	2	<b>0.03</b>
4-7 years	768	106,484			
8+ years	187	31,940			
<b>Education level</b>					

Primary level and below	124	56,859	10.33	1	<0.001
Secondary level and above	378	124,429			
<b>Health facility level</b>					
Secondary and above	516	126,152	0.12	1	0.73
Primary level	908	217,838			
<b>HIV caseload at facility</b>					
<1 000 patients in care	82	72,935	202.97	1	<0.001
1 000+ patients in care	1342	271,005			
<b>Province</b>					
Bulawayo	619	43,960	1533.60	8	<0.001
Harare	215	72,275			
Manicaland	1	13,985			
Mashonaland Central	2	25,431			
Mashonaland East	105	30,959			
Masvingo	46	46,996			
Matabeleland North	46	26,382			
Matabeleland South	3	23,359			
Midlands	387	60,733			
<b>Facility distribution</b>					
Urban	890	175,987	72.98	1	<0.001
Rural	534	168,003			

## 4.6 Simple Binary and Multivariable Logistic Regression Analysis of IPT Uptake

This section looks at patient-level and facility-level factors in turn.

### 4.6.1 Patient Level Variables Related To IPT Uptake

In terms of uptake of IPT by sex, see Table 5, there was a lower uptake of IPT by males which was statistically significant on simple binary analysis (OR 0.89, 95% CI: 0.86-0.92), but not so after multivariable logistic regression modelling.

Bivariate analysis had already shown that IPT uptake was associated with age using the chi-square method. Multivariable logistic regression corroborate this and show that clients 0-14years (aOR 0.16, 95% CI: 0.06-0.44); 15-19years (aOR 0.23, 95% CI: 0.08-0.63); 20- 30

years (aOR 0.62, 95% CI: 0.46-0.82) had significantly lower uptake of IPT when compared to their 50-59year old counterparts after adjusting for potential confounding.

With regard to functional status “ambulatory and bedridden” clients were significantly more likely to be put on IPT when compared to their working and school-going peers (OR 1.13, 95% CI: 1.08-1.19), and this was statistically significant before adjusting for other variables. However, this was not an independent predictor of IPT uptake after multivariable logistic regression.

Non-pregnant women living with HIV were more likely to be initiated on IPT than pregnant women and this was a statistically significant finding (OR 1.10, 95% CI: 1.02-1.18). However, this variable was not included in the final regression model to adjust for confounding.

In terms of the clinical picture at presentation, clients that presented to HIV clinics earlier before exhibiting any clinical symptoms had statistically significant higher uptake of IPT both before and after logistic regression (aOR 1.14, 95% CI: 1.05-1.23).

Clients already on ART (including having their regimens changed for whatever reason) had a significantly higher uptake of IPT when compared to the ART-naïve peers. However this effect was not sustained after multivariable regression modelling (aOR 0.99, 95% CI: 0.88-1.11).

For all clients in care analyzed for using logistic regression, clients enrolled into care for longer periods had a higher uptake of IPT than those on shorter duration across all the ranges analyzed for and this effect was sustained even after logistic regression. For those 4-7years since enrolments (aOR 1.21, 95% CI: 1.12-1.30), while for the more than eight years since enrolment (aOR 1.32, 95% CI: 1.16-1.50). This corroborates findings from the bivariate analysis described earlier.

#### 4.6.2 Facility Level Variables Associated With IPT Uptake

When the level of sophistication of health services described in the literature review is analyzed as a variable, those enrolled at higher levels of care had a significantly lower uptake of IPT when compared to those seen at primary level of care i.e. hospitals. The effect was significant after regression modelling, and in fact, was actually stronger after adjusting for potential confounding (aOR 0.46, 95% CI: 0.43-0.51).

Individuals enrolled at facilities with low HIV caseloads had significantly lower uptake of IPT compared to those enrolled in less busy facilities. This effect was sustained even after adjusting for potential confounding (aOR 0.49, 95% CI: 0.44-0.54).

There is geographical regional variation for uptake of IPT which was significant across all regions, when compared to Bulawayo, both before and after multivariable regression modelling except for Matabeleland North. However it is worth noting that one of the provinces- Mashonaland West- did not have any data for this analysis for reasons described earlier. In addition, Manicaland, Mashonaland Central and Matabeleland South had very few clients initiated on IPT that made their confidence intervals extremely wide.

