

**Tuberculosis Screening for Pregnant Women Living with HIV  
in UThungulu District,  
in 2011/2012**

**A dissertation submitted to the**

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“As the candidate’s supervisor I agree/do not agree to the submission of this dissertation”

Supervisor:.....

Date: .....

## **DEDICATION**

This dissertation is dedicated to all health workers in UThungulu District, without the assistance of whom it would not have been possible to complete this work.

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Above all I would like to thank God Almighty for being the light of my life throughout my studies.

## DECLARATION

I Sthandwa Octavia Mnqayi declare that:

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# **ABSTRACT**

## **Background**

Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) co-infection in pregnancy are risk factors that affect both maternal and perinatal outcomes. TB is preventable in pregnant women living with HIV by initiating Isoniazid (INH) prophylactic therapy (IPT) if there are no TB symptoms upon screening. This study analysed health system factors associated with TB screening of pregnant women living with HIV, in 2011/2012, in antenatal care services in UThungulu District, in the Province of KwaZulu-Natal.

## **Purpose**

To analyze health system factors associated with TB screening of pregnant women living with HIV in Basic Antenatal Care (BANC) services in UThungulu District.

## **Objectives**

To determine the proportion of pregnant women living with HIV screened for TB at initiation of BANC in health facilities in UThungulu District and to analyze health system factors associated with the TB screening.

## **Methods**

An observational cross-sectional study design, with descriptive and analytic components was carried out in health facilities in UThungulu District. Multi-stage sampling was used to select health facilities and then to select pregnant women living with HIV initiating BANC. An interviewer-administered structured questionnaire and data extraction tools were used to collect data. Data was analysed using descriptive and analytic statistics using mixed effect logistic regression with cluster

effect, and doer and non-doer analysis, with Fischer's exact analysis. The level of statistical significance was set at  $p=0.05$ .

## **Results**

The results of the study showed that pregnant women living with HIV were 3 times more likely to be screened for TB in clinics where personnel had been trained on TB management, on Antiretroviral Therapy (ART) for pregnant women, and on the Prevention of Mother to Child Transmission (PMTCT) of HIV; and in clinics with a full-time enrolled nurse. Furthermore, clinics where ALL pregnant women living with HIV were screened for TB were more likely to have: a full-time midwife; personnel at all levels trained on TB management, on ART for pregnant women, and on PMTCT; and a policy to trace pregnant women who do not adhere to their scheduled subsequent visit.

## **Conclusion**

Clinics with appropriate, and trained personnel, with a policy to follow-up pregnant women who do not adhere to scheduled appointments, are health system factors associated with the implementation of the National Department of Health Guideline and World Health Organisation recommendation for the screening of TB in pregnancy for women living with HIV.

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## DEFINITION OF TERMS

- Antenatal period shall mean the time from when a woman becomes pregnant until she goes into labour to deliver the baby.
- Basic antenatal care (BANC) shall mean health care provided to pregnant women at low risk during the antenatal period.
- Living with HIV shall mean a person who has tested positive for HIV after having had an HIV screening test and an HIV confirmatory test on-site, including those pregnant women who already knew their HIV status before initiation of BANC.
- Tuberculosis (TB) shall mean pulmonary tuberculosis.
- TB screening shall mean both symptomatic screening and bacteriological investigations.
- Barriers shall mean anything that obstructs or restrains progress or access to comprehensive BANC.
- Level one antenatal care service shall mean BANC provided in a District Hospital, Community Health Centre (CHC) or Primary Health Care (PHC) facility.
- Essential package of antenatal care service shall mean five scheduled visits integrated with Sexually Transmitted Infections (STI) prevention, counselling and treatment; onsite screening for syphilis and treatment; TB screening; and strategies for Prevention of Mother to Child Transmission (PMTCT)

## LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
BANC	Basic Antenatal Care
BCG	Calmette-Guérin bacillus
CD4	Cluster of Differentiation 4
CDC	Communicable Disease Control
DHIS	District Health Information System
DHMT	District Health Management Team
GA	Gestational age
HIV	Human Immunodeficiency Virus
INH	Isoniazid
IPT	INH prophylactic therapy
KZN	KwaZulu-Natal
LFT	Liver Function Test
MDR	Multi Drug Resistant
TB	Tuberculosis
WHO	World Health Organization
XDR	Extreme Drug Resistant

# CHAPTER 1: INTRODUCTION

## 1.1 Background

Tuberculosis (TB) is a communicable disease of global concern, with the greatest burden experienced in low- and middle-income countries [1-6]. Globally, gains in controlling the TB epidemic have been observed: between 2000 and 2015 the number of new TB cases decreased by about 1.5% per year, with an estimated 49 million lives saved through TB diagnosis and treatment [6-8]. The Global Tuberculosis Report 2016 expressed concern that the 1.5% decline needs to be accelerated to at least 4 – 5% by 2020 [8]. The progress towards reducing TB incidence has been varied, with some countries in the Americas, Western Pacific and East Asia regions showing major decline, while other countries in the south Asian and sub-Saharan regions showing a slower decline [6, 10]. In 2013, 56% of new TB cases reported were from the South East Asia and Western Pacific regions [6], while in 2015, 60% of new TB cases were from six (6) countries, that is India, Indonesia, China, Nigeria, Pakistan and South Africa [6, 8]. In the south Asian and African regions the high TB incidence is associated with a maturing HIV epidemic [6, 8]. Worldwide, in 2013, TB in women accounted for about 33% of TB incidence [6, 9] and by 2015, had increased to 34% [8].

Worldwide, a 22% decrease in TB-related deaths was observed between 2000 and 2015. However, TB remains a leading cause of death in ten (10) countries, that is: India, Indonesia, Nigeria, Pakistan, South Africa, Bangladesh, the Democratic Republic of the Congo, China, the United Republic of Tanzania and Mozambique [8]. In 2013, South Africa and India accounted for one third of global TB-related deaths [6, 10]. TB is a leading cause of death particularly in women [4, 6, 10]. In resource-limited settings, including South Africa, women of child-bearing age (especially between 15 and 24 years) are disproportionately affected by TB because of the high HIV prevalence in this age group [3, 11]. Globally in 2013, about half of all HIV-related TB deaths were among women [3].

TB incidence for the pregnant population is not available, but is expected to be the same as in the general population [3]. An increase in the incidence of TB in the general population may lead to a higher risk of TB among pregnant women [3, 11, 12]. Studies have shown that pregnancy alone is not associated with an increased risk of TB infection [3, 11]. However, worldwide, TB accounts for 6–15% of all maternal deaths [13, 14]. In South Africa, in the context of co-infection with HIV, TB is the third leading non-obstetric cause of maternal mortality [3, 14, 15], and in KwaZulu-Natal (KZN) TB is the second highest cause of death, accounting for 14% of maternal deaths [11, 15, 16].

In South Africa, TB prevalence was up to ten times higher in pregnant women living with HIV than in pregnant women without HIV infection [6, 17]. The relative risk of TB among pregnant women living with HIV, compared to those who are HIV uninfected, is 20- to 37-fold, depending on the state of the HIV epidemic and the pregnant women's CD4 cell count [18]. TB and HIV co-infection in pregnant women is the major non-pregnancy related cause of maternal mortality and it increases when direct obstetric causes are excluded [13, 19]. Furthermore, TB in pregnant women living with HIV increases the risk of vertical transmission of HIV [3, 13, 20, 21]. High child morbidity and mortality rates have been attributed to TB in infants, whether acquired during the antenatal or postpartum period [2, 7, 18, 22, 23] Furthermore, delayed diagnosis of TB and lack of treatment in pregnancy contributes to neonatal TB [3, 13, 24, 25].

Early detection and screening for TB in pregnancy in women living with HIV contributes to preventing maternal deaths due to TB, to preventing mother-to-child transmission of HIV, and to preventing neonatal morbidity and mortality due to TB [3, 9, 16, 26]. The World Health Organization (WHO) recommended that routine TB symptom-based screening should be implemented with pregnant women living with HIV in high HIV prevalence regions, as TB infection is high in such settings [3, 27-30]. WHO also recommended that pregnant women living with HIV should be systematically screened for active TB at each antenatal care visit [9]. The use of a simple screening questionnaire to exclude current cough, fever, weight loss, and night sweats should be used at initiation

of Basic Antenatal Care (BANC), and at each subsequent visit, to identify pregnant women living with HIV eligible for isoniazid preventive therapy (IPT) or for further TB investigation [3, 13]. TB is often not detected in pregnancy due to lack of symptoms, especially where there is co-infection with HIV, thus the need for repeated screening [13, 28, 31] at subsequent antenatal care visits [3, 32]. Studies have shown that failure to follow this protocol is a factor associated with the delay in the diagnosis of TB, delay in the initiation of treatment, and is contributory to TB-related maternal mortality [11, 30]. A study in Soweto, South Africa, showed that TB screening, through the use of a limited number of questions during routine BANC, was feasible and not time consuming [11].

