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UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

INCIDENCE AND DETERMINANTS OF TRANSFUSION–TRANSMISSIBLE INFECTIONS IN VOLUNTARY BLOOD DONORS IN MALAWI, 2005 – 2015

DR. CONSTANCE N. WOSE KINGE

A RESEARCH REPORT SUBMITTED TO THE FACULTY OF HEALTH SCIENCES, UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG, IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN EPIDEMIOLOGY (EPIDEMIOLOGY AND BIOSTATISTICS).

JOHANNESBURG, OCTOBER 2019

INCIDENCE AND DETERMINANTS OF TRANSFUSION–TRANSMISSIBLE INFECTIONS IN VOLUNTARY BLOOD DONORS IN MALAWI, 2005 – 2015

By

Dr. Constance N. Wose Kinge

(Student Number: 1918187)

Supervisors

Prof. Charles Chasela

School of Public Health, University of the Witwatersrand

Dr. Juliana Kagura

School of Public Health, University of the Witwatersrand

DECLARATION

I, **Dr. Constance N. Wose Kinge**, declare that this report: **Incidence and Determinants of Transfusion Transmission–Transmissible Infections in Voluntary Blood Donors in Malawi, 2005 - 2015**, is my own original work and that all sources that I have used have been indicated by complete references. This report is being submitted for the degree of Master of Science in Epidemiology at the University of the Witwatersrand, Johannesburg, South Africa. It has not been submitted before for any degree at this or any other University.



SIGNATURE

17 October 2019

DATE

DEDICATION

To my very special and wonderful family, and daughter Priscilla, whose presence especially, has given me so much joy and reasons to work even harder, I remain truly thankful for your loving support, care and encouragements over the years.

In memory of,

Theophilus N. Wose Kinge

(1974 – 2002)

Christiana M. Kinge

(1952 – 2006)

Emmanuel E. Wose Kinge

(1976 – 2006)

Ernest U. Iheneche

(1976 – 2010)

Tigris M. Wose Kinge

(1983 – 2014)

Life has been filled with many ups and downs in your absence but with each passing day, I have only become a stronger and better person. In your own special way, you all contributed greatly to the special woman that I am today and the memories we shared, will continue to be a great source of comfort.

PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS WORK

PRESENTATIONS

Two presentations by the same title (Incidence and Determinants of Transfusion–Transmissible Infections in Blood Donors in Malawi, 2005-2015) have been submitted for oral presentation at the Wits School of Public Health Research Day- “Public Health: Past, Present, Future”, Johannesburg, August 22, 2019 and the PHASA Conference- “The Right to Health: 25 years into our Constitutional Democracy”, Cape Town, 16–22 September, 2019.

PUBLICATIONS

1.) Wose Kinge CN, Kagura J, Chasela C. Incidence and Determinants of Transfusion–Transmissible Infections in Blood Donors in Malawi, 2005-2015. BMC Infectious Dis. 2019; xx (x): xxx (In preparation)

ABSTRACT

Introduction. Blood transfusion has been associated with a high risk of blood transfusion–transmissible infections (TTIs), which include: Human immunodeficiency virus (HIV), Hepatitis C virus (HCV), Hepatitis B virus (HBV), Syphilis, and malaria among others. These infections pose great threats to the global population particularly in sub-Saharan Africa (SSA) where the burden of disease is alarmingly high. This calls for the need to monitor blood supply safety, understand the trend of transmission routes, and develop effective donor behavioural screening. Therefore, the objectives of the study were to describe the baseline characteristics of the study population, determine the incidence of transfusion transmissible HIV, HCV and HBV infections, and to identify factors that are associated with the incidence of infection in blood donors in Malawi through the period of 2005 – 2015.

Methods. This was secondary data analysis of a cohort of blood donors from the Malawi Blood Transfusion Service (MBTS). The data were obtained from the MBTS database on blood donors registered from 2005 – 2015. The data was cleaned, and duplicate records checked. Baseline characteristics of donor participants by TTI, HIV, HBV and HCV status were described using frequency distribution tables. Age as a continuous variable was described using median and interquartile range (IQR) and histograms. Categorical variables were summarized using percentages. Kaplan-Meier plots were generated to assess the survival patterns for TTI, HIV, HBV and HCV and log-rank tests for equality of survivor function across strata for all exposure variables were performed. Bivariate and multivariate regression was used to determine risk factors for transfusion transmissible HIV, HCV and HBV infections. The odds ratio with a 99% confidence interval was calculated. A p-value< 0.02 was considered statistically significant.

Results. Overall, TTI incidence was 43.4 per 10,000, and this was significantly higher for donors aged 16–19 (IR= 49.81, 95% CI= 44.87–55.29), males (IR= 46.36, 95% CI= 44.76–48.03), unmarried donors (IR= 43.91, 95% CI= 42.40–45.48), unemployed (IR= 65.23, 95% CI= 51.43–82.74), living in the Southern region (IR= 49.09, 95% CI= 46.97–51.30), unprotected sex with multiple partners (IR= 49.13, 95% CI= 44.50–54.25), and malaria-positive donors (IR= 50.42, 95% CI= 47.91–53.05). There were statistically significant differences in survival experience with respect to age category, sex, marital status, unemployment status, region of residence, sex with multiple partners without condom use, and other TTIs. The risk of TTI increased with age and this was similar for HIV and HBV. For HCV, risk of infection decreased with increasing age. Age groups 16–19 (aOR= 1.82, 95% CI= 1.15–2.89), 20–24 (aOR= 2.15, 95% CI= 1.36–3.41), 25–29 (aOR= 2.13, 95% CI= 1.33–3.39), 30–34 (aOR= 2.69, 95% CI= 1.67–4.34), and 35–39 (aOR= 2.00, 95% CI= 1.19–3.35), and married status (aOR= 1.93; 95% CI= 1.38–2.69) was significantly associated with higher odds of TTI in the multivariate logistic model. Infection with syphilis was a common significant risk factor for incident HIV (aOR= 2.62, 95% CI= 1.57–4.38), HCV (aOR= 2.03, 95% CI= 1.04–3.98), and HBV (aOR= 1.71, 95% CI= 1.01–2.89).