The final variable assessed for association with IPT uptake was setting of the health facility with respect to whether it is situated in an urban or rural setting. As can be seen below, patients enrolled in facilities in urban settings had significantly higher likelihood of being initiated on IPT than their peers in facilities situated in rural settings (aOR 1.66, 95% CI: 1.47-1.87). This effect was sustained after controlling for other variables.

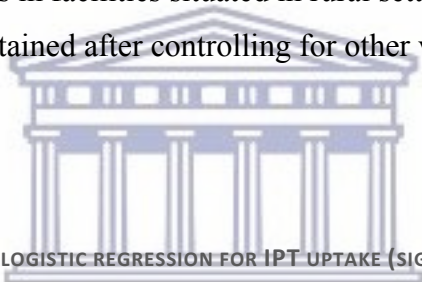


TABLE 5: OUTCOME OF MULTIVARIABLE LOGISTIC REGRESSION FOR IPT UPTAKE (SIGNIFICANT FINDINGS IN BOLD)

Characteristics	Number eligible for IPT	Number (%) on IPT	Unadjusted OR	p value	Adjusted OR	P value
<b>Sex</b>						
Female	221,900	954 (0.43)	Reference		Reference	
Male	123,514	470 (0.38)	<b>0.89 (0.86-0.92)</b>	<b>&lt;0.001</b>	8.76 (0.72-106.83)	0.089
<b>Age</b>						
50- 59 years	47,476	258 (0.54)	Reference		Reference	
0- 14 years	13,987	8 (0.09)	<b>0.99 (0.91-1.08)</b>	<b>0.003</b>	<b>0.16(0.06-0.44)</b>	<b>&lt;0.001</b>
15- 19 years	8,594	10 (0.12)	0.92 (0.82-1,02)	0.105	<b>0.23 (0.08-0.63)</b>	<b>0.005</b>



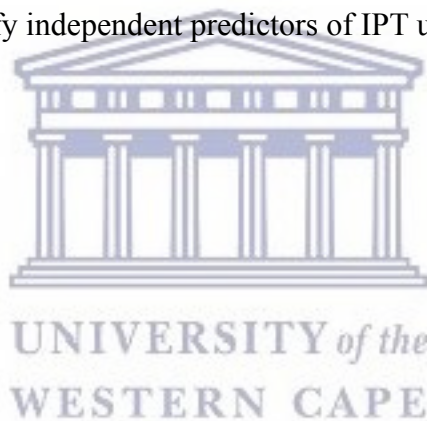
20- 29 years	45,554	113 (0.25)	0.96 (0.91-1.02)	0.219	<b>0.62 (0.46-0.82)</b>	<b>0.001</b>
30- 39 years	103,525	424 (0.41)	<b>1.06 (1.01-1.12)</b>	<b>0.015</b>	1.01 (0.81-1.25)	0.965
40- 50 years	101,437	490 (0.54)	<b>1.06 (1.01-1.11)</b>	<b>0.018</b>	1.05 (0.84-1.31)	0.664
60+ years	24,831	121 (0.49)	<b>1.17 (1.08-1.26)</b>	<b>&lt;0.001</b>	0.77 (0.54-1.11)	0.158
<b>Functional status</b>						
Working/school	308,248	1,213 (0.39)	Reference		Reference	
Ambulatory and bedridden	34,622	211 (0.61)	<b>1.13 (1.08-1.19)</b>	<b>&lt;0.001</b>	0.91 (0.73-1.12)	0.379
<b>Pregnancy status at eligibility</b>						
Pregnant	16,890	19 (0.11)	Reference			
Not Pregnant	188,445	927 (0.49)	<b>1.10 (1.02-1.18)</b>	<b>0.018</b>	N/A	
<b>WHO Stage</b>						
Stage 3 and 4	164,490	659 (0.40)	Reference		Reference	
Stage 1 and 2	180,445	764 (0.42)	<b>1.15 (1.13-1.16)</b>	<b>&lt;0.001</b>	<b>1.14 (1.05-1.23)</b>	<b>0.002</b>
<b>ART Status</b>						
Never initiated ART	19,680	26 (0.13)	Reference		Reference	
Ever initiated ART	325,625	1398 (0.43)	<b>1.34 (1.26-1.42)</b>	<b>&lt;0.001</b>	0.99 (0.88-1.11)	0.867
<b>Duration enrolled into care</b>						
≤3 years	206,008	469 (0.23)	Reference		Reference	
4 – 7 years	107,252	768 (0.72)	<b>1.32 (1.27-1.36)</b>	<b>&lt;0.001</b>	<b>1.21 (1.12-1.30)</b>	<b>&lt;0.001</b>