## **1.2 Problem statement**

Inadequate screening for TB during antenatal care in pregnant women living with HIV has been identified as one of the contributory factors to high maternal mortality due to Non-Pregnancy Related Infections (NPRI) [32-35]. The high burden of both HIV and TB in South Africa is expected to raise a clinician's suspicion and motivate the routine screening of all pregnant women for active TB, as per National Department of Health guideline and WHO recommendation [3]. TB in pregnant women living with HIV is often not detected due to: lack of TB suspicion; symptom screening not being offered to all pregnant women due to workload concerns by some health workers [12, 33, 34]; few signs or lack of symptoms during pregnancy [32, 36]; and/or due to expensive sputum culture [37].

In South Africa, TB screening data for pregnant women, including pregnant women living with HIV, is not routinely collected to determine case finding and to determine the TB case load in pregnant women [38]. BANC offers an opportunity for all pregnant women to be screened for symptoms of TB as per National Department of Health guideline and as recommended by WHO [22, 26, 30]. Therefore, the research question underpinning this study was: "What are TB screening practices during BANC in health facilities in uThungulu Health District for pregnant women living with HIV?"



### **1.3 Aim**

The aim of the study was to describe, and analyze factors associated with, TB screening for pregnant women living with HIV in BANC services in uThungulu District, in the KwaZulu-Natal Province of South Africa.

### **1.4 Objectives**

The objectives of this study were to:

- Determine the proportion of pregnant women living with HIV screened for TB at initiation of BANC in 2011/12, in health facilities in uThungulu District.
- Analyze health system factors associated with TB screening of pregnant women living with HIV at initiation of BANC in 2011/2012, in health facilities in the UThungulu District.

### **1.5 Significance of the study**

The study explored the health system factors associated with screening for TB in pregnant women living with HIV at initiation of BANC. The study was undertaken to identify possible areas of health system intervention to improve adherence to the National Guideline for the management of pregnant women living with HIV, at primary level health care facilities, thus improving the quality of care. TB screening implemented at initiation of BANC should contribute to early TB detection and management, which in turn should contribute to better maternal outcomes and a reduction in TB-related maternal mortality.

### **1.6 Overview of the dissertation**

Chapter 1 highlighted the study background, the problem statement, and the aim and objectives, and the significance of the study.

Chapter 2 shall present the literature reviewed and the conceptual framework that guided data collection.

Chapter 3 shall present an article manuscript, inclusive of the study results, that will be submitted to the BioMedical Central (BMC) Pregnancy and Childbirth journal.

Chapter 4 shall present an integrative discussion, inclusive of the study limitations, and recommendations that arise from the study.

Finally the annexures will be presented, which include: the study protocol (inclusive of the data extraction tool, information sheet and informed consent); the acknowledgment of registration of the study for degree purposes; the research ethics approval; the letter from the UThungulu Health District granting gatekeepers permission; and the instructions to authors for BMC Pregnancy and Childbirth.

## **CHAPTER 2: LITERATURE REVIEW**

### **2.1. Introduction**

This chapter presents a literature review on TB screening in pregnant women living with HIV. The first section of this chapter describes the literature search strategy. The body of the chapter will discuss the status of the TB epidemic, the epidemiology of TB, the signs and symptoms of TB, TB in pregnancy, Isoniazid Preventative Therapy (IPT), TB treatment, health system aspects in the delivery of quality TB care, and the conceptual framework guiding the data collection for study.

### **2.2. Literature search strategy**

A traditional narrative literature review was implemented to provide a summary of current literature relevant to the research question. The search terms used were: “tuberculosis”, “screening” and “HIV in pregnancy”. The electronic data bases searched were Google Scholar, PubMed, Science Direct, and BioMedical Central. Electronic journals searched were the Lancet, AIDS, Clinical Infectious Diseases, Reproductive Health Matters, International Journal of Gynecology & Obstetrics (IJGO) and Tuberculosis and Lung Disease. Limiters applied included the language of publication, which was English, and the year of publication, which was from 2000 to 2015. The period of publication was backdated to the year 2000 because of the limited number of published articles retrieved from 2010 onwards.

### **2.3. Status of the TB epidemic**

#### **2.3.1 Global status**

TB is a burden worldwide, second to HIV, with high mortality due to a single infectious agent [1-3, 5, 6, 39, 40]. TB was declared a global public health emergency in 1993 by the World Health Organization (WHO) [39, 41]. Through concerted public health efforts, the global incidence of TB decreased by about 1.5% each year from 2000 to 2013 [7]. Still in 2013, 9 million people developed

TB [7]. Of these, an estimated 3.3 million were women and 550 000 children [6, 10]. The GLOBAL TUBERCULOSIS REPORT 2014 showed a substantial burden of TB in terms of morbidity and mortality among adult women [10]. In resource-limited settings, women of child-bearing age (especially between 15 and 24 years) are disproportionately affected by TB because of the high HIV prevalence rates in this age group [1, 3, 7, 11, 39, 42].

A drop of 45% in overall TB mortality was observed between 1990 and 2013, [9, 10, 39], and by 22% between 2000 and 2015 [8]. The greatest burden of TB mortality is in the African and the South Asian regions, where three quarters of deaths happened [6, 7]. The countries with the greatest burden were South Africa and India, contributing a third of global deaths [6-8]. A large TB mortality burden was among women and children [6, 7, 10, 39]. Among women, those who are HIV infected have the greatest TB mortality compared to those who are uninfected [6, 8].

### **2.3.2 South African TB status**

With regards to TB incidence, South Africa ranks the highest, both globally and in sub-Saharan Africa, with a TB incidence of 593/100 000 in 2013 [38, 43]. However, there has been a gradual decline in the TB incidence in South Africa from 832/100 000 in 2009 to 593/100 000 in 2013 [43]. In 2013, ten of the 33 districts reporting a TB incidence higher than the national incidence were in the Province of KwaZulu-Natal (KZN) [38, 43]. Among the ten districts was the uThungulu District, which reported a TB incidence of 888/100 000 in 2013 [38, 43].

The TB case finding index in South Africa is 2.4% and in KZN it is 2.7% [38], with uThungulu District having the lowest case finding index in KZN at 2.6% [38]. The TB treatment success rate in South Africa increased from 76.1% in 2012 to 77.9% in 2013, slowly approaching the national target of 82% [43]. KZN was almost on target in 2013, with a TB success rate of 81.8%, which was also above the national average [43]. Albeit a high burden of TB in uThungulu district, the TB treatment success rate in 2013 was the highest in South Africa

at 90.1% [38, 43]. The more effective TB management in uThungulu District offers hope to the management of TB in pregnant women living with HIV [38].

#### **2.4. Epidemiology of TB**

TB is a treatable airborne disease caused by *Mycobacterium tuberculosis* [3, 44, 45]. The *tubercle bacillus*, which is the causative organism of tuberculosis, was demonstrated by Robert Koch in 1882, who was awarded the Nobel Prize in 1905 for his discovery [44-46]. In 1895 Wilhelm Roentgen developed X-rays which advanced diagnostics for TB [44]. In 1908, the French scientists Albert Calmette and Camille Guerin grew Koch's bacillus in several mediums to decrease virulence and increase the capacity to produce immunity [44]. This led to the vaccine called Bacillus Calmette–Guérin (BCG) named after the two founders [45, 46]. The BCG vaccine was introduced in France in 1921 [44-47]. In 1948, India and Pakistan became the first countries other than Europe to introduce trial BCG vaccinations [46]. The BCG campaign was extended to developing countries in the 1950s and first used by Greenland in 1955 [44, 45, 47].

Active tuberculosis can be contagious, while latent tuberculosis is not [3, 42, 47]. The TB incidence has risen with the rising burden of human immunodeficiency virus (HIV) [3, 11, 12, 22, 42], because people living with HIV, whose immune system is weakened, have 20–37 times the risk of developing opportunistic TB progressive disease compared with HIV negative individuals [3, 11].

TB is more common among men than women, affecting mostly adults in the economically productive age groups [8, 39]. In resource-limited settings, including in South Africa, women of child-bearing age (especially between 15 and 24 years) are disproportionately affected by TB because of the high HIV prevalence in this age group [3, 11]. An estimated one-third of deaths due to tuberculosis occur among women of childbearing age [12, 22]. TB infection in people living with HIV further increases the spread of extra-pulmonary TB [3].

