FACTORS INFLUENCING NON-ADHERENCE TO TUBERCULOSIS TREATMENT IN TB/HIV CO-INFECTED ADULTS AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA

BY

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A Dissertation Submitted In Partial Fulfilment Of The Requirement For The Award Of The Degree Of Master Of Science In Epidemiology.

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NOVEMBER, 2017

DECLARATION

I hereby declare that all the work in this dissertation is my own and has never been submitted for another degree in this or any other university or institution of higher learning.

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ABSTRACT

Zambia is a high TB/HIV prevalence country. The aim of this study was to explore barriers to TB treatment adherence and determine the prevalence of non-adherence in the Zambian capital of Lusaka. The factors under study were socio-economic and demographic, service-related and disease and treatment related factors.

A cross-sectional study was conducted on 239 TB patients co-infected with HIV, using an interviewer-administered structured questionnaire. Chi-square test was used for bivariate analysis of the outcome and independent variables. Logistic regression was used to obtain the best model because the study had a binary outcome.

The prevalence of non-adherence was found to be 8.4%. Factors that influenced adherence to TB treatment were response to treatment ($p=0.038$) and the affordability of transport costs ($p<0.001$) to the health-care facilities. The odds of a patient defaulting treatment due to their response to the TB drugs were up to 17 times higher for those with a poor response than those of a patient with an average response.

This study found a low level of non-adherence to TB treatment. Economic constraints and treatment factors pose a threat of non-adherence to TB treatment. Social support and intensive counseling might help to mitigate this threat. Further studies addressing sensitization, intervention and their impact assessment are recommended.

Keywords: Tuberculosis, HIV/AIDS, Non-adherence, co-infection

DEDICATION

In loving memory of my late father, Mr Juma Ramadhani, for ensuring I had a good and right start to my education and my late aunt Olive Kopolo for being an academic and career inspiration.

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First and foremost I want to thank God for according me the opportunity to complete this study program and for giving me strength and wisdom for every step.

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DEFINITIONS OF KEY CONCEPTS AND ABBREVIATIONS

Acquired Immunodeficiency Syndrome (AIDS) is a disease of immune system caused by infection with a retro virus HIV.

Active Tuberculosis - TB that has been confirmed by clinical and positive sputum smear or chest x-ray result suggestive of TB

Adherence - The extent of correspondence between the patient's actual dosing history and the prescribed regimen

Antiretroviral Therapy (ART) - A name given to treatment regimens recommended by leading HIV experts to aggressively suppress viral replication and progress of HIV disease.

Co-infection -The existence of two or more diseases in an individual at a time.

Concomitant treatment- Treatment regimens occurring during the same time period for an individual.

DOTS- Directly Observed Therapy, Short course

Human Immunodeficiency Virus (HIV)-is a virus that attacks the CD4 cells or T cells that are responsible for the body's defense system.

Latent Tuberculosis – Infection of tuberculosis but the patient does not suffer active disease and is not contagious.

MDR-TB – Multidrug resistant Tuberculosis

Non-Adherence – The number of doses not taken or taken incorrectly that jeopardizes the patient's therapeutic outcome

PLWHA- People Living With HIV/AIDS

Risk Factor- A feature of somebody's habits, socio-economic, environmental, genetic makeup or personal history that increases the probability of disease or harm to health.

Tuberculosis- is an infectious disease that causes small rounded Tubercles to form on mucous membranes, especially pulmonary tuberculosis that affects the lungs.

XDR-TB – Extensively drug resistant Tuberculosis

CHAPTER ONE: INTRODUCTION

1.1 Background

1.1.1 Tuberculosis Global Statistics

Tuberculosis (TB) is the most common illness among people living with HIV/AIDS (PLWHA), including those who are on antiretroviral treatment. There were an estimated 1.1 million HIV-positive new TB cases around the world in 2013. Around 78% of these people live in sub-Saharan Africa. At least a third of the 35 million people living with HIV worldwide are infected with latent TB. Globally, people living with HIV are on average 29 times (26 – 31) more likely to develop active TB disease compared to those without HIV. The two infections cause a rapidly progressive, self-sustaining burden on the immunity of the infected individual (Makanjuola et al., 2014, Pawlowski et al., 2012, Patel et al., 2007)

An estimated 37 million lives were saved through TB diagnosis and treatment between 2000 and 2013 and in addition, collaborative TB/HIV activities between 2005 and 2011 saved an estimated 1.3 million lives. Much more however, still needs to be done to achieve universal access to these life-saving measures and activities and subsequently eliminate HIV-associated TB deaths (World Health Organization, 2014).

1.2 Problem Statement

Tuberculosis (TB) and HIV infections act in synergy and place an immense burden on health care systems posing diagnostic as well as therapeutic challenges. Infection with HIV is the greatest known risk factor predisposing for Mycobacterium tuberculosis infection. It also propagates TB in its active state and increases the risk of reactivation of latent TB, 20-fold (Adane et al., 2013, Pawlowski et al., 2012). HIV/AIDS has markedly increased the TB incidence in sub-Saharan Africa, such that up to 60% of TB patients are co-infected with HIV and every year, 200,000 TB deaths are attributable to HIV co-infection (Williams and Dye, 2003).

Zambia is an example of a country with a high HIV burden in which TB notification in the last two decades has increased 5- fold, mainly due to the HIV epidemic. Of patients notified with tuberculosis, the HIV prevalence is approximately 70% (Ayles et al., 2009).

Lack of adherence to tuberculosis treatment is a significant problem in Zambia. Studies established that 29.8% in Ndola defaulted their treatment regimen once they started feeling

better (Kaona et al., 2004) and 19% in Lusaka defaulted mainly due to a bad drug-taking attitude (Mweemba et al., 2008).

These studies reveal a gap between the world-wide recommended regimen and patients completion of this well-known effective treatment.

1.3 Justification and Significance

The aim of this quantitative study is to determine and quantify the factors that influence non-adherence to TB treatment in TB-HIV co-infected patients in Lusaka.

DOTS, the existing strategy for TB treatment relies on detecting the most infectious cases as they pass through the existing health infrastructure and ensuring that adequate treatment inclusive of a short course rifampicin-containing regimen is taken. This strategy is succeeding in reducing both mortality and prevalence of tuberculosis in areas with low prevalence of HIV (Suarez et al., 2001) and it is important to continue and enhance it in order to cope with the increased burden in high HIV prevalent settings. However, what is clear is that DOTS is not enough and further measures must also be taken (De Cock and Chaisson, 1999).

Poor adherence to treatment is common despite many varied interventions to improve treatment completion. A lack of a comprehensive and holistic understanding of the factors that influence both adherence and non-adherence to treatment is currently a major barrier to finding effective solutions. Hence, one area of study becomes increasingly imperative: non-adherence to TB treatment in TB/HIV co-infected individuals (Gebremariam et al., 2010, Xu et al., 2009, Munro et al., 2007).

In order for Zambia to reduce the prevalence of TB and meet the 'Stop TB' strategy goals, all efforts available need to be consolidated. This study could serve as a baseline for further studies and the findings could benefit the Zambian community as a whole, the international bodies that are working towards reducing the global health burden of TB and policy makers.

1.4 Research Question

What factors are influencing non-adherence to TB treatment in TB-HIV co-infected adult patients in Lusaka?

1.5 General Objective

The main purpose of this study was to determine the common factors influencing non-adherence to TB treatment in TB-HIV co-infected adult patients in Lusaka.