8+ years	32,127	187 (0.58)	<b>1.39 (1.31-1.48)</b>	<b>&lt;0.001</b>	<b>1.32 (1.16-1.50)</b>	<b>&lt;0.001</b>
<b>Education level</b>						
Primary and below	56,983	124 (0.22)	reference		reference	
Secondary and above	124,807	378 (0.30)	<b>1.04 (1.02-1.08)</b>	<b>&lt;0.001</b>	N/A	
<b>Health Facility Level</b>						
Primary	218,746	908 (0.42)	Reference		Reference	
Secondary and above	126,668	516 (0.41)	<b>0.96 (0.93-0.99)</b>	<b>0.015</b>	<b>0.46 (0.43-0.51)</b>	<b>&lt;0.001</b>
<b>HIV caseload at facility</b>						
1 000+ patients in care	272,397	1,342 (0.49)	Reference		Reference	
<1 000 patients in care	73,017	82 (0.11)	<b>0.25 (0.24-0.27)</b>	<b>&lt;0.001</b>	<b>0.49 (0.44-0.54)</b>	<b>&lt;0.001</b>
<b>Province</b>						
Bulawayo	44,579	619 (1.39)	Reference		Reference	
Harare	72,490	215 (0.30)	<b>0.49 (0.46-0.51)</b>	<b>&lt;0.001</b>	<b>0.30 (0.26-0.34)</b>	<b>&lt;0.001</b>
Manicaland	13,896	1 (0.01)	<b>0.72 (0.67-0.78)</b>	<b>&lt;0.001</b>	<b>0.52 (0.43-0.63)</b>	<b>&lt;0.001</b>
Mashonaland Central	25,433	2 (0.01)	<b>0.09 (0.08-0.11)</b>	<b>&lt;0.001</b>	<b>0.13 (0.10-0.18)</b>	<b>&lt;0.001</b>
Mashonaland East	31,064	105 (0.34)	<b>0.63 (0.58-0.68)</b>	<b>&lt;0.001</b>	<b>0.71 (0.58-0.87)</b>	<b>0.001</b>
Masvingo	47,042	46 (0.17)	<b>0.04 (0.03-0.05)</b>	<b>&lt;0.001</b>	<b>0.06 (0.04-0.08)</b>	<b>&lt;0.001</b>
Matabeleland North	26,428	46 (0.17)	<b>0.77 (0.73-0.82)</b>	<b>&lt;0.001</b>	0.94 (0.78-1.14)	0.538
Matabeleland South	23,362	3 (0.01)	<b>0.08 (0.07-0.10)</b>	<b>&lt;0.001</b>	<b>0.07 (0.05-0.10)</b>	<b>&lt;0.001</b>

Midlands	61,120	387 (0.63)	<b>0.53 (0.50-0.56)</b>	<b>&lt;0.001</b>	<b>0.68 (0.56-0.81)</b>	<b>&lt;0.001</b>
<b>Facility distribution</b>						
Rural	168,537	534 (0.32)	Reference		Reference	
Urban	176,877	890 (0.50)	<b>2.00 (1.92-2.04)</b>	<b>&lt;0.001</b>	<b>1.66 (1.47-1.87)</b>	<b>&lt;0.001</b>

## 4.7 Summary

In this chapter a summary of the process from abstraction to the analysis was made through a flow diagram. Background characteristics were summarised, of both the participating PLHIV as well as facilities. Bivariate analysis was done to identify factors significantly associated with uptake of IPT using the chi-square test. Simple binary and multivariable logistic regression were used to identify independent predictors of IPT uptake using unadjusted and adjusted odds ratios.



# Chapter 5 - Discussion

In this chapter a discussion of the findings will be presented including an analysis of the extent to which each of the three objectives was achieved based on the study findings. For each of the three objectives comparisons will be made between the study findings and those from other research both on the continent and globally.

Based on the gaps in knowledge related to implementation of the IPT policy, the following objectives were outlined for this minithesis;

- Establish the coverage of IPT among eligible PLHIV in Zimbabwe
- Identify patient factors associated with implementation of IPT
- Identify facility factors associated with implementation of IPT.