## **2.5. Signs, symptoms and diagnosis of TB**

The general symptoms of TB disease include unexplained weight loss, loss of appetite, night sweats, fever, fatigue, and chills, and the symptoms of pulmonary TB include coughing for 3 weeks or longer, hemoptysis and chest pain [12, 22, 30, 48]. The clinical features of TB in pregnant women are the same as in non-pregnant women [3, 7, 12].

Several tests are used to diagnose TB, depending on the type of TB suspected. Medical history, physical examination, TB skin test or TB blood test, chest radiograph (X-ray), and appropriate laboratory tests may be used to exclude TB infection [42]. The diagnosis of TB in pregnancy is the same as in the general population: by taking a history to identify the risk factors for TB infection and using the specific symptomatology screening tool to identify the presence of symptoms which may be suggestive of TB [3, 7, 10, 28]. Screening for TB during pregnancy, while recommended, does not seem to be undertaken routinely, which contributes to a delay in diagnosis and increased mortality [22, 42].

Signs of maternal TB may vary from mild cough, fever and fatigue to weight loss and hemoptysis [3, 11, 28, 49, 50]. In South Africa, routine screening for TB in pregnancy is standard protocol at each antenatal care visit [26]. Pregnant women living with HIV and co-infected with TB are most likely to be identified through routine screening and to be asymptomatic [3, 32]. In South Africa, of the pregnant women reporting cough of two weeks or more, 60% were diagnosed with TB. Of these pregnant women, less than 30% had fever or night sweats [2, 49]. The absence of TB symptoms makes it difficult to suspect TB and has a negative predictive value of 90.0-97.7% [2, 49].

TB may affect any tissue of the body. However pulmonary TB is the most common form of the maternal disease with bronchopneumonia, cavitation, bronchiectasis, interstitial pneumonitis and/or pleural effusion [11, 12]. TB infection in pregnancy may be a challenge to diagnose as the early symptoms often are non-specific, such as malaise and fatigue, which may be attributed to pregnancy and not raise the suspicion of TB infection [11, 12, 40].

HIV/TB co-infection, multi/extensive drug resistant (MDR/XDR) TB, the complexity of TB/HIV co-infection and immune responses to TB contribute to the challenges of TB screening in pregnancy [51, 52].

## **2.6. TB in pregnant women**

Pregnant women are more susceptible to develop active TB than other population groups [1, 3, 53]. However, at all levels of health care in sub-Saharan Africa, diagnosis of TB in pregnant women is overlooked [53], even though TB is one of the leading non-obstetric causes of maternal mortality [3, 11, 19, 42, 49, 53]. TB incidence in pregnant women is expected to be the same as in the general population [1, 3]. TB is often not detected in pregnancy due to lack of symptoms [3, 32].

TB infection may be worse during pregnancy due to factors associated with poor nutrition, immunodeficiency and/or other coexisting disease [11, 12]. Pregnancy was previously thought to aggravate or slow down the course of TB but evidence has since shown that it is not the case [49]. However, in an era of HIV with its profound effects on the immune system, TB seems to be aggravated in pregnancy as a result of HIV [11, 49]. It is argued that the TB presentation in pregnant women is similar to non-pregnant individuals with pulmonary TB [11].

The critical step in making the diagnosis even in pregnancy is based on identification of risk factors for TB infection and on specific enquiry about symptoms suggestive of TB [11, 12, 22]. Active TB during pregnancy is associated with spontaneous abortion, a smaller uterine symphysis to fundal height for the expected gestational age, preterm labor and adverse perinatal outcomes [3, 22].

Few national programs collect or report pregnancy-specific tuberculosis data to the WHO [49].

## **2.7. TB/HIV co-infection in pregnancy**

TB/HIV co-infection leads to difficulties in the diagnosis and treatment of TB [54, 55]. HIV/TB co-infection is common in areas with high prevalence of TB especially in South Africa [22, 40]. TB is the most frequent fatal opportunistic disease affecting people living with HIV especially in the first three months of starting antiretroviral therapy (ART) [41]. Although ART reduces the likelihood of developing TB disease, studies have shown that TB incidence among people living with HIV receiving ART is still greater than in the general South African population [56]. The development of TB disease has been associated with increased HIV replication and reduced CD4 cell counts, possibly contributing to the advancement of HIV infection [57].

TB/HIV co-infection has emerged as a major non-obstetric cause of maternal morbidity and mortality [12, 18, 58]. Increases in TB-associated maternal deaths have been reported from South Africa and Lusaka in Zambia [3, 11, 22]. Both TB and HIV infection have been identified as contributing independently towards maternal mortality and poor perinatal outcomes [49, 57]. However in combination, TB and HIV infection have a greater harmful impact than their individual effects [49, 57]. The relative risk of death in mothers with TB and HIV co-infection compared to those with TB without HIV co-infection was 3.2 [19, 22, 59]. HIV-infected TB cases cause 10% of maternal deaths in Africa [12]. HIV and TB effects are more deadly in pregnancy, and may contribute significantly to maternal morbidity and mortality. Over 50% of the maternal mortality occurring in mothers with TB in pregnancy is due to TB/HIV co-infection [13, 22, 58]. Pregnant women living with HIV had 3.8 times increased risk of severe elevated Liver Function Tests (LFTs) compared to non-pregnant women, and hepatotoxicity from ART during pregnancy ranged from 0.5% to 25.9% [11].

### **2.7.1 Vertical transmission of HIV and TB**

TB/HIV co-infection in pregnancy is associated with higher vertical transmission of HIV compared to women with HIV alone [1, 21, 34, 51, 53, 60, 61]. In pregnant women who have TB, the fetus is exposed to the infection [12, 25].



The exact risk of transmission to the fetus/newborn is unknown, but progression from infection to disease is highest during the first year of life [12]. The extra pulmonary forms of TB disease, e.g. peritoneal, renal, lymph node and meningeal TB, constitute greater risk factors for congenital TB [5, 11, 40]. Extra pulmonary TB has also been shown to increase all-cause neonatal mortality [5, 40]. Congenital TB, though rare, is associated with high perinatal mortality [12].

TB-infected mothers had a 6.4 times higher perinatal mortality than those TB-uninfected [3, 11, 40]. Adverse outcomes were higher where the maternal TB was diagnosed in the third trimester, TB disease was in an advanced stage, or where the mother had been non-compliant with treatment intervention [3, 5, 40].

## **2.8. TB treatment**

Lessons learned from the HIV programme have shown that, since TB is curable, if the gap between those diagnosed with TB and those who are ill can be closed, reduction of TB can be accelerated towards global elimination [7]. The effectiveness of care is known only in about two-thirds of the estimated 8.6 million incident cases of TB [7, 10]. THE GLOBAL TUBERCULOSIS REPORT 2014 estimates that in 2013 there were 3 million people with active TB, either not diagnosed or not reported [6, 10]. The WHO recommends that the treatment of TB in pregnancy should be the same as that in non-pregnant women; the only exception being that streptomycin should be avoided in pregnancy as it is ototoxic to the fetus [11, 30]. Starting TB treatment late in pregnancy has been associated with neonatal mortality and extreme prematurity [11].

Early initiation of antenatal care and availability of diagnostic facilities for TB enhance TB screening, early diagnosis, and treatment for pregnant women living with HIV [52]. Provision of proper resources for integration of TB and HIV programmes contributes to improved screening and diagnosis of TB in pregnant women living with HIV [32, 59]. TB screening should be integrated into maternal care so that pregnant women living with HIV can receive preventative therapy [49, 59]. Even in settings where infrastructure and human resource capacity

were limited, there was compelling evidence for the utilization of the TB symptomatology screening tool [59].

It is argued that although the Communicable Disease Centre (CDC) and WHO recommend early treatment of latent tuberculosis in pregnant women living with HIV, on treatment pregnant women may be at particular risk for drug-induced liver injury [49].

## **2.9. Preventative therapy**

TB control is failing in South Africa due to the failure to treat latent TB infection, using INH prophylaxis in the general population, including in people living with HIV [62]. INH is administered to individuals with latent infection with TB in order to prevent progression to active TB disease. The eligibility criteria for isoniazid preventive therapy (IPT) is pregnant and breastfeeding women living with HIV and the duration depends on the Tuberculin Sensitivity Test (TST) [63]. If TST positive the duration is 36 months, negative and not done the duration is 12 months [63]. The INH dosage should be 5mg/kg/day and maximum of 300mg with Vitamin B6 25mg/day [63].

The benefits of IPT in preventing TB outweigh the risks [3, 12]. After excluding active TB disease, IPT can be started at any time during pregnancy and should be completed if a woman falls pregnant while taking IPT [3, 12]. IPT was incorporated by WHO in 2004 as one of the twelve collaborative TB/HIV activities and included in 2008 as part of the three “I’s” for TB/HIV which are IPT, infection control for TB, and intensified case finding [41, 50].