Conclusion. The overall incidence of TTIs in the Malawian donor population is low, however, the risk of TTI remains a cause for concern. The incidence of HIV, HCV and HBV was highest in males, the unemployed, donors living in the Central Region, engaging in unprotected sex with multiple partners, and co-infection with syphilis. HBV was most common among supposedly healthy donors, followed by HIV and HCV, which revealed a substantial risk of TTI. Age, male sex, married status were significant risk factors associated with TTI in Malawian blood donors. TTI therefore, remains a cause for concern toward availability and safe blood transfusion. An urgent need to continue monitoring the

incidence of TTI markers in the donor population through use of more contextualised screening questionnaires and the use of nucleic acid testing (NAT) in addition to serological tests is paramount.

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TABLE OF CONTENTS

DECLARATION ..... **iii**
DEDICATION ..... **iv**
PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS WORK ..... **v**
ABSTRACT ..... **vi**
ACKNOWLEDGEMENTS ..... **ix**
TABLE OF CONTENTS ..... **xi**
LIST OF FIGURES ..... **xiii**
LIST OF TABLES ..... **xiv**
LIST OF APPENDICES ..... **xv**
LIST OF ABBREVIATIONS AND ACRONYMS ..... **xvi**
CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW **1**
1.1 INTRODUCTION **1**
1.1.1 TRANSFUSION–TRANSMISSIBLE INFECTIONS 1
1.1.2 STATEMENT OF THE PROBLEM 2
1.1.3 JUSTIFICATION 4
1.2 LITERATURE REVIEW **5**
1.2.1 INTRODUCTION 5
1.2.2 HIV INFECTION AMONG BLOOD DONORS 6
1.2.3 HBV INFECTION AMONG BLOOD DONORS 6
1.2.4 HCV INFECTION AMONG BLOOD DONORS 7
1.3 AIMS AND OBJECTIVES **8**
1.3.1 STUDY AIM 8
1.3.2 SPECIFIC OBJECTIVES 8
CHAPTER TWO: METHODOLOGY **9**
2.1. INTRODUCTION **9**
2.2. STUDY SETTING **9**
2.3. STUDY DESIGN **11**
2.4. STUDY POPULATION **11**
2.5. SAMPLE SIZE **12**
2.6. DATA MANAGEMENT AND PROCESSING **12**
2.6.1 VARIABLES USED IN THE STUDY 13
2.7. RESEARCH QUESTIONS **16**
2.8. DATA ANALYSIS **16**
2.8.1 BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS 16
2.8.2 SURVIVAL ANALYSIS 16
2.8.3 COX PROPORTIONAL HAZARDS REGRESSION ANALYSIS 17
2.8.4 LOGISTIC REGRESSION ANALYSIS 18
2.9. ETHICAL CONSIDERATIONS **20**
CHAPTER THREE: RESULTS **21**
3.1 INTRODUCTION **21**

3.2 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS 23
3.2.1. BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY TTI STATUS 25
3.2.2 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY HIV STATUS..... 26
3.2.3 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY HCV STATUS ... 29
3.2.4 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY HBV STATUS ... 32
3.3 INCIDENCE OF TRANSFUSION TRANSMISSIBLE HIV, HCV AND HBV INFECTIONS 35
3.3.1 INCIDENCE OF TTI (HIV+, HCV+ or HBV+)..... 35
3.3.2 INCIDENCE OF HIV 39
3.3.3 INCIDENCE OF HCV 42
3.3.4 INCIDENCE OF HBV..... 46
3.4 COX PROPORTIONAL HAZARDS REGRESSION ANALYSIS 50
3.4.1 TESTING PROPORTIONAL HAZARD ASSUMPTION 51
3.5 LOGISTIC REGRESSION ANALYSIS 51
3.5.1 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF TTI 51
3.5.2 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF TTI . 53
3.5.3 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HIV 56
3.5.4 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HIV . 58
3.5.5 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HCV 59
3.5.6 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HCV 61
3.5.7 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HBV 63
3.5.8 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HBV 65
CHAPTER FOUR: DISCUSSIONS, CONCLUSIONS AND RECOMMENDATIONS 67
4.1 INTRODUCTION 67
4.2 SUMMARY OF MAIN FINDINGS 67
4.4. LIMITATIONS OF THE STUDY 71
4.5. STRENGTHS OF THE STUDY 72
4.6. CONCLUSION..... 72
4.7. RECOMMENDATIONS 73
REFERENCES 74
APPENDICES 83

LIST OF FIGURES

Figure 2.1: Map of Malawi showing the different geographical regions and districts 10