The next sections of this chapter will discuss each of these objectives in turn after a brief discussion of the data.

## 5.1 General findings

As mentioned previously, the male to female distribution of clients shows a 36:64 ratio is heavily skewed towards females. This could be simply a reflection of knowledge of HIV status which leans towards more women knowing their status. It could also be a reflection of the inequity in distribution of the HIV epidemic, in terms of both the incidence as well as the prevalence of HIV. One national public health impact assessment of HIV in Zimbabwe (ZIMPHIA) showed that HIV is more prevalent among females, at 16.7% (c.f. 12.4% for males). Similarly the annual of HIV incidence for females is 0.59% compared to 0.31% for males (ZIMSTAT, 2016).

A worrying data quality issue was the lack of documentation of education status for almost half of records analyzed. This is because education level has been shown to be an important factor in the uptake of preventive health services like immunization (Bugvi et al., 2014; Jani, De Schacht, Jani, & Bjune, 2008; Mohammed, 2015). However, for those with documented education level about 17% had education up to primary, while secondary level and beyond constituted 36%.

In the methodology section reference was made to the ePMS system targeting high volume facilities. This is further corroborated by the findings here in that 78.9% of the 345,414

clients analyzed for are being seen at HIV facilities that have HIV caseloads in excess of 1,000 clients per facility.

## 5.2 Coverage of IPT

The study found an uptake of IPT among eligible PLHIV of 0.4%. This is a less than ideal coverage of a preventive service proven to reduce especially morbidity and to a lesser extent mortality related to TB among PLHIV. This is in spite of applying the very strict criteria of eligibility as outlined by the WHO and national guidance (MOHCC, 2013; WHO, 2012) on who would be included as the “population at risk” of developing TB that would benefit from the six months of Isoniazid.

This low uptake is partly explained by the fact that since the piloting of the IPT program at ten facilities in 2013, the rollout has been growing exponentially as shown in Table 4 below. Therefore, this means that at the time of performing this study 78% of facilities just recently begun implementing the IPT policy. Their uptake would predictably be expected to be low, if not downright non-existent as facilities had recently begun implementation. This is corroborated by Teklay et al. (2016) who found that facilities that implemented rollout earlier had better uptake of IPT than the newer facilities although this was not statistically significant. A more refined analysis comparing IPT uptake by duration of implementation of the policy would have been ideal, as would have restricting the analysis to only the facilities that implemented in 2013 and 2014, but this information was not available from the ePMS nor was it availed on request and therefore this analysis was not possible.

TABLE 6: ROLLOUT OF IPT SHOWING CUMULATIVE NUMBER OF FACILITIES BY YEAR

Year	Cumulative number of facilities implementing IPT policy
2013	10
2014	46
2015	142
2016	634

Getahun et al. (2010) described the phenomenon of suboptimal uptake of IPT. In their paper they describe how very few countries were reporting IPT coverage in 2008, and how the few that did were reporting coverages among PLHIV of less than one percent. The MOHCC in Zimbabwe itself also reported concerns related to implementation of the IPT policy in the HIV Treatment and Care preliminary 2015 Annual Progress Report by noting that since the launch of the IPT policy in 2013 only 39,264 clients had been put on IPT out of the 879,271 that were on treatment at the time, translating to an uptake of 4.4% (MOHCC, 2016). The difference of a factor of ten with this study is easily explained by the fact that the 39,264 clients reported is a cumulative figure from when pilot begin in 2013, rather than of PLHIV who were on IPT at that point in time. Cronin et al. (2015) found a similar rate of uptake of less than one percent of eligible clients on IPT in Swaziland.

In 2013-14 in Shurugwi district, Makoni et al. (2015) found a much higher IPT coverage of 54% albeit among PLHIV that were on ART, a different population to that of this study which included those on ART as well as an ART-naïve group of PLHIV. This alone, along with the notable fact that the Makoni et al. (2015) study was done in only one district in the country as well as at a different time could explain the differences in uptake of IPT. Further, Makoni et al. (2015) performed their study on a mixture of ePMS and non-ePMS facilities also helping to further explain the discrepancy noted.

## 5.2 Patient Variables Associated With IPT Uptake

Three patient variables studied were found to independently predict uptake of IPT;

- Age
- WHO clinical stage at presentation
- Duration in care since enrolment into HIV care.