Detection of TB can be beneficial to pregnant women living with HIV and their unborn babies [1]. Antenatal care provides an important contact between pregnant women, regardless of HIV status, and the health system [1]. In India, active TB screening and targeted use of IPT among women living with HIV was recommended to prevent postpartum TB and mother to child transmission of TB [3, 25, 49]. Babies born to mothers with TB should be commenced on INH prophylaxis for six months, afterwards vaccinated with BCG if they test negative [3, 12].

In most countries, even with a supportive national policy for IPT, there is a gap between policy and implementation. Concerns exist by programme managers and health providers that INH monotherapy for undetected TB may cause development of INH resistance [41]. Yet studies have shown no significant increased risk of INH mono-resistance following IPT [41]. Concurrent administration of ART and IPT has demonstrated a TB risk reduction of 76–89% in observational studies from both South Africa and Brazil [59].

### **2.10. The health system aspects of the quality of TB care**

The high burden of maternal HIV/TB co-infection over burdens the health care system [20, 53, 64]. In some HIV endemic countries, gains in maternal mortality were reversed [64]. Pregnant women living with HIV, and who have comorbidity with active or subclinical TB are often overlooked [53]. Services for pregnant women living with HIV should incorporate routine TB screening and provision of IPT. IPT should not be viewed by the community as a stand-alone TB prevention intervention [41, 53]. TB screening and IPT indicators should be monitored with TB/HIV integration [41].

Effective integration of TB service provision should be advocated, while maintaining some vertical elements for essential functions, such as drug supply, monitoring, and surveillance. The vertical TB programme components may be restricted to a small central team providing general oversight [53]. Poorly functioning management systems in each health service should be addressed, including ensuring adequate human resources [50].

### **2.11. Conceptual Framework**

Maternal health care outcomes are dependent on health system functioning [65]. The WHO defines the health system as a system whose primary purpose is to promote, restore and maintain health [66]. In 2007 the WHO developed a framework for health systems, composed of six building blocks: leadership and governance; health care financing; human resources for health; medical products, vaccines and technology; health information systems; and health service coverage [65, 66]. Blaauw and Kekana have elaborated the WHO

conceptual framework, showing the relationship between the health system building blocks, essential packages of care and maternal outcomes [65, 67] (See Figure 1).

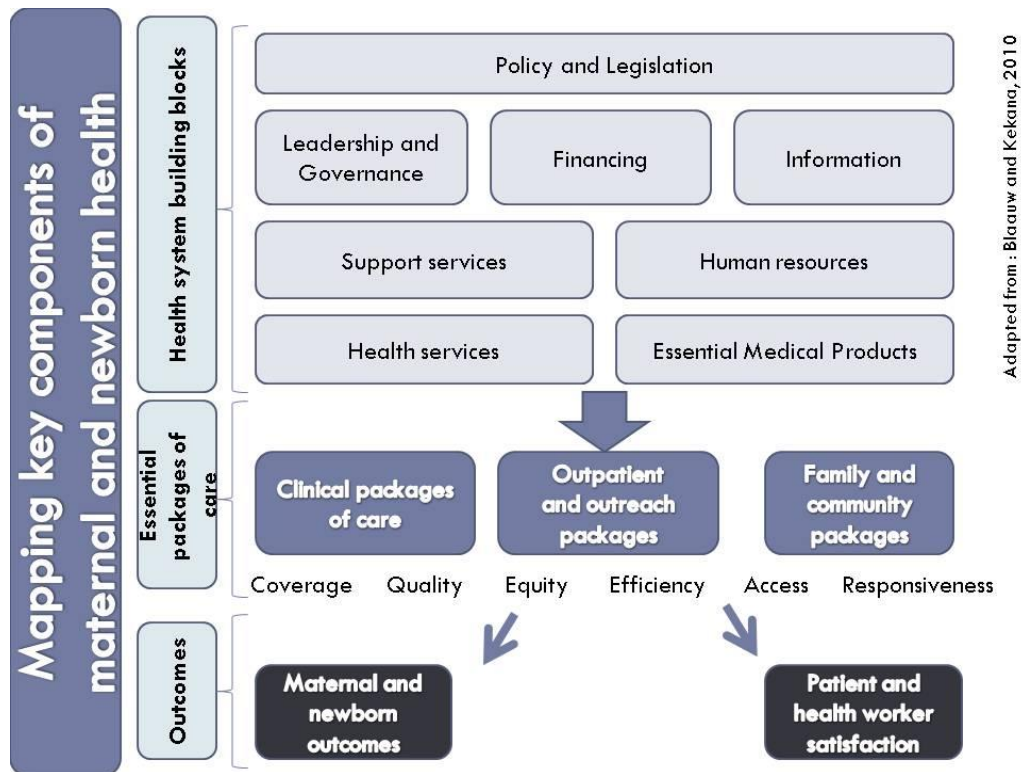


Figure 1: Map of key components of maternal and newborn health [65, 67]

The key health components contributing to maternal health, as depicted in the conceptual framework developed by Blaauw and Kekana [65] are explained as follows:

### 2.11.1 Leadership and governance

Leadership is a process of social influence, which maximizes the efforts of others, towards the achievement of a goal. Governance is the way to hold organizations accountable [68], with governance structures liaising with various stakeholders at different levels of the health system for the development of

conducive policies and environments of care, towards the promotion and protection of the health of communities [69].

Leadership and governance are viewed as key drivers in the provision of quality care for optimal maternal and newborn outcomes, as well as client and health worker satisfaction [65]. However should involve managers in positions of responsibility to effect change within organizations [70].

Effective leadership and governance contribute to health systems strengthening and include PHC supervision, PMTCT mentorship, clinical audit and the availability of an active clinic committee for ensuring accountability to community. Adequate financing is ensured by allocating a budget which is known by the clinic manager and staff for BANC services.

Supervision is an intervention provided by a senior member of a profession to a junior of same profession [68]. The relationship includes assessment of performance over time and has the concurrent purposes of monitoring the quality of professional services offered to the clients served and further improving professional functioning of lower ranking members [43] [38]. Primary Health Care (PHC) supervisory visits are intended to assist in identifying and addressing gaps in the provision of priority programs at clinics, Community Health Centers (CHC) and community day centers [38]. The South African target of at least one supervisory visit per month per facility was achieved in 80% of facilities nationally. In KZN it was met in 60% of facilities from 2011 to 2013, while in uThungulu it was met in 70% of facilities [38].

Clinical audit is a quality improvement process with the purpose of improving patient care and outcomes through a systematic review of care against explicit criteria, and through the implementation of corrective actions [71]. As IPT initiation has been shown to be beneficial to people living with HIV, supervisors should facilitate clinical audits to ensure that TB screening using the simple symptom-based clinical questionnaire is implemented for pregnant women living with HIV, and IPT is initiated for those eligible [41].

### **2.11.2 Policy and legislation**

Public policy development is a process that guided actions at different levels involving contests of interests within and outside government [69]. Legislation refers to laws which serve to legally guide certain actions and ensure others are carried out [69]. Policies provide a plan of action which act as a guide towards making sure legislation is complied with [69].

The number of countries that issued policies for IPT implementation increased from 8 to 102 between 2002 and 2009 [41]. However, a gap has been observed between policy formulation and its implementation, as only 50% of the countries with supportive IPT policies were reporting on IPT implementation to WHO [41]. In South Africa, TB screening for pregnant women living with HIV, with IPT initiation, was included in the national consolidated guideline for the prevention of Mother-To-Child Transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults, as a basic package of care, which is an example of how policy and legislation, and the implementation of the guideline has a potential to contribute towards good maternal and newborn outcomes.

### **2.11.3 Financing**

Health care financing has the potential to have a positive or negative impact on maternal health provision [72]. South Africa's district health service expenditure per capita increased from R659 in 2004/05 to R1 327 in 2012/13, with KZN below the national average at R1 301, while UThungulu District's per capita expenditure was R1 352 [38]. Competition for funds among programmes is fierce [73].

Global financial assistance to maternal and neonatal health was estimated at more than US\$663 million in 2003 [73]. An estimated extra US\$1 billion in 2006, increasing to US\$6.1 billion in 2015, was needed to increase financial coverage

to desired levels [73]. The estimates exclude the cost of incentives to improve quality of care, promoting staff retention in rural areas, and prevention of the imposed informal charges [69, 72-74].

The extent to which health system investment will affect maternal health is hard to quantify and is a challenge to cost-calculating exercises [73].