Figure 3:1: Flow chart diagram of blood donors enrolled in the study 22

Figure 3.2: Distribution of donors' age by TTI status (N= 47,075) 25

Figure 3.3: Distribution of donors' age by HIV status (N= 47,075) 27

Figure 3:4: Distribution of donors' age by HCV status (N= 47,075) 29

Figure 3.5: Distribution of donors' age by HBV status (N= 47,075) 32

Figure 3.7: Kaplan-Meier survival estimates of TTI, by sex (N= 47,075) 36

Figure 3.8: Overall Kaplan-Meier survival estimates of HIV (N= 47,075) 39

Figure 3.9: Overall Kaplan-Meier survival estimates of HIV, by sex (N= 47,075) 40

Figure 3.10: Overall Kaplan-Meier survival estimates of HCV (N= 47,075) 43

Figure 3.11: Kaplan-Meier survival estimates of HCV, by sex (N= 47,075) 44

Figure 3.12: Overall Kaplan-Meier survival estimates of HBV (N= 47,075) 47

Figure 3.13: Kaplan-Meier survival estimates of HBV, by sex (N= 47,075) 48

LIST OF TABLES

Table 3.1: Baseline characteristics of donor participants, by TTI status (N= 47,075)..... 24

Table 3.2: Baseline characteristics of donor participants, by HIV status (N=47,075)..... 28

Table 3.3: Baseline characteristics of donor participants, by HCV status (N=47,075) ... 31

Table 3.4: Baseline characteristics of donor participants, by HBV status (N=47,075) ... 33

Table 3.5: TTI incidence rates by potential risk factors and confounders (N=47,075).... 37

Table 3.6: HIV incidence rates by potential risk factors and confounders (N=47,075) ... 41

Table 3.7: HCV incidence rates by potential risk factors and confounders (N=47,075) . 45

Table 3.8: HBV incidence rates by potential risk factors and confounders (N=47,075) . 49

Table 3.9: Predictors of incident TTI in blood donors: univariate model (N= 47,075)..... 52

Table 3.10: Predictors of incident TTI in blood donors: multivariate model* (N= 47,075)..... 55

Table 3.11: Predictors for incident HIV in blood donors: univariate model (N= 47,032). 57

Table 3.12: Predictors for incident HIV in blood donors: multivariate model* (N= 47,032)..... 59

Table 3.13: Predictors of incident HCV in blood donors: univariate model (N= 47,075) 60

Table 3.14: Predictors of incident HCV in blood donors: multivariate model* (N= 47,075)..... 62

Table 3.15: Predictors of incident HBV in blood donors: univariate model (N= 47,032) 64

Table 3.16: Predictors of incident HBV in blood donors: multivariate model* (N= 47,032)..... 66

LIST OF APPENDICES

APPENDIX I: Plagiarism Declaration Form 83

APPENDIX II: MBTS Data Dictionary..... 84

APPENDIX III: Permission to use the MBTS Dataset..... 86

APPENDIX IV: Wits HREC Clearance Certificate 87

APPENDIX VI: Approval of Research Title 88

APPENDIX VI: Cox proportional regression model for factors associated with TTI: univariate model (N=47,075) 89

APPENDIX VII: Cox proportional regression model for factors associated with TTI: multivariate model* (N=47,075) 90

APPENDIX VIII: Test of Proportional Hazards Assumption..... 91

APPENDIX IX: Turnitin Report..... 92

LIST OF ABBREVIATIONS AND ACRONYMS

ELISA	Enzyme-linked Immunosorbent Assay
HBsAg	Hepatitis B surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HCC	Hepatocellular Carcinoma
HIV	Human Immune Deficiency Virus
IDU	Injection Drug Use
IQR	Interquartile Range
IR	Incident Rate
MBTS	Malawi Blood Transfusion Service
MER	Monitoring, Evaluation and Reporting
MWHSWM	Men Who Have Sex with Men
NAT	Nucleic Acid Testing
PWID	People Who Inject Drugs
STD	Sexually Transmitted Disease
SOP	Standard Operating Procedure
TB	Tuberculosis
TPHA	*Treponema pallidum* Haemagglutination
TTI	Transfusion Transmissible Infection
WHO	World Health Organization

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

This chapter provides an overview of the burden of transfusion–transmissible infections (TTIs) in blood donors, as well as the rationale for the study. It also provides an in-depth review of relevant literature on the subject.

1.1.1 TRANSFUSION–TRANSMISSIBLE INFECTIONS

Blood transfusion is a life-saving intervention especially in sub-Saharan Africa where the risk of TTIs is high due to limited resources, inadequate screening facilities and shortage of trained personnel (1, 2). Transfusion–transmissible infections such as the human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) pose great threats to blood safety (3). Recent estimates by Tagny *et al*. (4) and Fouelifack Ymele *et al*. (5), suggest that 5–10% of HIV infections are attributable to transfused blood and that an estimated 12.5% of patients who receive transfusion are more likely to develop post–transfusion hepatitis (6). As a result of the high burden of TTIs, there's a drop in the number of potential blood donors and a subsequent high risk of shortage of safe blood supply for transfusion.

HBV is highly infectious and transmission from one infected individual to another is easy. Worldwide, HIV, HBV, and HCV constitute the common chronic viral infections and share similar routes of transmission (7, 8). The modes of transmission include sexual contact, blood-to-blood contact, and injecting drug usage (IDU). The worldwide estimates by WHO of people living with chronic HBV and HCV sits at 257 and 71 million, respectively (9, 10).