1.6 Specific Objectives

The specific objectives of this study were to:

i. Estimate the level of non-adherence to TB treatment among TB/HIV co-infected adult patients.
ii. Identify socio-demographic, cultural and economic factors that influence non-adherence to TB treatment in TB/HIV co-infected adult patients.
iii. Determine the service factors influencing to non-adherence to TB treatment in TB/HIV co-infected adult patients.
iv. Determine the disease and treatment-related factors influencing non-adherence to TB treatment in TB/HIV co-infected adult patients.

CHAPTER TWO: LITERATURE REVIEW

2.1 Threat of Drug-Resistant TB

To reduce the likelihood of TB in PLWHA, preventive therapy is given. However, it may be more effective in people with less advanced immune-suppression (Mwinga et al., 1998).

People living with HIV also face the threat of drug-resistant TB. Delayed diagnosis as well as low adherence to TB treatment puts people living with HIV are at high risk of mortality from Multidrug-resistant (MDR-) and extensively drug-resistant TB (XDR-TB (Gandhi et al., 2010, Amuha et al., 2009, Corbett et al., 2006).

By definition, Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs. On the other hand, extensively drug-resistant tuberculosis (XDR-TB) is a form of multidrug-resistant tuberculosis that responds to even fewer available medicines, including the most effective second-line anti-TB drug (World Health Organization, 2014).

2.2 International Standard of TB treatment

DOTS, (directly observed treatment, short course), is the internationally recommended and recognized control strategy for TB. It is also the most effective strategy. Its delivery includes the direct observation of therapy (DOT), where a trained health care worker or any other designated person (DOT supporter) observes as the patient takes every dose. This strategy, promoted widely and implemented globally, has helped patients complete their TB therapy quickly, without unnecessary gaps thus decreasing the risk of developing drug resistance which results from incomplete or erratic treatment (World Health Organization, 1999). WHO has reported that over 30 million TB patients have been treated with this five-element DOTS strategy and the resulting cure rates greater than 80% were observed with default rates of less than 10% (Zignol et al., 2006).

The present TB vaccine, BCG which is administered in infancy, does not effectively prevent the most prevalent form of the disease, pulmonary TB in adults (Kaufmann and McMichael, 2005).

2.3 TB Treatment Challenges

There were an estimated 9 million new cases of TB in 2013 (including the 1.1 million cases among people with HIV) and an estimated 1.5 million deaths (including 360 000 people with HIV), making this disease one of the world's biggest infectious killers (WHO MDG 6, 2014).

TB is both treatable and curable. Active TB disease, when drug sensitive, is treated with a standard six-month course which consists of four antimicrobial drugs provided with information, supervision and support to the patient by either a health worker or trained volunteer. Without such supervision or support, adherence to treatment can be difficult, thus propagating the spread of the disease. A vast majority of TB cases can be cured if treatment is provided and taken properly (Bam et al., 2006).

Urquhart describes adherence to treatment as "the extent of correspondence between the patient's actual dosing history and the prescribed regimen". Poor adherence with rationally prescribed drug regimens attenuates the benefits of treatment, showing without a doubt that compliance is a key link between treatment and outcome of an illness (Urquhart, 1996).

Evidence shows that TB treatment can greatly reduce HIV and TB-related morbidity and mortality in co-infected patients. However, concomitant treatment is complicated by factors such as overlapping drug toxicities, drug-drug interactions and possible paradoxical reactions. The higher pill burden in concomitant treatment is highly implicated in poor adherence. Co-infected patients may thus be at risk for decreased adherence to either one or both treatments (Muture et al., 2011, Gebremariam et al., 2010, Amuha et al., 2009, Corbett et al., 2006)

Some cited significant factors contributing to non-adherence were forgetfulness, patient attitude, being in the continuation phases of chemotherapy, feeling better long before treatment has been completed and co-infection with HIV (Tesfahuneygn et al., 2015, Adane et al., 2013, Amuha et al., 2009, Mweemba et al., 2008).

Other studies have also reported that in addition to personal characteristics influencing adherence to treatment, other themes included:

i) Individual personal beliefs;
ii) HIV treatment and related issues;
iii) Socio-economic factors;
iv) Family and other social support factors, and
v) Relationships with health providers (Makanjuola et al., 2014, Gebremariam et al., 2010, Xu et al., 2009)

2.4 Impact of Non-adherence

Non-adherence is a big challenge in achieving high TB cure rates and ultimately increases healthcare costs in developing countries. This increases both TB and HIV mortality rates (Adane et al., 2013, Awofeso, 2008, Jakubowiak et al., 2007, Mishra et al., 2005). Efforts and interventions have been made to improve adherence and treatment completion but still poor adherence is a factor that is affecting the TB cure rates. This clearly shows that there's a gap in understanding the barriers and facilitators of treatment adherence (Munro et al., 2007)

2.5 TB in Zambia

Tuberculosis is a major public health risk factor of high mortality among patients in Zambia. The prevalence of tuberculosis among adults has more than doubled since the onset of the HIV/AIDS epidemic in Zambia, with most cases being victims of the 'twin epidemics'. (Kaona et al., 2004).

The steady rise of TB incidence in Zambia can in part be attributed to the lack of patient compliance to TB treatment. An increased prevalence of TB leads to an increased incidence of infection. This indicates a need to reduce the prevalence by understanding the problem of non-compliance with TB treatment. Compliance is one of the major determinants of TB control (Mweemba et al., 2008).