In the study, age groups from 0-29 years had a significantly lower uptake of IPT when compared to the older cohorts of clients. This is not surprising. For both conditions studied in this minithesis- TB and HIV- the paediatric age group has received, and indeed continues to receive, less coverage of lifesaving services to reduce Disability-Adjusted Life Years (DALYs) related to both conditions than their older counterparts above 30 years (Abrams & Strasser, 2015; Newton, Brent, Anderson, Whittaker, & Kampmann, 2008; eHospice, 2014).

The phenomenon of higher uptake of IPT by the clinically well PLHIV has not yet been corroborated by other studies. Further insights into this could be provided by both qualitative

and quantitative studies. To speculate, health workers might be more motivated to offer IPT to a clinically sound client compared to an ill one. Teklay et al. (2010) showed that clinicians were less likely to offer IPT because of fears of causing Isoniazid resistance by administering it to a client with active TB that would be clinically unwell. From a programming perspective, this would be a desirable finding. IPT is essentially secondary prevention of TB disease (Matias & Lozada, 2013). Therefore the earlier it is administered to “populations at risk” the better the overall performance of the programme. Waiting to administer IPT until clients’ risk profile for TB disease is very high would therefore defeat this endeavor. Identifying a potentially harmful precursor earlier before it has caused harm is in everyone’s best interest and should be rightly encouraged.

Clients that had been in care for longer demonstrated higher uptake of IPT compared to their counterparts that were newer to care. Again there is paucity of literature both regionally and globally on this and this issue would warrant further research to shed more light on it. All things considered, it is not unexpected that a client that is still active in care and adherent to other HIV management protocols would have a good relationship with health workers were they are seen. They would then be more likely to accept IPT when offered compared to a newly enrolled client that is still yet to establish a good relationship with health staff. Omesa et al. (2016) showed that a client that had a good relationship with the health workers was significantly associated with higher IPT uptake.

Although being ART-naïve proved not to be significant in affecting IPT uptake after adjustment for potential confounding, Durovni et al. (2010) found this to be a significant factor. In their paper they speculate that ART-naïve are less accustomed to taking daily medications, and are therefore less likely to accept IPT when offered, or to complete it successfully when started.

Similarly, for preventive services such as IPT, a higher educational status is associated with a higher uptake of preventive services like vaccinations and IPT (Bugvi et al., 2014; Jani et al., 2008; Mohammed, 2015). This was a finding of this study as well, although it was not significant after adjusting for potential confounding. A total of 47% of PLHIV in this study not having this data point might have led to this.

Other patient factors found in research to affect IPT uptake are fear of acquiring TB, receiving health education about benefits of IPT, and a good relationship with the healthcare worker offering the service (Omesa et al., 2016). The first two are not available on the ePMS



for this study to corroborate, while the third, that of a good relationship between health worker and client affecting IPT, was at least indirectly demonstrated in this study through the “duration in care since enrolment” variable. The hypothesis here would be that clients that have spent longer durations at the facility have better continuity of care, and therefore have better IPT uptake (Sudhakar-Krishnan & Rudolf, 2007).

Uptake of IPT was significantly higher for PLHIV with at least a secondary education and above when these were compared to group that had attained lower levels of education (OR 1.04, 95% CI: 1.02-1.08). However, this result needs to be interpreted with care as 47% of clients were missing data on this variable, and these are bound to be different from the ones that did. For this reason, this variable was also not included into the final regression model.

### 5.3 Facility Variables Associated With IPT Uptake

Similar to patient variables identified that independently predict IPT uptake, several facility level variables were also identified to independently predict higher IPT uptake, as part of a model including all factors;

- Level of facility (Primary care level with higher uptake)
- HIV caseload of facility (1 000 clients in care with higher uptake)
- Geographical region the facility is situated in
- Whether the facility is in an urban area or rural.

PLHIV seen at facilities offering the most basic services in the hierarchy of the Zimbabwean health system had a significantly higher uptake of IPT when compared to hospitals. In contrast, the Ethiopian study between 2011 and 2014 showed hospitals to have had a higher uptake of IPT when compared to small facilities, although this finding was not statistically significant (Teklay et al., 2016).