Globally, the frequency of HBV infection in HIV-infected individuals is 7.4%, which is similar across different groups especially among the high risk populations like persons who inject drugs (PWID, 7.0%) and men who have sex with men (MWHSWM, 6.1%) (11). Due to their common routes of transmission, people who are HIV positive are at greater risk of co-infection with HCV, which is the leading cause of hepatitis/liver-related deaths in HIV-infected individuals. In the presence of an HIV infection, the natural history of HCV is altered, which results in a rapid progression of liver disease accounting for high deaths (10, 12).

More so, HIV infection quickens the progression of liver disease caused by chronic HBV infection, which leads to end-stage liver disease and increased risk of hepatocellular carcinoma (HCC). HIV and HCV co-infection accounts for a global estimate of 2.3 million cases (13). The highest burden of HIV and HCV co-infection is recorded in Eastern Europe and central Asia, where an estimated 607,700 cases exist, predominantly in PWID. Sub-Saharan Africa accounts for 19% of cases, of which 429,600 cases are as a result of high HIV prevalence (13). Co-infection with HIV, HBV and HCV is associated with increased advancement of liver fibrosis and death compared to HCV mono-infection, with liver disease accounting for the majority of non-AIDS-related deaths among HIV-infected and co-infected individuals (10, 14).

1.1.2 STATEMENT OF THE PROBLEM

Safe and reliable transfusion services remain largely unavailable to the world's poorest populations, particularly in sub-Saharan Africa (13). In response to the WHO's call for member states to develop and coordinate national blood transfusion services based on

voluntary and unpaid blood donations and to improve the availability of safe blood supplies in sub-Saharan Africa, the Malawi Blood Transfusion Service (MBTS) was established in 2003. The MBTS collects blood from volunteer blood donors and supplies it to all approved health facilities that perform blood transfusion within the country. Despite this, the need for blood is massive and the MBTS is failing to meet this need. The shortage of readily available safe blood at the MBTS has contributed to loss of lives (15). In 2014, the MBTS data showed a decrease in blood donation per-capita, meeting only a third of the country's blood products needed. Currently, the country's annual blood need is 120,000 units per year (15). The decrease in adequate safe blood supply has been attributed to a number of reasons including lack of proper storage facilities for long-term storage, shortage in financial resources to run the MBTS, difficulties in recruiting and maintaining blood donors. Most importantly is the high prevalence of HIV, HCV and HCV in the country (16). HIV in the general population is estimated at 12%, HCV varying between 0.7–16.5% by subpopulation (16) and hepatitis B virus (HBV) ranging from 8.1 to 36% in certain parts of the Country. The incidence of these infections limits the number of potential donors who can donate safe blood and a subsequent shortage in safe blood supply.

While several studies have focused more on looking at the prevalence of these infections in high-risk groups as well as the general population (16-18), to the best of our knowledge little or no available research looking into the incidence of these infections in the donor population exits. It is hoped that this research will provide knowledge on the burden and risk factors of transfusion-transmissible HIV, HBV and HCV infections in the blood donor population, which can be used to monitor blood supply safety, understand the trend of transmission routes, and develop effective donor behavioural screening.

1.1.3 JUSTIFICATION

Providing safe and sufficient blood and blood product supplies is of key public health importance. Generally, blood products are required in major surgical operations, accidents, burns, injuries, obstetric haemorrhages, traumas, blood substitution in neonates, prematurity, as well as additional triggers of severe and prolonged anaemia (20). The treatment of cancer resulting in anaemia similarly calls for the need of transfusion (19). A previous study observed that “10–40% of cancer patients develop anaemia of chronic diseases, which results from long term medical condition that could affect production and lifespan of red blood cells” (20). Therefore, the availability of sufficient blood supplies contributes to preventing deaths in women and children (14).

In Malawi, the main conditions requiring blood transfusion in decreasing order include malaria, maternal bleeding, emergency surgery and road traffic accidents, elective surgery and cancer (15). Despite high demands for blood supplies, Malawi faces a serious problem of inadequate blood supplies collected from voluntary blood donors due to the high burden of HIV and endemicity of HBV and HCV in the general population as well as other infectious diseases including malaria and tuberculosis (15). As a result, there’s a substantial decrease in the number of potential voluntary blood donors and a subsequent shortage of safe blood supplies. This shortage of blood greatly contributes to high maternal death rate in the country, which currently seats at 510 deaths per 100,000 live births. Pregnancy-related complications are the major contributing factors of death due to excessive loss of blood and inability to provide blood transfusion (18, 21-24). Therefore, accurate epidemiologic knowledge on the incidence of transfusion-transmissible HIV, HCV and HBV infections in the blood donors permits an assessment of the occurrence of infections and consequently the safety of the donated blood (22).

1.2 LITERATURE REVIEW

1.2.1 INTRODUCTION

A thorough literature search was done on PubMed, Google Scholar and Scopus for studies reporting the incidence of transfusion–transmissible infections in blood donors. Publications that reported prevalence estimates were included. The electronic databases were sought for publications from 2005 to date using the MeSH (medical subject headings) search terms: “transfusion transmissible infections and blood donors”, “transfusion transmissible infections and Malawi” “hepatitis C virus and blood donors and Malawi”, “hepatitis B virus and blood donors and Malawi”, “HIV and blood donors and Malawi”. A manual search was also done for the references and related articles of every included study for other possible citations. All searched publications were limited to English–language.