Studies have shown that there has been an increase in the availability of funds to support collaborative TB/HIV activities through the President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to AIDS, TB and Malaria (GFATM) [41]. Provision of IPT to people living with HIV has been found to be more cost effective than the cost of medical care and social costs. However the study, conducted in South Africa, excluded those who were also on ART [41]. It was therefore recommended by the Global TB Drug Facility that INH should be available as a TB prevention commodity for people living with HIV as part of core services [41].

#### **2.11.4 Human resources**

Understaffing, particularly in rural, poor areas impacts negatively on maternal and newborn outcomes [75]. Furthermore, the quality of care provided to pregnant women, and whether standard protocol of management are followed, determine maternal and newborn outcomes [72]. The existing personnel may experience increased workloads and job dissatisfaction, and may have to assume tasks for which they are not trained. Therefore shortages of maternal health professionals should be addressed within an overall human resources policy [75].

Human resource capacity can be increased through in-service training, increased output from training institutions of health care workers competent to work at primary level, task shifting, increased flexibility in health service roles, and reliance on community based health care workers [50].

In a cross sectional operational study conducted in Soweto (South Africa), the obstacles to integrating TB screening with PMTCT services included poor morale of clinical staff and low motivation in staff to take on new responsibilities without additional remuneration [1]. Additional training and supportive supervision could potentially improve identification and investigation of TB suspects [1].

#### **2.11.5 Information**

Information management is central to health care delivery [76, 77]. The success of health care depends on the collection, verification, analysis, exchange and utilization of information, within and beyond the organization [74, 77, 78]. However the electronic TB register does not have segregated data for pregnant women.

A TB Suspect Register is used in some countries and in Malawi it is called the Chronic Cough Register [79]. The Register, under the control of the district or health facility TB officer became very helpful in tracking patients that presented for investigation of chronic cough [79]. A pregnant woman living with HIV who has any one of the Pulmonary TB symptoms of cough, fever or weight loss should be clinically assessed and initiated on cotrimoxazole preventive therapy [79].

Many resource-restricted countries have not established a system to monitor and evaluate the implementation of IPT [41]. TB screening and IPT provision indicators should be adopted by all HIV implementers [41]. The strength of a health system offers a key and sustainable mechanism to influence priority population level indicators of health [66].

#### **2.11.6 Support services**

A referral system is defined by WHO as “a process in which a health worker at any one level of the health system, having insufficient resources (drugs,



equipment, skills) to manage a clinical condition, seeks the assistance of a better or differently resourced facility at the same or higher level to assist in, or take over the management of, the client's case" [80]. Components of a referral system include, among others, clarity of level and role of each facility, availability of communication and transport, referral register to monitor follow-up and gather statistics, back referral and consistency of follow-up [80].

A functional referral continuum can increase client and provider satisfaction [81]. At the public health level, linkages between integrated packages can maximise the efficiency with which the scarce human and financial resources available for health care are used [81]. The continuum of care is the basis of health care in many countries, especially those with government-funded health-care systems [81].

#### **2.11.7 Package for indirect obstetric care**

A health package can refer to an entire national health package or to specific interventions designed to address a particular outcome [81]. For antenatal care to be effective, all pregnant women need a minimum of four focused visits, at specific times during the pregnancy, and with evidence-based content [81]. Care for women during pregnancy improves health through preventive measures, and by prompt detection and management of complications [81]. Essential components of a focused antenatal-care package include screening for and treatment of disorders including screening and management of HIV and TB in pregnancy [81].

TB screening for pregnant women living with HIV and provision of IPT should be part of core services [41].

#### **2.11.8 Community package**

A family and community care package aims to improve healthy home behaviours and to increase demand for outreach and clinical services. Effective

behavioural and preventive interventions that can be delivered through this package which includes prevention and promotion of health [66, 81].

Meaningful engagements of pregnant women living with HIV and their communities should be conducted in planning and implementation of TB screening and IPT [41]. IPT should be advocated in communities as an evidence based effective intervention to prevent TB in women living with HIV and communities should be empowered to demand IPT when they are in contact with PMTCT providers [41].

There is little country specific research that has been done to explore ways in which health system elements do impact on maternal health outcomes [66, 72]. The health system building blocks aim to support a health system to ensure coverage in the prevention and management of illness and to preserve mental and physical well-being for all individuals, equitably and efficiently, within a specified geographic area [66]. The health system activities range from direct quality service provision through accessible clinics and hospitals to communities that will respond to prevention strategies and health education. [65]. The expected outcomes are maternal and newborn health, and patient and health worker satisfaction [65].

TB management is one of the required services in the essential package of care for pregnant women attending BANC at any level of the health system [26]. According to the national HIV, TB and PMTCT guidelines, pregnant women living with HIV should be screened of TB at every visit and provided with IPT or TB treatment whichever is appropriate [26]

## **2.12. Summary of the literature review section**

Through the review of the literature it has been shown that TB is a burden globally and in South Africa. It has also been shown that there are concerns about maternal and neonatal complications associated with TB, especially if there is co-infection with HIV. There was no specific literature available to determine TB incidence during pregnancy, and so it was assumed to be as

prevalent as in the general population. TB symptomatic screening has been shown to be effective in identifying pregnant women living with HIV without TB, for whom IPT is indicated, and for those with symptoms, for further investigation and initiation of TB treatment. The components of the conceptual framework underpinning the study have shown the relationship between health system building blocks and health outcomes.

## **CHAPTER 3: JOURNAL MANUSCRIPT**

**Title: Factors associated with tuberculosis screening for pregnant women living with HIV in a health district in KwaZulu-Natal, South Africa: An observational analytic cross-sectional study design**

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## **Abstract**

### **Background**

Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) co-infection in pregnancy are risk factors for both maternal and perinatal outcomes. TB is preventable in pregnancy in women living with HIV by initiating Isoniazid (INH) prophylactic therapy (IPT) after TB has been excluded upon screening. This study explored health system factors associated with TB screening of pregnant women living with HIV in the basic antenatal care (BANC) services in a health district in the Province of KwaZulu-Natal, South Africa.

### **Methods**

An observational cross-sectional design, with descriptive and analytic components, was carried out. Multi-stage sampling was used, firstly to select health facilities and then to select pregnant women living with HIV initiating BANC. A structured interviewer-administered questionnaire and data extraction tools were used to collect data. Data was analysed using descriptive and analytic statistics, using mixed effects logistic regression with cluster effect, and doer and non-doer analysis and Fischer's exact analysis. The level of statistical significance was set at  $p=0.05$ .

### **Results**

The results of the study showed that pregnant women living with HIV were three (3) times more likely to be screened for TB in clinics where personnel had been trained on TB management, on Antiretroviral Therapy (ART) for pregnant women, and on the Prevention of Mother to Child Transmission (PMTCT) of HIV; and in clinics with a full-time enrolled

nurse. Furthermore, clinics where ALL pregnant women living with HIV were screened for TB (doers) were more likely to have: a full-time midwife; personnel at all levels trained on TB management, on ART for pregnant women, and on PMTCT; and a policy to trace pregnant women who do not adhere to their scheduled subsequent visit.

### **Conclusions**

Health system factors associated with the implementation of the National Department of Health Guideline and World Health Organisation recommendation for the screening of TB in pregnancy for women living with HIV include appropriate, and trained, personnel, with a policy to follow-up pregnant women who do not adhere to scheduled appointments.

**Key words:** HIV, isoniazid preventative therapy, pregnant women, screening, tuberculosis, basic antenatal care, health system factors

## **Background**

Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) co-infection in pregnancy are risk factors for both maternal and perinatal outcomes [1, 12, 13, 64, 82, 83]. TB is preventable in pregnancy by initiating Isoniazid (INH) prophylactic therapy (IPT) after TB has been excluded [3, 17, 49, 79]. In South Africa, TB is the third highest non-pregnancy related avoidable cause of maternal death, while in KwaZulu-Natal (KZN) TB is the second highest, accounting for 14% of maternal deaths [11, 15, 16]. Delayed diagnosis of TB, and delayed or lack of treatment in pregnancy contributes to neonatal TB [34, 35]. Studies have shown that TB in pregnant women living with HIV increases maternal and perinatal morbidity and mortality, including the risk of vertical transmission of HIV [3, 13, 20, 21].