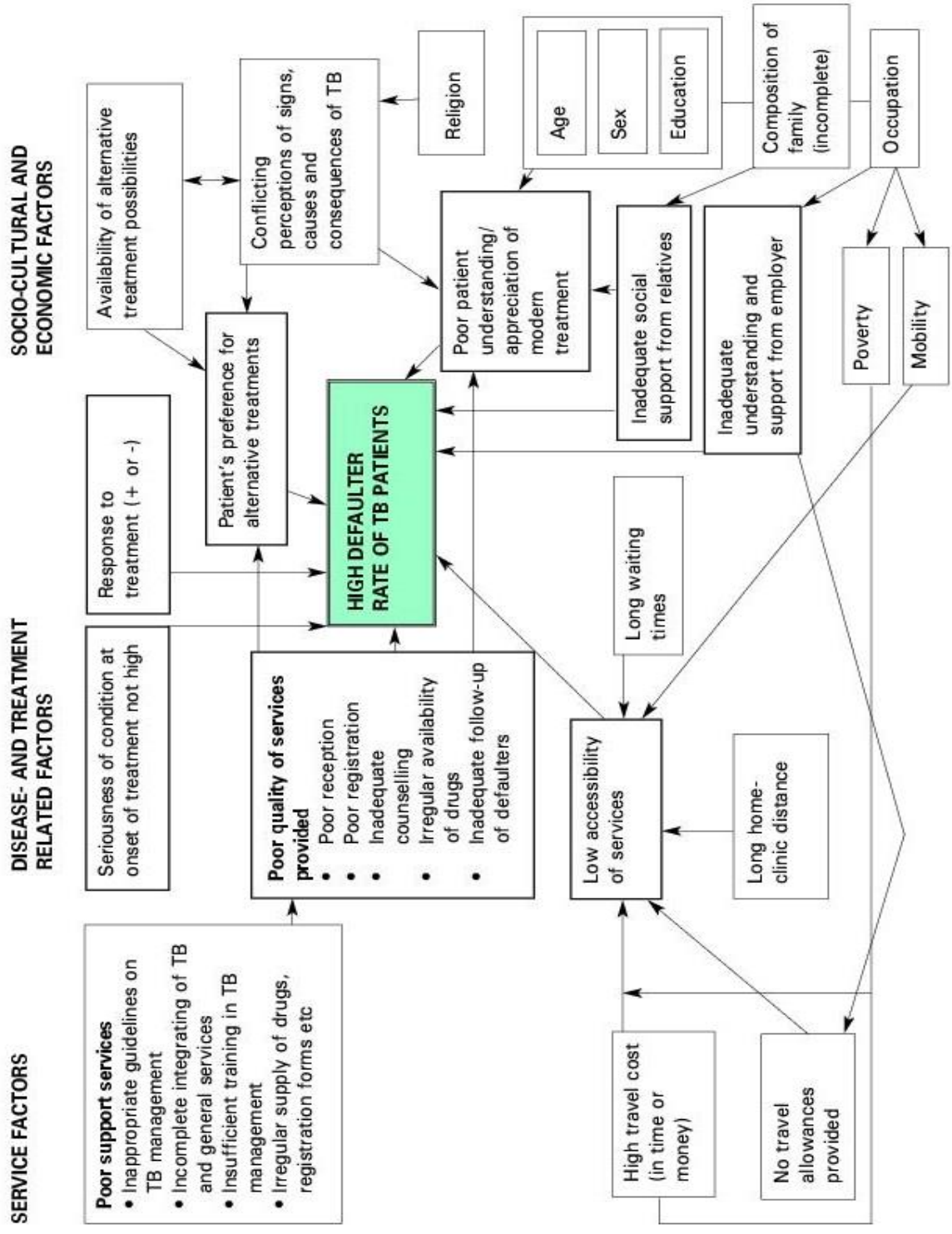

Figure 1: Conceptual Framework
(Varkevisser et al., 1993)

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Research Design

A cross-sectional study was used to determine factors that influence non-adherence to TB treatment in adult TB/HIV co-infected patients.

3.1.1 Research setting and Period

This study was conducted in Lusaka, the capital of Zambia, at the University Teaching Hospital (UTH). Information was gathered from patients seeking treatment for the first time and after relapses or treatment failure. Also included in the study were patients with multi-drug resistant TB. More information was obtained from clinic records and health-care workers where need arose. A timeframe of about three (03) months was taken for data collection. This was between November 2015 and February 2016.

3.2 Study Procedure

This section describes the population, sample and sample size, methods of data collection and data analysis. It shows the techniques used to gather and analyze information aimed at answering the research question.

3.2.1 Sampling Procedure and sample size

Convenient sampling was used.

Sample size calculation was as follows:

$$n = \frac{z^2 \times p(1-p)}{d^2}$$

- z= 1.96
- d= 0.05
- 19% proportion (p) as in a previous study by Mweemba et al.
- 80% power
- 0.05 precision
- Sample size = 237 (minimum)

3.2.2 Sampling Criteria

The population of this study included all TB/HIV co-infected persons in Lusaka who were above 18 and seeking treatment at UTH.

In this study the following inclusion criteria was used;

- TB patients who were 18 and above.
- TB patients who were seeking treatment at UTH in the duration of data collection.
- Patients who were willing to give their informed consent to participate in the study.

The following exclusion criteria were used;

- Patients who were too sick and unable to communicate.

3.3 Data Collection

Data collection was conducted at the University Teaching Hospital in ART and chest clinics using a structured questionnaire after obtaining informed consent from each participant. This was performed by the researcher. To identify co-infected participants, patient records were used with consent from both the institution and the participants. Data was collected on socio-demographic characteristics which included age, sex, religion, marital status, level of education and residence. Health service-related factors included distance to health institution, attitude of health workers etc. while disease and treatment-related factors included drug availability, disease relapses, adverse drug reactions and whether or not patients were on antiretroviral therapy. The objective of the study was explained to each participant and the data collection was conducted in a private set up. The participants did not need to be literate.

3.3.1 Data Collection instrument

A structured questionnaire was used to gather information on factors that influence patients' non-adherence to TB treatment.

3.3.2 Data Entry

In this study, a single entry system was used for data collection. Only the researcher 3.3.3 Data Analysis

Stata version 12 was used for data cleaning and statistical analysis. Analysis of categorical variables included summary statistics such as frequency distributions. Continuous variables were summarized as means and standard deviations since they were normally distributed.

Normality was determined by a q-plot. Associations between variables were determined using the Mantel-Haenszel chi-square or Fisher's exact test.

Since this study had a binary outcome variable, logistic regression was used for analysis of association between explanatory variables and the outcome variable which was non-adherence to TB treatment. This study reported results at 5% level of significance.

The independent variables in this study were analysed by univariate analysis before being included in the multiple logistic regression model. Backward regression was used to obtain the final best fit model.

3.4 Ethical Considerations

3.4.1 Ethical Clearance and informed consent

This study was presented to UNZABREC for ethical approval. In addition, a letter of introduction was obtained from the University of Zambia Public Health department in order to get institutional (UTH) consent.

3.4.2 Specific Ethical Issues

In relation to the research topic (Non-adherence to TB treatment in TB/HIV co-infected adult patients), ethical issues that were considered and addressed were as follows;

- Individuals had the right to choose whether or not to participate and to know about the personal risks and consequences of joining the study. In the execution of this study, participants were informed about their right to decide voluntarily whether to participate or not. They were informed that there would be no risk or penalty for non-participation prior to data collection.
- Participants were furnished with adequate information regarding the research to enable them to comprehend and have the power of free choice. Written informed consent was obtained from the study participants before they were interviewed.
- In this study a pledge was made, that information obtained from participants would not be publicly reported in a manner that identified them. Confidentiality of the participants and their information was secured by using codes instead of participants' names throughout the study to ensure anonymity.
- The interviews were all conducted in a private room, one participant at a time.

CHAPTER FOUR: RESULTS

Table 1 shows descriptive statistics for the sample population under study. This was disaggregated by ART status (whether on ART or not).

Table 1: Characteristics of study population in the research on factors influencing non-adherence to TB treatment in TB/HIV co-infected adults at UTH in Lusaka: a cross sectional study.

VARIABLE	Overall n=239	On ART n=225	Not On ART n=14
SOCIODEMOGRAPHIC, CULTURAL & ECONOMIC FACTORS	n= 100%	n= 94.14%	n= 5.86%
Age groups:			
23-33	74 (30.96)	68 (30.22)	6 (42.86)
34-38	80 (33.47)	77 (34.22)	3 (21.43)
39-56	85 (35.56)	80 (35.56)	5 (35.71)
		N=225	N=14
Sex:			
Male	105 (43.93)	98 (43.56)	7 (50)
Female	134 (56.07)	127 (56.44)	7 (50)
Marital Status:			
Single	20 (8.37)	19 (8.44)	1 (7.14)
Married	173 (72.38)	160 ((71.11)	13 (92.86)
Divorced	18 (7.53)	18 (8.00)	0
Widowed	28 (11.72)	28 (12.44)	0
Education Status:			
None	105 (43.93)	99 (44)	6 (42.86)
Primary	97 (40.59)	91 (40.44)	6 (42.86)
Secondary	26 (10.88)	24 (10.67)	2 (14.29)
Tertiary	11 (4.60)	11 (4.89)	0
Occupation Status:			
Unemployed	48 (20.08)	46 (20.44)	2 (14.29)
Self-employed	113 (47.28)	104 (46.22)	9 (64.29)
Employed	75 (31.38)	72 (32)	3 (21.43)
Retired	3 (1.26)	3 (1.33)	0
Community Stigma:			
No	218 (91.21)	206 (91.56)	12 (85.71)
Yes	21 (8.79)	19 (8.44)	2 (14.29)
Cultural Conflict:			
No	230 (96.23)	216 (96)	14 (100)