In the developing countries, there is an increasing record of donor-recipient HBV, HIV and HCV transmission due to the unavailability of routine screening tests for donors (23). This led to the World Health Organization’s (WHO) recommendation for all blood transfusion services to screen donated blood using routine screening tests for transfusion transmissible infections (TTIs), including HBV, HIV, HCV and syphilis so as to lower the risk of transmission of these infections (25-27). As a result, donors tests results could be used not only as marker of a safe blood supply (26) but also to determine the HBV, HIV and HCV prevalence rates in the donor population. This knowledge in turn provides help to healthcare providers in understanding the epidemiology of these infections within the community (25, 27).

1.2.2 HIV INFECTION AMONG BLOOD DONORS

In sub-Saharan Africa, HIV epidemic is alarmingly high, and the prevalence varies greatly between regions and countries. In 2012, people living with HIV were estimated at about 25 million accounting for closely 70% of the global total. In the same year, new HIV infections and AIDS-related deaths were estimated at 1.6 million and 1.2 million, respectively. South Africa has the largest HIV epidemic in the world, with 19% of people living with HIV, 15% and 11% of new infections and AIDS-related deaths, respectively. The total number of persons living with HIV in South Africa has increased from an estimated 4,94 million in 2002 to 7,06 million in 2017. The 2017 estimate of the total population living with HIV is 12,6% (28). In one study conducted by Okoroiwu *et al*. (29), the prevalence of HIV among donors in Nigeria was 4.2%. In Malawi, HIV/AIDS constitute a major health challenge with a country prevalence of 8.8% (30). In 2012, the prevalence in the donor population was 22% (31). The 2015 HIV prevalence rate as reported by M'baya et al. (32) was 1.9% with age greater or equal to 25 years and being out school being associated risk factors for HIV.

1.2.3 HBV INFECTION AMONG BLOOD DONORS

HBV is hyperendemic in Sub-Saharan Africa with 8% of the population positive for the hepatitis B antigen (HbsAg). However, the endemicity of hepatitis B infection varies ranging from 5-10% in Ivory Coast Kenya, Liberia, Senegal, Sierra Leone and Zambia (33). In West Africa, seroprevalence levels ranging from 3 to 22% have been reported among blood donors (34). The prevalence of HBV among donors in Nigeria was 4.1% (29). The high endemicity corresponds to a high incidence of hepatocellular carcinoma in the region. Despite the initiation of the HBV vaccine introduced in 1982, which has been

adopted widely in most countries, HBV prevalence in the blood donor population is still high (27). The lifetime and death risks due to hepatitis B infection are estimated at about 60 and 25%, respectively, in these regions (30).

1.2.4 HCV INFECTION AMONG BLOOD DONORS

HCV is the main cause of post-transfusion hepatitis with a worldwide prevalence varying from 0.2% to 40% across countries (35). Infection with HCV could lead to chronic infections, cirrhosis, and HCC. In developing countries HCV prevalence is high among blood donors possibly due to low quality in screening procedures, dangerous medical practices, and IDU among drug users who share common needles. Egypt alone has a prevalence of 22% (36) while Central Africa is sitting at 6% with Cameroon seeing a prevalence of 13.8% (37). Unlike HBV, no vaccine to prevent HCV infection exists, and regimens for HCV infection is expensive. Thus, prevention of primary HCV infection is critical and any approach toward preventing HCV infection should be founded on accurate data, including information about its prevalence.

Malawi's HIV, HBV and HCV prevalence varies. In 2006, it was estimated that one million Malawians were living with HIV, giving rise to 24,000 deaths due to AIDS-related illnesses (38). The HIV prevalence in the adult population (aged 15-49) is estimated at 9.2%. However, limited epidemiological data on transfusion-transmissible HBV, HCV and HIV infections exist among blood donors in Malawi. Previous research revealed a 7.6% HBV and 10.7% HIV prevalence among blood donors (18). The safety of blood for transfusion is a major challenge of Malawi and is not well addressed. As a result, use of unsafe blood products puts the recipients at risk of acquiring many TTIs with an increased risk of

transmission to the community and subsequent increase in disease and financial burden to diagnose and treat these diseases (39). To ensure the safety and adequacy of the national blood supply in Malawi, it is imperative to enrol and recruitment low-risk, unpaid blood donors, as well as the use of highly sensitive and specific methods to screen for TTIs in the donated blood. Therefore, assessing the incidence and associated risk factors of transfusion-transmissible HIV, HBV and HCV infections can be used to assess the safety of blood supply and help develop approaches aimed at decreasing the burden of disease in the communities. This will ensure the availability and accessibility of safe and adequate blood supply to transfusion centres.

1.3 AIMS AND OBJECTIVES

1.3.1 STUDY AIM

The aim of the study was to determine the burden and associated factors of transfusion-transmissible HIV, HCV and HBV infections in blood donors in Malawi from 2005 to 2015.

1.3.2 SPECIFIC OBJECTIVES

The specific objectives of the study were to:

1. Describe the socio-demographic characteristics of the study population from 2005 to 2015.
2. Investigate the incidence of TTIs in voluntary blood donors in Malawi from 2005 to 2015.
3. Assess the factors associated with TTIs in voluntary blood donors in Malawi from 2005 to 2015.

CHAPTER TWO: METHODOLOGY

2.1. INTRODUCTION

This chapter provides a detailed review of the study setting, design, study site and population, as well as the sampling, data sources, data management and analysis, and ethical considerations. Data analysis was in two-phase namely descriptive statistics, and survival analysis using Kaplan-Meier estimates, and regression analyses.