In terms of how busy the facilities were as measured through HIV caseloads, clients seen at busier facilities had significantly higher uptakes of IPT compared to the less busy counterparts. This is yet another finding that needs further investigation as it is quite paradoxical. Intuitively, it would be expected that busy facilities would tend to be overwhelmed with work and therefore less likely to take up an additional service that would further make the workload there more precarious. O’Neill et al. (2015) demonstrated a similar finding among clinics offering HIV services in New York State. When they compared

how well facilities adhered to the state HIV guidelines, they found that facilities that had caseloads of less than 20 clients had poorer adherence to guidelines when compared to the busier clinics with more than 20 clients (O'Neill et al., 2015).

The fact that facilities situated in different regions had significant differences in the uptake of IPT was expected. The ZIMPHIA referred to in earlier sections has shed a lot of light on the presence of regional variations of not only differences in prevalence and incidence of HIV, but also differences in terms of uptake of HIV testing, ART initiation and viral suppression (ZIMSTAT, 2016). It is therefore not surprising that uptake of IPT would follow similar trends as IPT is a service offered within an HIV service delivery setting. Bulawayo had the highest IPT uptake. This trend was significant both before and after multivariable logistic regression except for Matabeleland North. Midlands, the province with the second highest uptake of IPT, also happens to be the setting for the Makoni et al. (2015) study. The team found a much higher uptake of IPT than this study, although in their study they only considered PLHIV that were also on ART. In addition, Shurugwi was one of the pilot districts, while this study assessed uptake for facilities that were in the pilot and also ones that began implementation very recently (Makoni et al., 2015).

Facilities in urban areas had significantly higher uptake of IPT than their rural counterparts both before and after multivariable logistic regression. This is not unheard of. In Canada, Jandoc et al. (2016) noted consistently higher uptake of new formulations of several medicines among urban populations than with rural populations (Jandoc, Mamdani, Lévesque, & Cadarette, 2016). There is however a paucity of literature explaining the mechanism at play.

Other facility level factors noted in literature to affect IPT uptake include a health worker issues like lack of supervisory capacity, fear of toxicity to Isoniazid (INH), fear of generating INH-resistant strains of TB, lack of standardised tools to track IPT, as well as competing priorities at the point of service delivery (Getahun et al., 2010). None of these factors have variables in the current ePMS that could be used to refute or corroborate- even through use of proxies.

## 5.4 Study Limitations

This study was originally intended to include all PLHIV from IPT-implementing facilities with ePMS across the country. However, data from one of the ten provinces- Mashonaland West- was not available even after a month-long effort to access the data. However, due to

the impressive amounts of data from the other nine provinces in terms of both numbers of facilities and numbers of patients themselves the sample sizes proved more than adequate for the purposes of this minithesis although inferences of the results cannot be made about IPT uptake in the province that did not provide data.

The epidemiological study design selected for this minithesis, an analytical cross-sectional study design, has several limitations that need to be borne in mind. One of these being that the IPT coverage is not static over time, but fluctuates as time progresses, with times in which it is well done, and other times when it may be done less effectively. So, timing of this study design will affect the results depending on the particular time chosen to implement it. What is obtained may not be necessarily true at another time. It could be reasonably considered that as the IPT policy implementation matured over time, and health workers more confident of its effectiveness, and clients less afraid of the adverse effects, that the uptake would improve over time. In this case, WHEN the study is done will affect the outcome, depending on whether the policy had been given a chance to “take” or “institutionalise”.

In relation to the third objective of the study, that of facility level factors affecting uptake of IPT, an analysis of health worker characteristics like their Knowledge-Attitudes-Practice (KAP) would have been insightful. This is because there are bound to be some differences in individual health worker implementation of the IPT policy both within a facility; as well as between health workers implementing the IPT policy working at different facilities.

However, by design, the ePMS does not afford an analysis with this level of granularity.

As noted in the results section, use of odds ratios to estimate prevalence ratios tends to overestimate the size of the effect. This is especially so when the prevalence of the condition being sought, or of the coverage of a service being calculated, is high. Fortunately, the coverage of IPT in this study, of 0.4%, is in the range in which this exaggeration of the effect is at its minimal (Barros & Hirakata, 2003; Coutinho et al., 2008).

Finally, having analyzed for IPT uptake only at facilities with ePMS has limitations in terms of any inferences made about IPT uptake at facilities without ePMS. This is because facilities offering IPT but without ePMS, whether intentionally or not, will be inherently different from their peers that have the ePMS. This will limit the external validity of the study. No reasonable conclusions can be made about IPT uptake at facilities without ePMS.