Yes	9 (3.77)	9 (4)	0
SERVICE-RELATED FACTORS			
Cost of trip affordable?			
No	20 (8.37)	18 (8)	2 (14.29)
Yes	219 (91.63)	207 (92)	12 (85.71)
Free to ask questions			
No	10 (4.18)	10 (4.44)	0
Yes	229 (95.82)	215 (95.56)	14 (100)
Reception after skipping			
Good	12 (60)	12 (60)	0
Poor	8 (40)	8 (40)	0
DISEASE& TREATMENT FACTORS			
Times infected			
Once	219 (91.63)	205 (91.11)	14 (100)
Twice	18 (7.53)	18 (8.00)	0
Three times	2 (0.84)	2 (0.89)	0
Diagnosis:			
Screening	9 (3.77)	9 (4)	0
Symptoms	19 (7.95)	18 (8)	1 (7.14)
Very ill	211 (88.28)	198 (88)	13 (92.86)
Response to treatment			
Good	216 (90.38)	205 (91.11)	11 (78.57)
Average	16 (6.69)	15 (6.67)	1 (7.14)
Poor	7 (2.93)	5 (2.22)	2 (14.29)
Drugs available:			
No	6 (2.51)	6 (2.67)	0
Yes	233 (97.49)	219 (97.33)	14 (100)
Duration on ART:			
<1 year	16 (6.69)	16 (7.11)	0
1-2 years	19 (7.95)	19 (8.44)	0
>2 years	190 (79.5)	190 (84.44)	0
N/A	14 (5.86)	0	14
Patients experience of dual treatment			
No Problems	194 (81.17)	194 (86.22)	0
Side Effects	31 (12.97)	31 (13.78)	0

N/A	14	0	14
Changes with ART			
Improved	215 (89.96)	215 (95.56)	0
Got ill	8 (3.35)	8 (3.56)	0
No change	2 (0.83)	2 (0.89)	0
N/A	14 (5.86)	0	14
Changes with TB treatment			
Improved	226 (94.56)	212 (94.22)	14
Got ill	9 (3.77)	9 (4)	0
No change	4 (1.67)	4 (1.78)	0

The mean age of participants this study was 37 with a standard deviation of 6.65. The minimum and maximum ages were 23 and 56, respectively. The prevalence of non-adherence was 8.37% (4.8-11.9%).

Majority of the participants (72.38%) were married. The married participants also accounted for the majority of those on ART (71.11%). There were more females overall (56.07%) than males (43.93%). The same was case among those on ART (56.44% female vs 43.56% male). Majority of the respondents reported having no education (43.93%) and being self employed (47.28%). Very few participants reported experiencing stigma in their communities (8.79%) or having cultural beliefs that were in conflict with modern treatment (3.77%).

About 92% of the participants afforded the cost of trip to the health facility for their medication and about 96% were free to ask personnel any questions they had concerning their treatment.

In this study, most participants reported having suffered TB once (91.63%) and this included all (14) those who were not on ART. Majority (88.28%) were diagnosed after becoming very ill as opposed to those who were diagnosed after experiencing some symptoms (7.95%) or during a general body screening (3.77%).

About 90% of the participants reported a good response to treatment while 97.5% reported that drugs were readily available every time they went to their health facility. Of those on ART, the majority (79.5%) had been on therapy for more than two years and most of them (81.17%) reported no side effects with the dual treatment.

Of the 239 participants in this study, 94.14% were on concomitant treatment for TB as well as HIV while 5.86% were only on TB treatment. The age-groups in this study were created in such a way as to have equal populations in each group.

Table 2 : Bivariate analyses of Outcome variable (adherence to TB treatment) and independent variables using the Chi square test.

VARIABLE	ADHERED N (%)	DEFAULTED N (%)	p-value
SOCIODEMOGRAPHIC, CULTURAL & ECONOMIC FACTORS			
Age group			
23-33	69 (93.24)	5 (6.76)	0.520
34-38	71 (88.75)	9 (11.25)	
39-56	79 (92.94)	6 (7.06)	
Sex:			
Male	94 (89.52)	11 (10.48)	0.298
Female	125 (93.28)	9 (6.72)	
Marital Status:			
Single	19 (95)	1 (5)	*0.940
Married	158 (91.33)	15 (8.67)	
Divorced	17 (94.44)	1 (5.56)	
Widowed	25 (89.29)	3 (10.71)	
Education Status:			
None	98 (93.33)	7 (6.67)	
Primary	89 (91.75)	8 (8.25)	*0.403
Secondary	23 (88.46)	3 (11.54)	
Tertiary	9 (81.82)	2 (18.18)	
Occupation Status:			
Unemployed	44 (91.67)	4 (8.33)	
Self-employed	103 (91.15)	10 (8.85)	*0.414
Employed	70 (93.33)	5 (6.67)	
Retired	2 (66.67)	1 (33.33)	
Community Stigma:			
No	203 (93.12)	15 (6.88)	0.007
Yes	16 (76.19)	5 (23.81)	
Cultural Conflict:			
No	211 (91.74)	19 (8.26)	*0.551
Yes	8 (88.89)	1 (11.11)	

SERVICE-RELATED FACTORS			
Cost of trip affordable?			
No	12 (60.0)	8 (40.0)	<0.001
Yes	207 (94.52)	12 (5.48)	
Free to ask questions			
No	8 (80.0)	2 (20.0)	*0.200
Yes	211 (92.14)	18 (7.86)	
DISEASE&TREATMENT FACTORS			
Times infected			
Once	210 (95.89)	9 (4.11)	*<0.001
Twice	9 (50)	9 (50)	
Three times	0	2	
Diagnosis:			
Screening	6 (66.67)	3 (33.33)	*0.039
Symptoms	17 (89.47)	2 (10.53)	
Very ill	196 (92.89)	15 (7.11)	
Response to treatment			
Good	204 (94.44)	12 (5.56)	
Average	9 (56.25)	7 (43.75)	*<0.001
Poor	6 (85.71)	1 (14.29)	
Drugs available:			
No	4 (66.67)	2 (33.33)	*0.081
Yes	215 (92.27)	18 (7.73)	
Duration on ART:			
<1 year	14 (87.50)	2 (12.5)	
1-2 years	17 (89.47)	2 (10.53)	*0.630
>2 years	174 (91.58)	16 (8.42)	
N/A	14 (100)	0	
Patients experience of dual treatment			
No Problems	183 (94.33)	11 (5.67)	<0.001
Side Effects	22 (70.97)	9 (29.03)	
Changes with ART			
Improved	195 (90.70)	0	
Got ill	8 (100)	20 (9.30)	*0.723
No change	2 (100)	0	
N/A	14 (100)	0	

Changes with TB treatment			
Improved	209 (92.48)	17 (7.52)	*0.029
Got ill	8 (88.89)	1 (11.11)	
No change	2 (50.0)	2 (50.0)	

* Used Fisher's exact test because they did not satisfy chi-square assumptions.

In the bivariate analysis, variables that significantly influenced non-adherence to TB treatment included community stigma (p=0.007), affordability of the cost of the trip to the health facility (p<0.001), the number of times a participant had had TB (p<0.001), what led to the diagnosis (p=0.039), a participant's response to treatment (p<0.001), their experience of dual treatment (p<0.001) as well as the changes in a participant's health with TB treatment (P=0.029). The rest of the variables were not statistically significant. There were 20 out of the 239 participants who did not adhere to their TB treatment.