2.2. STUDY SETTING

The Malawi Blood Transfusion Service (MBTS) with headquarters in Blantyre, Southern Malawi, was founded in 2003 with goals to provide safe and adequate blood and blood products for all patients in all authorized clinics in Malawi. Malawi, a country in southern Africa, is the least developed in the continent with an area of approximately 120,000 km^2 and a population of 17 million. The country borders Zambia to the west, Mozambique to the south and Tanzania to the north (40). There are three main regions– Northern (with Mzuzu being the capital city), Central (with Lilongwe City being the country's national and administrative capital) and Southern (with Blantyre City being the provincial and commercial) regions as shown {Figure 2.1- source: (41)}.

Three regional branches in Lilongwe, Mzuzu and Balaka have as responsibilities to collect, prepare, storage and distribute blood components (42). Following international guidelines, the MBTS receives and encourages regular blood donation from voluntary unpaid donors only.

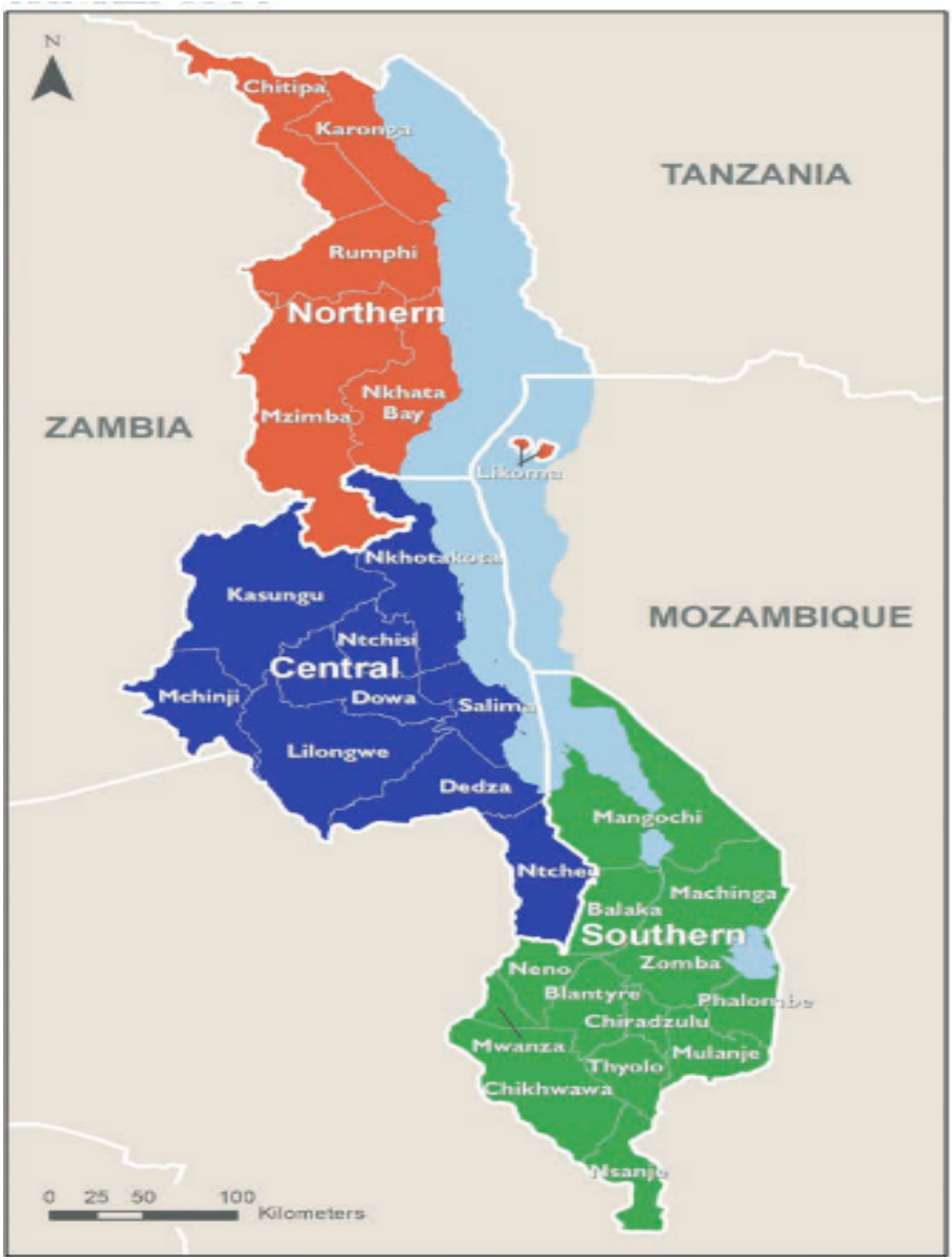


Figure 2.1: Map of Malawi showing the different geographical regions and districts

Primary data collection included socio-demographic, past medical history and risk behaviour captured using self-administered questionnaires. Screening for HIV, Hepatitis B and C, syphilis and malaria are performed on all donated blood. One pint of blood drawn from each donor is screened using laboratory tests for blood-borne infections, and blood grouping. HIV is tested using the enzyme-linked immunosorbent assay- ELISA (p24 antigen and antibodies for HIV 1 and 2), hepatitis B virus (HbsAg), HCV (anti-HCV antibodies) and syphilis (*Treponema pallidum* hemagglutination-TPHA test). Blood films are screened for malaria parasites. All routine tests are integrated and performed using standard operating procedures (SOPs) to minimize errors (17) in Blantyre. Additional tests performed on donated blood included ABO blood grouping and rhesus D (RhD) antigens.