To facilitate the early detection and management of TB in pregnant women living with HIV, the National Department of Health in South Africa has issued guidelines, as per the World Health Organization (WHO) recommendation, to screen all pregnant women living with HIV for TB [26]. The guidelines call attention to the fact that pregnant women living with HIV often have other health issues. Therefore, the necessity of integrating HIV services with Primary Health Care (PHC), and with maternal, newborn and child health (MNCH) and TB services, in order to provide more client-centred care [26]. Pregnant women living with HIV should be screened for TB and if there is any symptom suggestive of TB, appropriate investigation using sputum/Gene-Xpert and TB culture should be used [26]. However, inadequate screening for TB during antenatal care in pregnant women



living with HIV has been identified as one of the contributory factors to adverse maternal and perinatal outcomes [32-35]. TB screening is part of the essential package of care to be provided during antenatal care to pregnant women living with HIV [13, 15, 41, 64, 65]. Health system performance influences the provision of care [22, 31, 83]. The conceptual framework proposed by Blaauw and Kekana [65] (see Figure 1) formed the basis for attaining the purpose of this study, which was to evaluate health system components associated with TB screening for pregnant women living with HIV initiating basic antenatal care (BANC), in 2011/12, in a District in the Province of KwaZulu-Natal. The health system components comprised: policy and legislation; leadership and governance; health financing; human resources for health; information system; and support services [65].

## **Methods**

An observational cross-sectional study design, with descriptive and analytic components, was conducted in primary level clinics that provide BANC services, in a Health District in the Province of KwaZulu-Natal, South Africa.

The study population comprised pregnant women living with HIV initiating BANC in health facilities in the District. Pregnant women aged 18 years and older who were confirmed to be living with HIV at initiation of BANC were included in the study. Pregnant women testing negative for HIV at initiation of BANC were excluded from the study.

Multi-stage cluster sampling was implemented. Firstly, all six Level One public sector hospitals in the Health District were selected. Secondly, a simple random sample was drawn of fixed clinics providing antenatal care services within the catchment area of each Level One hospital. Fifteen (15) of a total of 46 fixed clinics were selected using probability proportionate to size. The number of 15 fixed clinics was based on sample of 30%, which is the required sample size in a descriptive study not testing a hypothesis [84, 85]. Thirdly, within the randomly sampled clinics, systematic sampling was implemented to select every third pregnant woman living with HIV, recorded in the BANC register as having initiated BANC between April 2011 and March 2012, and as being counselled, tested and positive for HIV. A total of 845 records of pregnant women living with HIV were sampled.

To assess the proportion of pregnant women living with HIV who were screened for TB, a data extraction tool was used to retrieve data from the BANC register held in the clinic. To assess health system factors associated with TB screening, data collection comprised: structured interviews, utilising an interviewer-administered questionnaire, with antenatal care clinic managers on duty on the day of data collection; and a data extraction tool for extracting data from clinic administrative records. Data was collected from September 2013 to March 2014.

Outcome and exposure variables were collected simultaneously, reducing the expense of the study [86]. All data was cleaned, coded, and entered on a Microsoft excel spreadsheet. The data was double entered, and the two files compared for any discrepancies. Discrepancies were corrected

against the original paper records. Data was exported to the IBM SPSS™ 21 software for analysis. At the individual level, mixed effects logistic regression with cluster effect was used to measure the strength of association between outcome (pregnant women living with HIV screened for TB) and exposure variables (health system factors) [87]. At the clinic level, doer and non-doer analysis was implemented to determine the relationship between outcome (ALL pregnant women living with HIV screened for TB) and exposure variables (health system factors) [87]. A clinic where ALL pregnant women living with HIV were screened for TB was classified as a 'doer' and one where not all were screened for TB was classified as a 'non-doer'. Fischer's exact analysis was used to measure the probability of a clinic being classified as a doer or a non-doer in relation to the exposure variables.

The basic principles of research ethics, that is: beneficence, which is ensuring protection for participants; autonomy, which respects a person's decision to participate or not to participate in the study; non-maleficence, that is doing no harm; and justice, which is random selection of participants, were applied in this study. Ethical clearance was obtained from the UKZN Biomedical Research Ethics Committee (Reference number BE142/11). Permission to conduct the study in the clinics was obtained from the District Health Manager. Participants were provided with full information on the study and were asked to sign an informed consent form when they agreed to participate in the study. They were assured of confidentiality and also were assured of no negative consequences should they decline to participate in the study at any stage.

## **Results**

### **Demographic characteristics and obstetric history of pregnant women living with HIV**

The mean age for the pregnant women living with HIV was 26 years. The mean gravidity was 2 and mean parity was one. Gestational age (GA) at initiation of BANC ranged from 4 to 39 weeks, with a mean GA of 19 weeks. The proportion of women who initiated BANC before 20 weeks GA was 47% (See Table 1).

### **TB screening of pregnant women living with HIV**

Of the 845 pregnant women living with HIV, 76% (n=645) were screened for TB. However, only 19% (n=124) of those who had no TB symptoms were initiated on IPT. Only 9% (n=11) pregnant women living with HIV who had symptoms of TB had sputum collected for TB diagnosis.

Of the fifteen clinics sampled, one third (n=5) implemented TB screening for ALL the sampled pregnant women living with HIV and were classified as 'doers'.

### **Health system factors associated with TB screening of pregnant women living with HIV**

#### **Leadership and governance, financing and information**

Descriptive analysis revealed that 60% (n=9) of clinics reported being visited by the PHC supervisor in the previous month, and 13% (n=2) by the PMTCT mentor. Pregnant women living with HIV were more likely to

be screened if attending a clinic that had been visited by: a PHC supervisor (OR 4.1;  $p=0.50$ ; 95%CI 0.65-265.46) and a PMTCT mentor (OR 2.1;  $p=0.81$ ; 95%CI 0.004-1217.6) although neither association was found to be statistically significant. Among the clinics, 80% of doers compared to 50% of non-doers reported being visited by the PHC supervisor in the previous month, although the probability of being classified as a doer was not statistically significant ( $p=0.58$ ).

The proportion of clinics reporting to have conducted a BANC record audit in the previous month was 13% ( $n=2$ ). Only 20% of clinic managers knew the budget allocation for the clinic. All the required registers and data collection tools were generally available. A majority of clinics, 88% ( $n=13$ ), had clinic committees, and of those 62% ( $n=10$ ) reported the committee had met as scheduled. None of these health system factors were found to have an association with the likelihood of pregnant women living with HIV being screened for TB and with the probability of clinics being classified as doers or non-doers.

### **Policy and legislation**

The availability of national guidelines was assessed. In 80% ( $n=12$ ) of clinics both the Maternity Care Guidelines 2007 and the PMTCT Guidelines were available, while the National TB Manual, National TB Control Practical Guideline and the TB Training Manual were available in all clinics. There was no association between the availability of national guidelines and likelihood for pregnant women living with HIV being

screened for TB nor with the probability of clinics being classified as doers or non-doers.

### **Support services**

A tracing policy for pregnant women who do not adhere to their scheduled BANC appointments was reported in 27% (n=4) of clinics. In the presence of a policy to trace pregnant women who do not adhere to their scheduled appointment, the likelihood of pregnant women living with HIV being screened for TB was higher, but with borderline statistical significance (OR 13.5; p=0.06; 95%CI 0.87-207.63). Furthermore, the probability of a clinic being classified a doer was of borderline statistical significance (p=0.07).

### **Human resources**

The influence of the human resource building block was assessed by measuring the association between the availability, mix and training of personnel in the BANC services, and TB screening. With regard to availability, the number of midwives per clinic ranged from 2 to 15, representing a midwife-to-patient ratio that ranged from 1:2 to 1:7. With regard to staff mix: one-third (n=5) of clinics had a sessional medical officer; all clinics had a full-time midwife; 87% (n=13) had a full-time enrolled nurse; one-third (n=5) had a full-time enrolled nursing assistant; all had a full-time lay counselor; and 87% (n=13) had a full-time community health worker or community care giver. With regard to training, of the 75 midwives providing BANC in the 15 clinics, 52% (n=39) were

trained on TB management, 75% (n=56) on ART for pregnant woman, and 59% (n=44) on PMTCT.

Following logistic regression (Table 3), pregnant women living with HIV were more likely to be screened for TB in clinics: where midwives had been trained on ART for pregnant women (OR 3.1; p=0.005; 95%CI 1.42-6.67) and on PMTCT (OR 3.0; p=0.05; 95%CI 1.01-8.98); with full-time enrolled nurses (OR 3.1; p=0.04; 95%CI 1.06-8.77); and with enrolled nurses trained on TB management (OR 7.9; p=0.001; 95%CI 2.24-27.92).

In Table 4 is shown the proportion of clinics classified as doers and non-doers, in the presence of the availability and training of different categories of staff. Clinics with midwives, registered nurses, enrolled nurses and community health workers trained on TB management, on ART for pregnant women and on PMTCT had a statistically significant probability of being classified as doers and providing TB screening to ALL pregnant women.