# Chapter 6: Conclusion and recommendations

## 6.1 Conclusion

The uptake of IPT in Zimbabwe, specifically at facilities with both ePMS and also implementing the IPT policy, was extremely low at 0.4% against a target of 100%. This uptake was significantly lower among the following patient variables- younger PLHIV, clinically unwell PLHIV at enrolment (WHO stage 3 and 4), as well as those new to care at their respective facilities. Facility level variables that were identified as independent predictors of lower IPT uptake were the health facility being a hospital rather than a clinic, having an HIV caseload of less than 1000 PLHIV in care at that facility, as well as the facility being situated in all the other provinces except Bulawayo. It goes without saying that both the marginalized groups of PLHIV in terms of IPT uptake, and underperforming facilities in terms of IPT uptake need systematic targeting to address these inequities in TB/HIV services. Suggestions are made in the next sections of the actions that can be taken.

## 6.2 Recommendations

### 6.2.1 Recommendations for data quality

In terms of data quality about 1.4% of records abstracted could not be analyzed as they were missing critical demographic information like sex and TB status. While this figure speaks to a decent level of data completeness, there is still room for improvement. Two data points had worrying levels of missing data- 71% of records of clients on ART that were analyzed for were missing date of initiation. Similarly, 47% of records were missing level of education of the client. This warrants urgent corrective action in the form of development of standard operating procedures to prevent such data gaps occurring in future as well as more frequent supportive supervision visits focusing on data quality. Some gaps in terms of timeliness of data submission to national level, partially due to the fact that these submissions are done by physically bringing the data to ministry through use of flash-drives, led to one province not being abstracted and analyzed for. Secure internet connectivity is required to enable timely data submission to enable use of data for action while it is still relevant.

## 6.2.2 Recommendations for overall IPT uptake

The target for IPT uptake among eligible populations is 100% (WHO, 2014; MOHCC, 2013). An IPT uptake of 0.4%, while partially explained by the phased rollout of the policy in which 80% of facilities assessed had only started a few months prior to this study, is low.

Efforts need to be made to improve the screening of PLHIV for TB to identify those infected early and institute therapy; as well as enable prescribing of IPT for those without the disease as per national and international guidelines referred to in earlier sections. Specifically, activities like trainings and mentorship of health workers on TB case management and IPT, developing IEC materials on TB screening and other TB/HIV collaborative activities, as well as availing IPT guidelines would go a long way in improving performance on TB screenings (Chehab, Vilakazi-Nhlapo, Vranken, Peters, & Klausner, 2012).

## 6.2.3 Recommendations for patient level factors

Speaking to the second objective of the study, younger PLHIV, clients with clinical symptoms at enrolment, as well as those are still new to care at HIV facilities were shown to have less likelihood of being on IPT. In addition to warranting further research into reasons for this, there is a need to intentionally and systematically target these three groups as further rollout of the IPT program is being carried out. For example, the Ministry of Health currently has several dynamic platforms for supporting children and adolescents on treatment that can be leveraged to not only educate children and adolescents on the benefits of IPT, but these platforms can also be used to deliver IPT to convenient locations for these groups. For the very young children that are still being seen at Family Child Centres for immunizations, the ministry of health can capitalize on these visits to market this intervention to the children's caregivers. For the adolescents, the Community Adolescents Treatment Supporters role can be reviewed to also include discussing IPT as well as supporting adolescents to adhere to prescribed IPT. Another option to consider includes sending of bulk Short Message Service (SMS) to younger groups of PLHIV hailing the benefits IPT (Cole-Lewis & Kershaw, 2010).

As was mentioned previously, having healthier cohorts- WHO clinical stage 1 and 2- being put on IPT is not necessarily undesirable. The whole point of a screening intervention is to identify potentially malevolent precursors and prevent them from progressing to cause morbidity and mortality. This finding should be disseminated as part of feedback to health workers at the annual IPT review meetings so that this practice continues.



To address the issue of clients that are new to care having lower uptake of IPT, the scope of primary counsellors needs to be revised so that their counseling services are not only about HIV and ART but also about benefits of IPT as this has been shown to improve IPT uptake (Woldeyohannes, Wasie, & Mulugeta, 2015). If the root cause for clients declining IPT is because of inadequate information on the benefits of IPT then counselling will address this gap, especially in the context of counselors specifically and intentionally targeting groups marginalized from preventive services like these cohorts that are new to care.