There were more participants (11.25%) who did not adhere in the 34-38 age-group than the other age-groups. More males (10.48%) defaulted treatment compared to females (6.72%). The widowed had a higher default rate than other groups with respect to marital status followed by those who were married. Participants who had attained tertiary education had a higher default rate (18.18%) than all the other classes of education status.

There was a higher default rate (20%) among those who were not free to ask health personnel questions compared to those who were (7.86%). Participants who had been on ART for less than a year defaulted more (12.5%) than those who had been on ART more than two years.

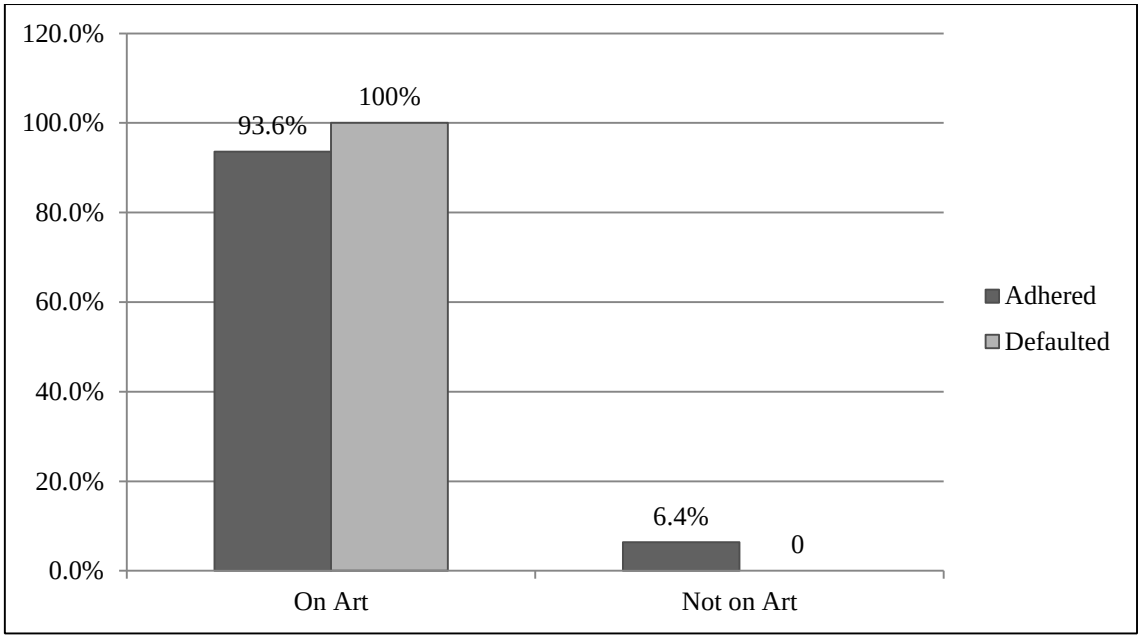

Figure 2: Participants who defaulted versus those who adhered to TB treatment disaggregated by whether or not they were on ART.

The figure above shows that all those who did not adhere to TB treatment were on Anti-Retroviral Treatment and all participants who were not on ART adhered to their TB treatment.

Table 3: Logistic regression model fitting all significant variables from the Univariate analysis

VARIABLE	ODDS RATIO (CI)	P-value
SOCIODEMOGRAPHIC, CULTURAL & ECONOMIC FACTORS		
Age groups:		
23-33	1.00	-
34-38	1.44 (0.29 - 7.18)	0.655
39-56	0.33 (0.05 – 2.17)	0.251
Sex:		
Male	1.00	-
Female	0.54 (0.13 – 2.07)	0.367
Marital Status:		
Single	0.68 (0.006 -72.33)	0.872
Married	2.88 (0.07 - 123.7)	0.582
Divorced	1.00	-
Widowed	10.34(0.16 - 651.37)	0.269

Education Status:		
None	1.00	-
Primary	1.77 (0.37 - 8.40)	0.472
Secondary	2.59 (0.32 - 21.21)	0.376
Tertiary	8.90 (0.59 - 134.67)	0.115
Occupation Status:		
Unemployed	0.41 (0.03 – 6.54)	0.528
Self-employed	1.99 (0.38 -10.26)	0.409
Employed	1.00	-
Retired	13.88 (0.25 – 778.98)	0.200
Community Stigma:		
No	1.00	-
Yes	0.47 (0.04 -6.10)	0.561
Cultural conflict:		
No	1.00	-
Yes	0.11 (0.002 – 5.95)	0.281
SERVICE-RELATED FACTORS		
Cost of trip affordable?		
No	1.00	-
Yes	0.04(0.003 – 0.618)	0.02
Free to ask questions		
No	1.00	-
Yes	0.26 (0.016 – 4.14)	0.341
DISEASE & TRT FACTORS		
Diagnosis:		
Screening	1.00	-
Symptoms	0.05 (0.003 0.83)	0.037
Very ill	0.10 (0.01 -1.05)	0.055
Response to treatment		
Good	0.04 (0.006 – 0.21)	<0.001
Average	1.00	-
Poor	0.005(0.00005–0.59)	0.029
Drugs available:		
No	1.00	-
Yes	0.59 (0.01 – 20.05)	0.771
Changes with TB treatment		

Improved	0.73 (0.02 – 30.02)	0.870
Got ill	1	-
No change	9.29(0.07 – 1205.1)	0.369

Table 4: Final nested model showing predictors of Non-adherence using Backward Stepwise Regression.

VARIABLE	ODDS RATIO (CI)	P-VALUE
Cost of trip affordable	0.09 (0.03 – 0.32)	<0.001
Response to treatment		
Good	0.09 (0.03 – 0.34)	<0.001
Average	1.00	-
Poor	0.06 (0.004 – 0.86)	0.038

In the multivariate analysis, variables that were statistically significant were affordability of the cost of trip to the health facility (p=0.02) and a patient's response to treatment (good response-p<0.001 and poor response-p=0.029). The variable 'what led to the diagnosis' was borderline (p=0.055). When the final model was done, affordability of transport costs (p<0.001) and response to treatment (good-p<0.001 and poor-p=0.038) were still significant.

CHAPTER FIVE: DISCUSSION

We set out to determine what factors influence non-adherence to TB treatment in adult patients at UTH in Lusaka and the current prevalence of non-adherence. Results indicate that service-related factors as well as disease and treatment related factors were important barriers to patients' adherence to TB treatment. The specific risk factors under these classes of factors were: the cost of the trip to the health care facilities where patients got their drugs and the patients' response to treatment.

Prevalence of Non-adherence

Prevalence of non-adherence in this study was 8.37%. This is 56% lower than it was eight years ago in a study on "Knowledge, attitudes and compliance with Tuberculosis treatment" (Mweemba et al., 2008). Our study adopted a 100% level of compliance to treatment as being adherent. Even though this ideal level of compliance is rarely achieved in current clinical practices (Chirwa et al., 2013), it was used in order to minimize any measurement bias that could arise from the patients' recall of how often they defaulted.

Factors that influenced defaulting treatment

The cost of the trip to the health facility was found to be a risk for non-adherence, much more during the intensive phase of treatment when patients are required to travel to the health facility daily for their directly observed treatment. Other studies report similar findings (Shargie and Lindtjorn, 2007, Bam et al., 2006, Mishra et al., 2005, Rubel and Garro, 1992). With the odds of defaulting being 11 times higher in patients who cannot always afford the cost of transport, our study agrees with other studies (Gebremariam et al., 2010, Raviglione and Uplekar, 2006, Spence et al., 1993) that TB is a disease that afflicts the poor.