### **Health services**

The assessment of the provision and organisation of BANC services relied on verbal reporting by the clinic manager. New clients, i.e. clients initiating BANC, were reported to be catered for on a daily basis in 53% (n=8) of clinics, with the remaining clinics accommodating clients initiating BANC only on specific days (see Table 6). Offering, and recording the results of HIV counseling and testing for all pregnant women initiating BANC, and initiating all eligible women on antiretroviral therapy, was reported in all clinics. Providing TB services daily was reported in all clinics; however the TB services were not integrated in BANC services. Providing TB

screening for ALL women living with HIV was reported in 87% (n=13) of clinics. Initiating eligible women on INH, or collecting sputum for bacteriological test, and, for those with positive sputum, initiating TB treatment, was reported in all clinics. None of these health system factors showed an association with the likelihood of pregnant women living with HIV being screened for TB and with the probability of clinics being classified as doers or non-doers.

## **Discussion**

The mean age for pregnant women living with HIV in the study was 26.7 years. The results are similar to a study conducted by Gounder and colleagues on active TB case finding in Soweto in 2008, which also found the median age of 26 years among pregnant women living with HIV [1]. The results show that 47% women booked for antenatal care before 20 weeks. The results differ slightly from a study by Massyn which showed that in South Africa ANC initiation before 20 weeks of gestation was 45% and has been consistently so since 2002 [38].

The National Guideline and WHO recommendation for TB screening of pregnant women living with HIV are not consistently being followed. Just over three quarters of pregnant women living with HIV were offered TB screening when initiating antenatal care, and of those who screened negative for TB symptoms only about one-in-five were initiated on IPT. Furthermore, of the women who screened positive for TB, in only one-in-ten was sputum collected for further investigation. Studies have shown that the benefits of IPT are greater than the risks even during concurrent



administration with ART has shown a TB risk reduction of 76–89% [3, 12, 59].

The availability of national guidelines alone does not translate into implementation. The main purpose served by guidelines is to provide decision making support to health care providers, and promote uniform, evidence based practice and standards of care [88]. It is important to ensure the same standard of care is delivered to all women, whatever clinic they attend. Not only the proportion of pregnant women living with HIV screened for TB must increase, but also the proportion of clinics that provide TB screening to ALL pregnant women living with HIV. Training in guidelines of care has been shown to have a mixed effect in changing practice. In this study, having nursing staff at all levels trained in TB management, in ART for pregnant women and in PMTCT was significantly associated with the greater likelihood of pregnant women living with HIV being screened for TB, and the greater probability of clinics being classified as doers, i.e. providing TB screening for ALL pregnant women living with HIV. Training can only be regarded as the first step to implement changes towards evidence-based practice [89, 90]. One of the challenges with training activities is ensuring that, within a context of high staff turnover [89], a core group of trained staff is retained in the health system [75, 91]. In this district, among the midwives working in the clinics sampled, just half had received training in TB management, and three-quarters in antiretroviral therapy for pregnant women.

Even with training, adherence to guidelines for ALL women living with HIV does not occur. Further health systems interventions are required such as

supervision, audit of BANC records and a tracing policy for women who do not adhere to follow up antenatal care. Audit may help to reduce the discrepancy between what health care managers think and say is done, and what is actually done. In this study 100% clinics self-reported to be screening ALL pregnant women living with HIV for TB, initiating IPT to those eligible and taking sputum specimen to those with any of the TB symptoms. On record review only 33% clinics implemented TB screening for ALL pregnant women living with HIV. The discrepancies increased with regard to IPT initiation and collection of sputum, where 100% of clinics report adherence to guidelines, while the review of records showed that in only 10% and 20% respectively of pregnant women living with HIV were the guidelines actually implemented.

Audit provides a more realistic representation of the actual practice and ensuring that each of the elements of TB care in pregnant women living with HIV is instituted, like IPT initiation, sputum collection and initiation of TB treatment beyond the initial screening. Audit, combined with feedback, training and supervisor visits has shown moderate to strong effects in changing health worker practice [90]. However, audit was not an established practice in the clinics included in the study, although a higher proportion of doers than non-doers reported conducting an audit.

Furthermore, TB screening was more likely in clinics that had received PHC supervision and PMTCT mentorship, although this result was not found to be statistically significant in this study, probably due to the small sample of clinics.

Human resource mix and training showed a higher likelihood of TB screening among pregnant women living with HIV, and a higher probability of clinics providing TB screening for ALL pregnant women living with HIV. However, the presence of a sessional doctor had a negative association with TB screening, which requires more exploration.

None of the factors in the health service component showed an association with the likelihood of pregnant women living with HIV being screened for TB and with the probability of clinics being classified as doers or non-doers. However the health service component should be assessed in conjunction with other key components of maternal and newborn health, as it depends on a fully functioning health system [72].

This study should be regarded as a pilot study, describing current TB screening practices in one District in KZN, and exploring the association with health system factors. A larger study, drawing on a larger sample of clinics, could begin to test hypotheses that arise from this study; for example that supervision and mentorship visits, clinical audit, and a tracing system, are positively associated with TB screening. In addition, the association of the organisation of services and TB screening practices needs to be explored further.

## **Conclusion**

Training of staff in the management of TB, ART for pregnant women living with HIV, and on PMTCT, is a key building block in the health system.

Together with other building blocks, such as leadership, which includes

clinics receiving supervisory and mentoring support, health care workers are more likely to implement TB screening for ALL pregnant women living with HIV. There is need for the Ministry of Health to invest in strengthening health system activities such as ensuring availability of skill mix, training, supervision and mentorship so as to improve quality of care provided to pregnant women living with HIV and ensuring healthcare workers satisfaction.

### **List of abbreviations**

ART	Antiretroviral treatment
BANC	Basic Antenatal Care
BCG	Calmette-Guérin bacillus
HIV	Human Immunodeficiency Virus
INH	Isoniazid
IPT	Isoniazid prophylactic therapy
KZN	KwaZulu-Natal
PHC	Primary Health Care
PMTCT	Prevention of mother-to-child transmission
TB	Tuberculosis

### **Competing interests**

The authors declare that they have no competing interests

### **Author's contributions**

SM conceptualized the study, data collection and drafted manuscript

FN assisted with data analysis and reviewed the data analysis in the manuscript

AV contributed to designing the study and interpreting the results, and reviewed the manuscript

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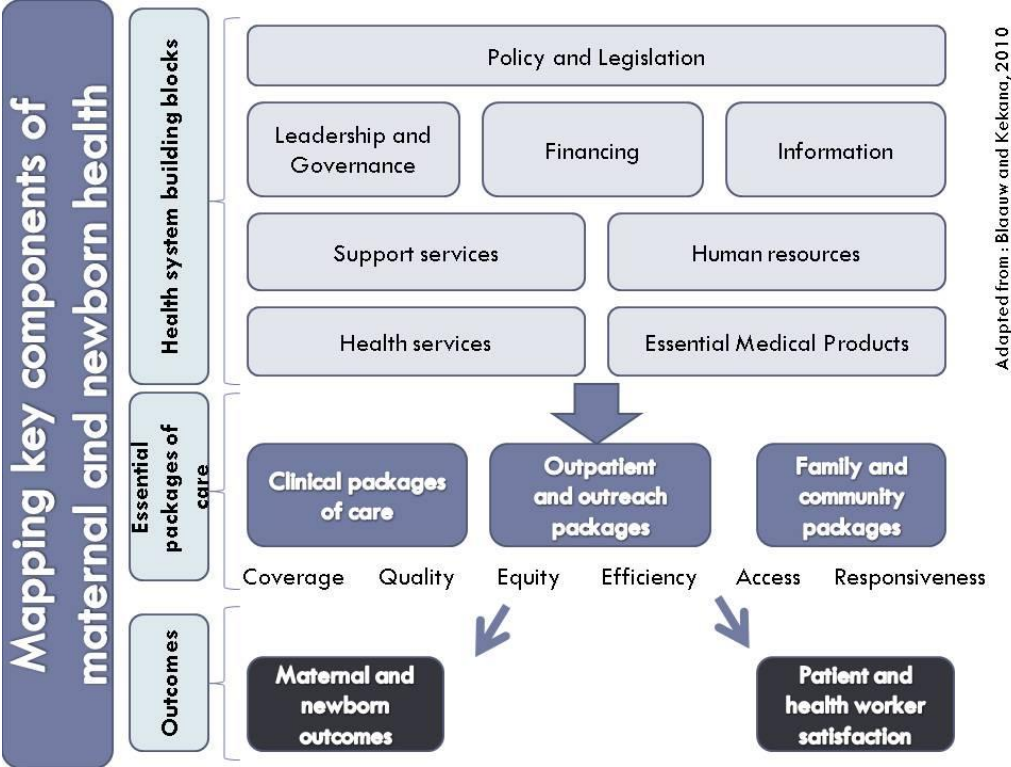
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**Figure legends**