Development of Information, Education, and Communication (IEC) messages on IPT for both social media, print media and broadcasting would also empower PLHIV with information about the benefits of IPT. Finally, the clients that have been in care for long periods and now fully conversant about HIV programming, the so-called “expert patients” could form support groups with newer clients so that they mentor the newer clients about benefits of IPT, as well as issues of retention and adherence. Indeed such models have worked very well in prevention of vertical transmission of HIV from mothers to their children in a role in which they are called “mentor mothers” (Futterman et al., 2010).

#### 6.2.4 Recommendations for facility level factors

At the health system level, hospitals and facilities with HIV caseloads below 1000 PLHIV in care were shown to have lower IPT uptake. Further research needs to be done to unravel the mechanism by which this is happening so appropriate policy decisions can be made to address this inequity. Meanwhile, until this happens, what can be done right away is to arrange fora in which health workers from both high and low HIV caseload clinics can meet and exchange implementation ideas with their peers on IPT implementation. This “cross-pollination” of ideas has been shown to be effective as a teaching tool for health workers (Rooyen, Hugo, & Marcus, 2017). Exchange visits in which health workers visit their peers and see how they are implementing policies like IPT would be beneficial. The hosts as well as the guests can both “learn while they teach”.

A recommendation to address the geographic differences in IPT uptake is to convene monthly meetings with managers of these regions. The point of the meetings is two-fold. First, to facilitate diffusion of innovation through peer learning as referenced above. The slow-adopters begin to realize that implementation of IPT is not as difficult as they perceived because their peers are executing it well. Second, managers from the lower uptake regions

will be motivated to spur the health workers within their jurisdiction to action. This approach hinges on the competitive nature of managers.

If the lower uptake is mostly because rural populations decline IPT when it is offered, then rural clinics could add a health education session to their roster so that their clients will have a better understanding of the benefits of IPT and hopefully become more receptive when it is offered. In addition, the strong community presence of Village Health Workers (VHW) could be leveraged to also promote IPT in the community. In addition, after appropriate lobbying and advocacy efforts, the same VHWs could have their terms of reference revised so that it also includes them performing TB screening in the community and prescribing IPT for the non-presumptive cases. Presumptive cases can then be referred to a health centre. With this approach the community would be empowered to take the responsibility of their health into their own hands in line with the Primary Health Care approach. Indeed this is the direction that HIV programming is moving towards, dubbed Differentiated Service Delivery models that will bring health care closer to the community, involve lay community health workers more, while at the same time de-congesting the health facilities (WHO, 2016).





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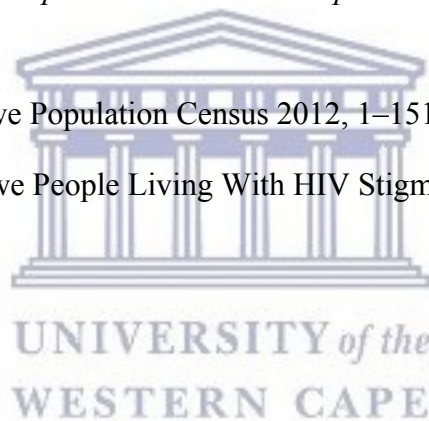
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## Appendix 1: UWC Senate Research Committee Ethical Approval



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19 January 2017

Mr BB Khabo  
School of Public Health  
**Faculty of Community and Health Sciences**

**Ethics Reference Number:** BM/17/1/31

**Project Title:** Factors associated with uptake of Isoniazid Preventive Therapy among Human Immunodeficiency Virus-infected clients in Zimbabwe.

**Approval Period:** 15 December 2016 – 15 December 2017

I hereby certify that the Biomedical Science Research Ethics Committee of the University of the Western Cape approved the scientific methodology and ethics of the above mentioned research project.

Any amendments, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval. Please remember to submit a progress report in good time for annual renewal.

The Committee must be informed of any serious adverse event and/or termination of the study.

A handwritten signature in black ink that reads 'Josias'.

*Ms Patricia Josias  
Research Ethics Committee Officer  
University of the Western Cape*

**PROVISIONAL REC NUMBER -130416-050**