We found another risk factor of importance was patients' response to treatment. Interestingly, both those who responded well and those who responded poorly defaulted on their treatment. This is also in line with other studies previously done (Muture et al., 2011, Kaona et al., 2004). The odds of non-adherence for those who responded poorly to treatment were lower than the odds of non adherence for those who responded well. It can be understood that those who default due to poor response to treatment, do so because of the side effects. However, there are different reasons for not adhering when patients feel better. These include forgetfulness and ignorance of the requirement that one needs to be on treatment for the

entire six months, regardless of the improvement (Muture et al., 2011, Amuha et al., 2009, Bam et al., 2006).

The study population included only individuals who had completed their intensive phase of treatment, with the rationale that their reasons for default would be much more varied. It is known that the majority default in the intensive phase (Liam et al., 1999) but our study aimed at finding out the minority's reasons as well.

Statistical Analysis

In the bivariate analysis, one factor under socioeconomic, cultural and demographic factors was significantly influencing non-adherence to TB treatment. This was community stigma. Even though TB is curable, there is still a lot of stigma that surrounds it (Xu et al., 2009, Rubel and Garro, 1992). This poses a risk of a patient not adhering to treatment (Mishra et al., 2006) as they avoid being seen or known to be on treatment. However, this factor was not significant in the multivariate analysis.

In the category of disease and treatment-related factors, two variables were statistically significant in bivariate analysis. These were the non-availability of drugs at the health centers and being on concomitant treatment with ART. These are key factors in treatment compliance even though they were not statistically significant in the multivariate analysis.

TB drugs, though free, are not always available in health facilities and this was reported by some studies to be a barrier to treatment compliance (Muture et al., 2011, Xu et al., 2009, Daniel et al., 2006). We found that this factor was independently associated with non-adherence but was not significant in the multivariate analysis. However, logically, we can assume that when drugs are not available, it is most probable that a patient will default treatment. Being on concomitant treatment for TB and HIV is a factor that has been highly implicated to be a barrier to treatment adherence in a number of studies (Makanjuola et al., 2014, Adane et al., 2013, Gebremariam et al., 2010, Awofeso, 2008). They have reported among other reasons that there are possible adverse drug interactions, pill burden and over-lapping drug toxicities.

This study showed that the group most affected by the dual epidemic is that between ages 34 and 38. This finding was in agreement with another study in Ndola (Kaona et al., 2004). Though it was not statistically significant, this group also had the least rate of adherence, contrary to a finding that adherence to treatment increases with age (Mehta et al., 1997). The

34 to 38 age group are a productive age, in the prime of their life and their lack of adherence to treatment could be due to various commitments like businesses and jobs in order to make a living and they might not have the time to wait in line at clinics to be attended to (Jin et al., 2008). However, as in other studies age was not statistically influential in patients' non-compliance in this study.

With regard to sex, there were less male participants in the study and the rate of defaulting was higher among them. However this was not statistically significant. A Russian study was consistent with this result (Jakubowiak et al., 2007). Other studies however, found that default was more common among men than among women (Jin et al., 2008, Wares et al., 2003, Mehta et al., 1997). In this regard, it may be assumed that male patients do not comply probably due to their view on masculinity. Illness and treatment taking may be seen as a 'weakness' and this may be a reason for default. Additionally, many men are the providers in their homes, making them subject to differently placed priorities as earlier alluded to with regards to the productive age group.

There was no association found between patients' marital status and drug-taking habits. This finding matches that in Ndola when a similar study was done (Kaona et al., 2004). However, it was found that the highest percentage among defaulters were those who were widowed whereas the highest percentage among those who complied were the divorced participants.

Education status was not a significant facilitator or barrier to treatment adherence in our study. This is in agreement with some other studies (Jin et al., 2008, Liam et al., 1999). Unlike some studies (Gelmanova et al., 2007, Jakubowiak et al., 2007, Chang et al., 2004), this study found that occupation status was not a significant social factor in non-adherence (Liam et al., 1999).

Interestingly, cultural beliefs in this study were not found to influence adherence to treatment. Nine out of the 239 participants had some opposing cultural views against 'western medicine' but out of those, eight reported that they did not default treatment. This was in contrast to other studies that found that erroneous beliefs or misconceptions bore importance on a patient's treatment taking habits (Jin et al., 2008).

We also found that whether or not patients had a good relationship with Health Care Workers did not have a significant effect on their adherence to treatment. This was contrary to other studies which reported that lack of respect, confidentiality and adequate communication with

health professionals as well as aggressive responses resulted in default of treatment (Gebremariam et al., 2010, Xu et al., 2009, Mishra et al., 2006, Wares et al., 2003). In this study, it was found that these negative factors were only reported after patients had defaulted, making it difficult to determine if this could be a risk factor for non-adherence.

In this study, the number of times a patient had had TB was not a significant factor in whether or not they adhered to treatment. In addition, contrary to other findings (Liam et al., 1999) which report that previous patient education on treatment compliance may have contributed to their compliance in subsequent TB infections, our study found that those who suffered disease relapse did not adhere to their dosage. However, there was no statistical significance to this finding.

Limitations of the study

This study was not without limitations. It was a facility-based study so the findings cannot be generalised to Lusaka. Self-reporting by participants could have led to inaccurate information either by recall bias or not wanting to be viewed as negligent in their drug-taking. Sensitivity (stigma) of the two infections under study could have led to participants giving inaccurate information. There was no way to objectively quantify some of the factors that were included in the questionnaire, for example, response to treatment: good, average and poor. This could have led to misclassification of participants, causing increase in some classes and reduction in others. Factors like community stigma were not determined whether they were experienced or perceived. If perceived stigma was reported where participants were asked about experienced stigma, this could have increased the number of participants who reported having experienced stigma in their communities.

However, the study also had strengths. The study sample included only participants who had been on treatment for more than two months, making their reasons for defaulting much more varied because of their different experiences over time. The level of compliance adopted for adherence was 100%. This cut down on errors that could have arisen from misclassifying participants in different levels of adherence due to recall bias.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Our findings suggest that economic constraints and treatment factors influence non-adherence to TB treatment. The prevalence of non-adherence was found to be 8.37%, which is a reduction from the 19% that was found in a similar study eight years ago. Further studies addressing social interventions and assessment of their impacts are recommended.

6.2 Recommendation

This study highlights the need for health professionals and policy makers to be aware of barriers to TB treatment compliance in TB/HIV co-infected patients. In a high TB/HIV prevalence setting as well as low-middle income country like Zambia (Ayles et al., 2009), this knowledge and its application is vital in effectively cutting back on healthcare costs that arise from non-compliance and its effects. Incentives and minimal support to meet transport costs could be provided in addition to counseling in order to facilitate adherence. This has been successful in other countries where strong social support has improved treatment compliance and ultimately treatment outcomes (Jakubowiak et al., 2007, Davidson et al., 2000).

It cannot be over-emphasized that continued counseling, particularly for those on a dual treatment regime for TB and HIV, is a necessary part of patient management. This could help patients to comply despite experiencing side effects to treatment (Liam et al., 1999) Educating the public as well may reduce TB and HIV related stigma (Adane et al., 2013, Gebremariam et al., 2010).

REFERENCES

ADANE, A. A., ALENE, K. A., KOYE, D. N. & ZELEKE, B. M. 2013. Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in Northwest Ethiopia. *PloS one,* 8**,** e78791.

AMUHA, M. G., KUTYABAMI, P., KITUTU, F. E., ODOI-ADOME, R. & KALYANGO, J. N. 2009. Non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara Hospital Uganda: Prevalence and associated factors. *African health sciences,* 9.