2.3. STUDY DESIGN

The study was secondary data analysis of a cohort of blood donors from the Malawi Blood Transfusion Service (MBTS) who donated blood over a 10-year period from 2005 to 2015.

2.4. STUDY POPULATION

In Malawi, the legal and acceptable age for blood donation is 16 to 65 years (43). Hence, this study comprised of voluntary blood donors, both males and females aged 16 to 65 years registered with the MBTS and who donated blood at the regional centres in Malawi from 2005 to 2015.

2.5. SAMPLE SIZE

A total of 47,075 blood donor records were retrieved for this study. To be eligible for blood donation, every donor is tested for HIV and other TTIs at every donation, hence repeat donors provide a convenient source of longitudinal data for estimating the incidence of viral HIV, HBV and HCV infections (44).

The following eligibility criteria were employed:

- Donor ID=1 (minimum of two blood donations)
- Aged 16 to 65
- Complete data on HIV or HCV or HBV status
- Negative for HIV, HCV or HBV at time of first donation

2.6. DATA MANAGEMENT AND PROCESSING

The MBTS data, captured into STATA as "*mbtswithcords.dta*" file, was accessed with approval from the MBTS Director. The data were cleaned, checked for consistency and duplicate records. No duplicate records were present. A unique ID (donor ID) for each donor was generated based on the number of blood donations contributed throughout the study period. All donors with donor ID less that one (that is only donated once and became infected), below the age of 16 and older than 65, were dropped. Also, donors with missing HIV, HCV or HBV status or who tested positive for HIV, HCV or HBV at first donation were dropped.

2.6.1 VARIABLES USED IN THE STUDY

2.6.1.1 Outcome Variables

The four outcome variables of interest for this study were:

a) **TTI (transfusion–transmissible infection)**: defined as a donor who tested positive for either HIV, HBV or HCV after the first donation. TTI was generated and categorized as a binary variable with two outcomes:

- ‘0’ = Uninfected (HIV^- or HCV^- or HBV^-)
- ‘1’ = Infected (HIV^+ or HCV^+ or HBV^+)

b) **HIV**: A binary variable with two outcomes:

- ‘0’ = Uninfected (HIV^-)
- ‘1’ = Infected (HIV^+)

c) **HCV:** A binary variable with two outcomes:

- ‘0’ = Uninfected (HCV^-)
- ‘1’ = Infected (HCV^+)

d) **HBV:** A binary variable with two outcomes:

- ‘0’ = Uninfected (HBV^-)
- ‘1’ = Infected (HBV^+)

2.6.1.2 Explanatory or Predictor Variables

The explanatory or predictor variables included in this study were socio-demographic characteristics and clinical information of donors.

2.6.1.2.1 Socio-Demographic Characteristics

- **Age:** Age (in years) at time of testing was calculated by subtracting the date of birth from the TTI test date and dividing by 365.25. To account for missing age, firstly,

the maximum number of blood donations for each donor was computed and used to compute the average age. Next, the average age was replaced if age was missing and donor ID=1 and where the date of birth was missing, it was imputed with the age multiplied by 365.25 and subtracted from the TTI test date. The variable age was then categorized into 8 levels based on the United States President's Emergency Plan for AIDS Relief (PEPFAR) monitoring, evaluation, and reporting (MER) disaggregated standardized seven-year age bands as follows:

- ‘1’ = 16-19,
- ‘2’ = 20-24,
- ‘3’ = 25-29
- ‘4’ = 30-34
- ‘5’ = 35-39
- ‘6’ = 40-44
- ‘7’ = 45+

- **Sex:** Sex of donor was categorized as a binary variable:
  - “0’ = Female
  - ‘1’ = Male
- **Marital Status:** A categorical variable encoded as;
  - ‘1 = Married
  - ‘2’= Not Married (included those who were single, separated, widowed or divorced)
- **Employment Status:** Employment status was categorized into three levels as follows:
  - ‘0’ = Employed
  - ‘1’ = Unemployed

- ‘2’ = Unknown

- **Region of Residence:** Defined as the place of residence and encoded as
  - ‘0’ = Central region
  - ‘2’ = Northern region
  - ‘3’ = Southern region
  - ‘4’ = Unknown
- **Risk:** The variable “*riskyess*” was defined as sex with multiple partners without condom use. It was a categorical variable with two outcomes;
  - ‘0’ =No
  - ‘1’ = Yes

2.6.1.2.2. Clinical Information

- **ABO blood group**: A categorical variable with five levels:
  - ‘0’ = A
  - ‘1’ = B
  - ‘2’ = AB
  - ‘3’ = O
  - ‘4’ = Missing
- **Other TTIs**: The variable “*OtherTTIs*” was created, defined as a donor with syphilis or malaria and categorized into three levels;
  - ‘0’ = None,
  - ‘1’ = Syphilis
  - ‘2’ = Malaria

The sources of all socio-demographic as well as clinical information variables were contained in the MBTS data dictionary (Appendix II).

2.7. RESEARCH QUESTIONS

a) What is the incidence of transfusion–transmissible TTI, HIV, HCV and HBV infections in the blood donor population in Malawi?

b) What are the risk factors associated with transfusion–transmissible HIV, HCV and HBV infections in the Malawian blood donor population?

2.8. DATA ANALYSIS

All statistical analysis was performed using STATA/SE 15.1 for Mac.