**Figure 1: Map of key components of maternal and newborn health [65, 67]**

**Tables**

**Table1: Demographic characteristics and obstetric history of the study population (N=845)**

	Mean (95%CI)	Median	Range (min–max)	SD (95% CI)
Age	26.7 (26.3–27.1)	26	28 (18–44)	5.7 (5.4–5.9)
Gravidity	2.4 (2.3–2.5)	2	7 (1–8)	1.2 (1.1–1.3)
Parity	1.4 (1.3–1.5)	1	7 (0–7)	1.2 (1.1–1.3)
GA at first booking	19.8 (19.3–20.2)	19	35 (4–39)	6.8 (6.4–7.1)

**Table 2: TB management practices**

	Number (n)	%
Screened for TB (N=845)	645	76.3
Initiated on IPT (N=645)	124	19.2
Patients whose sputum was collected (N= 122)	11	9.0

**Table 3: Leadership and governance factors associated with TB screening of pregnant women living with HIV**

Predictor variable	Odds ratio	p-value	95%CI	
Clinics visited by PHC supervisor in the last month	4.1	0.50	0.65	265.46
Clinics visited by PMTCT mentor in the past month	2.1	0.81	0.004	1217.6

**Table 4: Human Resource factors associated with TB screening of pregnant women living with HIV**

Predictor variable	Odds ratio	p-value	95%CI	
Clinics with midwives trained on:				
TB management	2.9	0.15	0.67	12.55
ART for pregnant women	3.1	0.005*	1.42	6.67
PMTCT	3.0	0.05*	1.005	8.98
Clinics with full time ENs	3.1	0.04*	1.06	8.77
Clinics with ENs trained on TB management	7.9	0.001*	2.24	27.92
Clinics with PMTCT guidelines available	0.9	0.95	0.008	86.62

\* Statistically significant results

**Table 5: Human resource factors associated with women living with HIV being screened for TB, in 2011/2012 in the District**

	TB Screening for ALL pregnant women living with HIV				Fischer's 2-sided p-value
	Non-doers (No)		Doers (Yes)		
	n	%	n	%	
Sessional medical officer	5	50	0	0	0.022
Full time Registered Midwife	10	100	5	100	0.005*
Registered midwife trained on:					
TB	7	70	5	100	0.114
ART	9	90	5	100	0.391
PMTCT	7	70	5	100	0.165
Full time Registered Nurse	0	0	2	40	0.095
Registered Nurse trained on:					
TB	0	0	2	40	0.095
ART	0	0	2	40	0.095
PMTCT	0	0	2	40	0.095
Full time Enrolled Nurse	8	80	5	100	0.029*
Enrolled Nurse trained on:					
TB	4	40	5	100	0.043*
ART	0	0	3	60	0.022*
PMTCT	0	0	3	60	0.022*
F/T Enrolled Nurse Assistant	4	40	1	20	0.760
ENA trained on:					
TB	2	20	0	0	1.000
ART	0	0	0	0	
PMTCT	0	0	0	0	
Full time Lay Counselor (LC)	10	100	5	100	1.000
LC trained on TB	1	10	3	60	0.022*
LC trained on ART	1	10	3	60	0.022*
LC trained on PMTCT	1	10	3	60	0.022*
Full time Community Health Worker (CHW)/ Community Care Giver (CCG)	8	80	5	100	0.532
CHW/CCG trained on TB	3	30	4	80	0.017*
CHW/CCG trained on ART	1	10	4	80	0.017*
CHW/CCG trained on PMTCT	1	10	3	60	0.022*
Full time Nutrition Advisor	6	60	3	60	1.000
Nutrition Advisor trained on TB	0	0	0	0	
Nutrition Advisor trained on ART	0	0	0	0	
Nutrition Advisor trained on PMTCT	0	0	0	0	

\*statistically significant results

**Table 6: Leadership and governance, finance, information, support services and health services factors associated with women living with HIV being screened for TB, in 2011/2012 in the District**

	TB Screening for ALL pregnant women living with HIV				
	Non-doers		Doers		Fischer's 2-sided p-value
	n	%	n	%	
<b>Leadership and governance</b>					
Was the facility visited by a PHC supervisor in the past month?	5	50	4	20	0.580
Was the facility visited by a PMTCT mentor in the past month?	1	10	1	100	1.000
Were BANC records audited in the past month?	1	10	1	20	1.000
Does the facility have a clinic committee?	9	90	4	80	1.000
How often does the committee meet?	8	80	4	80	1.000
Did the committee meet as scheduled?	5	50	3	60	1.000
<b>Policy and Legislation</b>					
Maternity care guideline 2007 available?	8	80	4	80	1.000
PMTCT guidelines available?	7	70	4	80	1.000
SA National TB control Practical guideline	10	100	5	100	
TB training manual/ module available?	10	100	5	100	1.000
National TB Programme manual?	10	100	5	100	1.000
<b>Finance</b>					
Is the facility budget known?	1	10	2	40	0.242
<b>Information</b>					
PHC minimum data collection tools?	10	100	5	100	
<b>Support services</b>					
Does the facility have a tracing policy?	1	10	3	60	0.077*



Table 6 (continuation)

	TB Screening for ALL pregnant women living with HIV				
	Non-doers		Doers		Fischer's 2-sided p-value
	n	%	n	%	
<b>Health services</b>					
1st ANC available daily or on special days	6	60	2	40	0.608
TB service available daily or special days?	10	100	5	100	
Was TB covered in patient health education in the past month?	5	50	4	80	0.580
Is TB symptom screening done?	8	80	5	100	0.524
If there are signs of TB, is sputum collected for bacteriological test?	10	100	5	100	1.000
If there are no signs of TB, is IPT initiated?	10	100	5	100	1.000
If client has positive sputum is TB treatment initiated?	10	100	5	100	1.000
TB suspects register?	10	100	5	100	1.000
TB symptomatology form?	9	90	5	100	
BANC register to record all pregnant women?	10	100	5	100	
Maternity case records?	10	100	5	100	

## CHAPTER 4: INTEGRATIVE DISCUSSION

Inadequate screening for TB during antenatal care in pregnant women living with HIV, a contributory factor to high maternal mortality due to NPRI, motivated this study. In the presence of national, evidence-based guidelines for the management of TB in pregnancy, this study explored health system factors associated with the TB screening of pregnant women living with HIV. The study was located in BANC services in a health district in the Province of KwaZulu-Natal, South Africa.

An observational cross-sectional study design was carried out. Multi-stage sampling was used, firstly to select health facilities and then to select pregnant women living with HIV initiating BANC. A structured interviewer-administered questionnaire and data extraction tools were used to collect data. Data was analysed using descriptive and analytic statistics. Health system factors associated with the likelihood of TB screening among pregnant women living with HIV were identified using mixed effect logistic regression with cluster effect. Health system factors associated with the likelihood of clinics screening ALL pregnant women living with HIV were identified through doer and non-doer analysis and Fischer's exact analysis.

The study showed that pregnant women living with HIV were three (3) times more likely to be screened for TB in clinics where personnel had been trained on TB management, on ART for pregnant women, and on the PMTCT of HIV; and in clinics with a full-time enrolled nurse. Furthermore, clinics where ALL pregnant women living with HIV were screened for TB (doers) were more likely to have: a full-time midwife; personnel at all levels trained on TB management, on ART for pregnant women, and on PMTCT; and a policy to trace pregnant women who do not adhere to their scheduled subsequent visit.

The implementation of the guidelines for the screening of TB in pregnancy for women living with HIV in this study was shown to be associated with health system factors within the human resource and support services component of

the conceptual framework of of key components of maternal and newborn health care as proposed by Blaauw and Kekana.

### **Limitations**

The doer and non-doer analysis has made a contribution towards assessing whether standardised protocols of management are implemented for ALL pregnant women living with HIV. However, the small sample of clinics available for analysis resulted in wide confidence intervals, and an inability to discriminate statistically significant associations in the range of health system factors assessed.

The cross-sectional study design, relying on data extracted from the BANC register, was useful for this pilot study. A stronger study design, using observational, real-time data, could provide greater insights into the TB management in clinics of pregnant women living with HIV.

### **Further research required**

A larger study, drawing on a larger sample of clinics, could begin to test hypotheses that arise from this study: for example that supervision and mentorship visits, clinical audit, and a tracing system, are positively associated with TB screening. In addition, the association of the organisation of services and TB screening practices needs to be explored further.

### **Recommendations**

It is therefore recommended that there is need for the Ministry of Health to invest in strengthening health system activities such as ensuring availability of skill mix, training, supervision and mentorship so as to improve quality of care provided to pregnant women living with HIV and ensuring healthcare worker satisfaction.