AWOFESO, N. 2008. Anti-tuberculosis medication side-effects constitute major factor for poor adherence to tuberculosis treatment. *Bull World Health Organ,* 86**,** B-D.

AYLES, H., SCHAAP, A., NOTA, A., SISMANIDIS, C., TEMBWE, R., DE HAAS, P., MUYOYETA, M. & BEYERS, N. 2009. Prevalence of tuberculosis, HIV and respiratory symptoms in two Zambian communities: implications for tuberculosis control in the era of HIV. *PloS one,* 4**,** e5602.

BAM, T., GUNNEBERG, C., CHAMROONSAWASDI, K., BAM, D., AALBERG, O., KASLAND, O., SHIYALAP, K. & SRISORRACHATR, S. 2006. Factors affecting patient adherence to DOTS in urban Kathmandu, Nepal. *The International Journal of Tuberculosis and Lung Disease,* 10**,** 270-276.

CHANG, K., LEUNG, C. & TAM, C. 2004. Risk factors for defaulting from anti-tuberculosis treatment under directly observed treatment in Hong Kong. *The International Journal of Tuberculosis and Lung Disease,* 8**,** 1492-1498.

CHIRWA, T., NYASULU, P., CHIRWA, E., KETLOGETSWE, A., BELLO, G. & DAMBE, I. 2013. Levels of Tuberculosis Treatment Adherence among Sputum positive Pulmonary Tuberculosis Patients Attending care at Zomba Central Hospital, Southern Malawi. *PloS one,* 8.

CORBETT, E. L., MARSTON, B., CHURCHYARD, G. J. & DE COCK, K. M. 2006. Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment. *Lancet,* 367**,** 926-37.

DANIEL, O. J., OLADAPO, O. T. & ALAUSA, O. K. 2006. Default from Tuberculosis Treatment Programme in Sagamu, Nigeria. *Nigerian Journal of Medicine,* 15.

DAVIDSON, H., SCHLUGER, N., FELDMAN, P., VALENTINE, D., TELZAK, E. & LAUFER, F. 2000. The effects of increasing incentives on adherence to tuberculosis directly observed therapy. *The International Journal of Tuberculosis and Lung Disease,* 4**,** 860-865.

DE COCK, K. & CHAISSON, R. 1999. Will DOTS do it? A reappraisal of tuberculosis control in countries with high rates of HIV infection [Counterpoint]. *The International Journal of Tuberculosis and Lung Disease,* 3**,** 457-465.

GANDHI, N. R., NUNN, P., DHEDA, K., SCHAAF, H. S., ZIGNOL, M., VAN SOOLINGEN, D., JENSEN, P. & BAYONA, J. 2010. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. *The Lancet,* 375**,** 1830-1843.

GEBREMARIAM, M. K., BJUNE, G. A. & FRICH, J. C. 2010. Barriers and facilitators of adherence to TB treatment in patients on concomitant TB and HIV treatment: a qualitative study. *BMC Public Health,* 10**,** 651.

GELMANOVA, I., KESHAVJEE, S., GOLUBCHIKOVA, V., BEREZINA, V., STRELIS, A., YANOVA, G., ATWOOD, S. & MURRAY, M. 2007. Barriers to successful tuberculosis treatment in Tomsk, Russian Federation: non-adherence, default and the acquisition of multidrug resistance. *Bulletin of the World Health Organization,* 85**,** 703-711.

JAKUBOWIAK, W., BOGORODSKAYA, E., BORISOV, E., DANILOVA, D. & KOURBATOVA, E. 2007. Risk factors associated with default among new pulmonary TB patients and social support in six Russian regions. *The international journal of tuberculosis and lung disease,* 11**,** 46-53.

JIN, J., SKLAR, G. E., OH, V. M. S. & LI, S. C. 2008. Factors affecting therapeutic compliance: A review from the patient's perspective. *Therapeutics and clinical risk management,* 4**,** 269.

KAONA, F. A., TUBA, M., SIZIYA, S. & SIKAONA, L. 2004. An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. *BMC Public health,* 4**,** 68.

KAUFMANN, S. H. & MCMICHAEL, A. J. 2005. Annulling a dangerous liaison: vaccination strategies against AIDS and tuberculosis. *Nat Med,* 11**,** S33-44.

LIAM, C., LIM, K., WONG, C. & TANG, B. 1999. Attitudes and knowledge of newly diagnosed tuberculosis patients regarding the disease, and factors affecting treatment compliance. *The International Journal of Tuberculosis and Lung Disease,* 3**,** 300-309.

MAKANJUOLA, T., TADDESE, H. B. & BOOTH, A. 2014. Factors associated with adherence to treatment with isoniazid for the prevention of tuberculosis amongst people living with HIV/AIDS: a systematic review of qualitative data. *PLoS One,* 9**,** e87166.

MEHTA, S., MOORE, R. D. & GRAHAM, N. M. 1997. Potential factors affecting adherence with HIV therapy. *Aids,* 11**,** 1665-1670.

MISHRA, P., HANSEN, E., SABROE, S. & KAFLE, K. 2005. Socio-economic status and adherence to tuberculosis treatment: a case-control study in a district of Nepal. *The international journal of tuberculosis and lung disease,* 9**,** 1134-1139.

MISHRA, P., HANSEN, E. H., SABROE, S. & KAFLE, K. K. 2006. Adherence is associated with the quality of professional–patient interaction in Directly Observed Treatment Short-course, DOTS. *Patient education and counseling,* 63**,** 29-37.

MUNRO, S. A., LEWIN, S. A., SMITH, H. J., ENGEL, M. E., FRETHEIM, A. & VOLMINK, J. 2007. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. *PLoS Med,* 4**,** e238.

MUTURE, B. N., KERAKA, M. N., KIMUU, P. K., KABIRU, E. W., OMBEKA, V. O. & OGUYA, F. 2011. Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: a case control study. *BMC public health,* 11**,** 1.

MWEEMBA, P., HARUZIVISHE, C., SIZIYA, S., CHIPIMO, P., CRISTENSON, K. & JOHANSSON, E. 2008. Knowledge, attitudes and compliance with Tuberculosis treatment, Lusaka, Zambia. *Medical Journal of Zambia,* 35.

MWINGA, A., HOSP, M., GODFREY-FAUSSETT, P., QUIGLEY, M., MWABA, P., MUGALA, B. N., NYIRENDA, O., LUO, N., POBEE, J., ELLIOTT, A. M., MCADAM, K. P. & PORTER, J. D. 1998. Twice weekly tuberculosis preventive therapy in HIV infection in Zambia. *AIDS,* 12**,** 2447-57.

PATEL, N. R., ZHU, J., TACHADO, S. D., ZHANG, J., WAN, Z., SAUKKONEN, J. & KOZIEL, H. 2007. HIV impairs TNF-alpha mediated macrophage apoptotic response to Mycobacterium tuberculosis. *J Immunol,* 179**,** 6973-80.

PAWLOWSKI, A., JANSSON, M., SKOLD, M., ROTTENBERG, M. E. & KALLENIUS, G. 2012. Tuberculosis and HIV co-infection. *PLoS Pathog,* 8**,** e1002464.

RAVIGLIONE, M. C. & UPLEKAR, M. W. 2006. WHO's New Stop TB Strategy. *The Lancet,* 367.

RUBEL, A. J. & GARRO, L. C. 1992. Social and cultural factors in the successful control of tuberculosis. *Public health reports,* 107**,** 626.

SHARGIE, E. B. & LINDTJORN, B. 2007. Determinants of Treatment Adherence Among Smear-Positive Pulmonary Tuberculosis Patients in Southern Ethiopia. *PLoS medicine,* 4.

SPENCE, D. P., HOTCHKISS, J., WILLIAMS, C. S. & DAVIES, P. D. 1993. Tuberculosis and Poverty. *BMJ*.

SUAREZ, P. G., WATT, C. J., ALARCON, E., PORTOCARRERO, J., ZAVALA, D., CANALES, R., LUELMO, F., ESPINAL, M. A. & DYE, C. 2001. The dynamics of tuberculosis in response to 10 years of intensive control effort in Peru. *J Infect Dis,* 184**,** 473-8.

TESFAHUNEYGN, G., MEDHIN, G. & LEGESSE, M. 2015. Adherence to Anti-tuberculosis treatment and treatment outcomes among tuberculosis patients in Alamata District, northeast Ethiopia. *Pubmed*.

URQUHART, J. 1996. Patient non-compliance with drug regimens: measurement, clinical correlates, economic impact. *Eur Heart J,* 17 Suppl A**,** 8-15.

VARKEVISSER, C. M., PATHMANATHAN, I. & BROWNLEE, A. T. 1993. *Designing and conducting health systems research projects*, IDRC.

WARES, D., SINGH, S., ACHARYA, A. & DANGI, R. 2003. Non-adherence to tuberculosis treatment in the eastern Tarai of Nepal. *The international journal of tuberculosis and lung disease,* 7**,** 327-335.

WILLIAMS, B. G. & DYE, C. 2003. Antiretroviral drugs for tuberculosis control in the era of HIV/AIDS. *Science,* 301**,** 1535-1537.

WORLD HEALTH ORGANIZATION 1999. What is DOTS?: A guide to understanding the WHO-recommended TB Control Strategy Known as DOTS.

WORLD HEALTH ORGANIZATION 2014. Tuberculosis: fact sheet no. 104, updated October 2013.

XU, W., LU, W., ZHOU, Y., ZHU, L., SHEN, H. & WANG, J. 2009. Adherence to anti-tuberculosis treatment among pulmonary tuberculosis patients: a qualitative and quantitative study. *BMC health services research,* 9**,** 1.

ZIGNOL, M., HOSSEINI, M. S., WRIGHT, A., LAMBREGTS–VAN WEEZENBEEK, C., NUNN, P., WATT, C. J., WILLIAMS, B. G. & DYE, C. 2006. Global incidence of multidrug-resistant tuberculosis. *Journal of Infectious Diseases,* 194**,** 479-485.

APPENDICES

APPENDIX I: INFORMED CONSENT

TOPIC: FACTORS INFLUENCING NON-ADHERENCE TO TUBERCULOSIS TREATMENT IN TB-HIV COINFECTED ADULT PATIENTS IN LUSAKA.

INTRODUCTION

I, Asha Ramadhani, a Master of Science in Epidemiology student from the University of Zambia, am requesting for your participation in the research study mentioned above.

PURPOSE OF THE STUDY

You are being asked to take part in a study which is aimed at determining the factors that affect drug adherence to TB treatment among adult TB/HIV co-infected patients.

VOLUNTARY PARTICIPATION

Your participation in this study is purely voluntary. This means that you are free to decline to participate in the study without any consequences. Furthermore, if you wish to discontinue, you are free to do so without facing any penalties.

RISKS AND DISCOMFORT

The probable risk that the study may pose is disclosure of information.

BENEFITS

There are no monetary benefits for participating in this study. You will benefit by knowing the factors that affect drug adherence among TB/HIV patients.

CONFIDENTIALITY

I would like to reassure you that the personal information that you will entrust me with will not be disclosed to any third party unless legally required to do so and with your consent. Your identity will be kept anonymous.

INFORMATION AND CLARIFICATION

Please be informed that if you at any time need some clarification over the research study, direct your concerns to:

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APPENDIX II: CONSENT FORM

I agree that the purpose of the study has been explained to me. The risks and benefits have been clarified and I understand that participation or not will not affect my job security or health care at this institution. I freely and voluntarily choose to participate. I also understand that my rights and privacy will be maintained.

I …….... (Names)

agree to take part in the study designed to find out factors that affect drug adherence to TB treatment in TB/HIV co-infected patients.

Signed……..Date……...(Participant)

Signed……..Date……..(Witness)

Signed……..Date……..(Researcher)

APPENDIX III: RESEARCH QUESTIONNAIRE:

SOCIO DEMOGRAPHIC, CULTURAL AND ECONOMIC FACTORS

No.	QUESTIONNAIRE	CATEGORY
1	Age	Write in numbers_____
2	Sex	1. Male 2. Female
3	Religion	1. Christian 2. Muslim 3. Hindu 4. Other (specify) _____
4	Marital status	1. Single 2. Married 3. Divorced 4. Widowed 5. Other (specify) _____
5	Education status	1. No education 2. Primary education 3. Secondary education 4. Tertiary education
6	Occupational status	1. Unemployed 2. Employed 3. Self-employed 4. Retired 5. Other (specify) _____
7	Meals afforded per day	1. 1 2. 2-3 3. 3 or more
8	Where do you usually go for medical care when you are sick?	1. Private Clinic 2. Government clinic 3. Traditional healer 4. Other (specify)_____
9	In your community, how is a person who has TB and/or HIV infection usually regarded/treated?	1. Most people reject him/her 2. Most are friendly but try to avoid him/her 3. Most offer support and help him/her 4. Other (specify) _____
10	Any cultural perceptions that conflict with modern treatment?	1. Yes 2. No

SERVICE-RELATED FACTORS

No.	QUESTIONNAIRE	CATEGORY
11	Are you a resident of Lusaka?	1. Yes 2. No
12	If no to q201, are you in Lusaka specifically for treatment?	1. Yes 2. No
13	How long does it take you to reach the health institution from your residence?	1. Less than 1 hour 2. 1-2 hours 3. More than 2 hours
14	Is the cost of the trip to the health institution affordable?	1. Yes 2. No 3. Not always
15	Do you feel free to ask the health personnel who attend to you any questions you might have?	1. Yes 2. No
16	Have you been informed about the importance of your compliance to treatment in order to recover from TB?	1. Yes 2. No
7	Have you ever skipped treatment because you couldn't make it to this institution?	1. Yes 2. No
18	If yes to q207, how was the reception of the health personnel when you made it to the health institution?	1. Poor 2. Average 3. Good

DISEASE AND TREATMENT-RELATED FACTORS

No.	QUESTIONNAIRE	CATEGORY
19	How many times have you had TB?	1. Once 2. More than once
20	How did you find out you had TB the first time?	1. Routine screening 2. Became sick and symptoms prompted to immediately get tested 3. Was sick for a long time and TB testing was suggested/became imperative.
21	How did you respond to treatment the first time?	1. Very well 2. Average 3. Poorly
22	Were drugs readily available after your diagnosis?	1. Yes 2. No
23	Are you on ART?	1. Yes 2. No
24	If yes to q305, how long have you been on ART?	1. < 1 year 2. 1-2 years 3. > 2 years
25	What was your CD4 count when you commenced on TB treatment?	Write in numbers _____
26	If yes to q305, what is your experience, taking ART and TB treatment at the same time?	1. Too many drugs 2. Side effects when drugs are combined 3. No problems
27	If yes to q305, what change have you seen in your health after you started taking ART?	1. No change 2. Improved 3. Got severely ill
28	What change have you seen in your health after you started taking TB treatment?	1. No change 2. Improved 3. Got severely ill
29	Do you have preference for alternative treatment?	1. Yes 2. No 3. Sometimes

Thank you for your participation.