2.8.1 BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS

Baseline characteristics of donor participants were described using frequency distribution tables. Age as a continuous variable was described using median and interquartile range (IQR) and histograms. All categorical variables were described using percentages. The baseline characteristics were compared between those uninfected and infected with TTI, HIV, HCV and HBV and Pearson Chi-square test was used to compare frequencies between groups. Where the expected cell numbers were less than five, a Fischer's exact test was used.

2.8.2 SURVIVAL ANALYSIS

Survival analysis was done to determine the time until the occurrence of TTI, HIV, HCV and HBV. Disease incidence for the period from 2005-2015 was calculated by dividing the

number of new cases over the study period by the total person-years at risk as previously described (45).The cases, person-years at risk and incidence rates per 10,000 person-years were reported with 95% confidence intervals. The Kaplan-Meier estimates were used to compute the survival time and the overall survival probability as well as the survival probability by sex was calculated as the number of surviving donors divided by the donors at risk. The Kaplan-Meier curves were plotted to determine the proportionality of the survival functions. The log-rank test for equality of survivor functions across strata was done.

2.8.3 COX PROPORTIONAL HAZARDS REGRESSION ANALYSIS

The Cox proportional hazards (PH) regression was used to identify factors associated with TTI, HIV, HCV, and HBV. In a univariate analysis each explanatory variable was used to determine the predictors for TTI, HIV, HCV, and HBV. Categorical variables that were statistically significant at a *p*-value<0.2 in the log-rank test and any priori biologically plausible covariates were considered important determinants and included in the multivariate PH regression analysis.

For the multivariate modelling all variables that were statistically significant at a *p*-value<0.2 were included in the model. A backward stepwise model building process was performed using all the variables from the univariate analysis. All variables were modelled as categorical with interaction terms included. Models were compared using the likelihood ratio (LR) test (*lrtest*). Potential confounders were adjusted in the multivariate model. The final model, with estimates of the hazards ratios of TTI, HIV, HCV, and HBV and corresponding 95% confidence intervals, was attained using a LR *p*-value of 0.05.

Proportional hazards assumptions were then tested graphically on cumulative hazards plots as well as on the Schoenfeld and scaled Schoenfeld residuals using the Grambsch-Therneau test. Finally, to assess the overall goodness of fit using the Cox-Snell residuals of a Cox proportional hazards regression model the cumulative observed versus the cumulative expected number of events for subjects with observed (not censored) survival times was plotted. According to Arjas (46) a model with adequate fit should have points that follow a 45-degree line beginning at the origin.

2.8.4 LOGISTIC REGRESSION ANALYSIS

The generated Cox proportional hazard model violated the assumption of proportionality using the Grambsch-Therneau test. While optional methods exist to text the assumption of proportionality such as the inclusion of the time-dependent variable for the non-proportional predictors and stratifying on the non-proportional predictor, these could not be applied in this study. Reasons being that three (age group, sex and Other TTIs) out of six predictors violated the proportionality assumption and were not time-dependent variables. After consultation with a Biostatistician in the school, the use of a binary logistic model to determine the risk factors associated with incident TTI, HIV, HCV or HBV was deemed appropriate since all four outcome variables (TTI, HIV, HCV and HBV) are binary outcomes.

2.8.4.1 UNIVARIATE LOGISTIC REGRESSION ANALYSIS

Univariate logistic regression analyses were done for all variables to determine the predictors of disease. Statistically significant variables at a *p*-value <0.2 and any priori

biologically plausible covariates were considered important factors to be included in the multivariate regression analyses.

2.8.4.2 MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

For the multivariate modelling all variables that were statistically significant at a *p*-value<0.2 were included in the model. A backward stepwise model building process was performed using significant variables from the univariate analysis. All variables were modelled as categorical with interaction terms included. Models were compared using the likelihood ratio (LR) test (*lrtest*). Potential confounders were adjusted for in the multivariate model. The final model, with estimates of the odds ratios of TTI, HIV, HCV, and HBV and corresponding 95% confidence intervals, was attained using a LR *p*-value of 0.05 and the Akaike's information criterion (AIC) and Bayesian information criterion (BIC).

2.8.4.3 MODEL DIAGNOSTICS

Model specification error was assessed using the *linktest* command to ascertain that the linear predicted value and linear predicted value squared of the final models were correctly specified. A significant linear predictive value squared denotes a significant linktest and this depicts a specification error. The Box-Tidwell model (using the *boxtid* command), which transforms a predictor using power and exponential transformations were also used to find the best power for model fit based on maximum likelihood estimates. An insignificant *p*-value for the test of non-linearity depicts that the predictors be modelled as linear terms.

To assess the goodness-of-fit of the final model, the Hosmer-Lemeshow test and Pearson Chi-square tests were performed. Multi-collinearity was assessed using the variance inflation factor (VIF) and tolerance level. Variables with a VIF greater than 10 and tolerance level less than 0.1 were considered to be perfectly collinear. Outliers and influential observations were assessed using the studentized Pearson and deviance residuals as well as the Pregibon's (hat) leverage and influence statistics (47).

2.9. ETHICAL CONSIDERATIONS

Permission to use the MBTS data (at no cost) was obtained in writing from the MBTS Medical Director (Appendix III). Prior to receiving the dataset, all donor identifiers were coded with unique donor numbers to maintain anonymity. Ethics for this study was approved by the Human Research Ethics Committee (Medical), University of the Witwatersrand (Clearance Certificate Number: M181008; Appendix IV) after the research title was approved (Appendix V).

CHAPTER THREE: RESULTS

3.1 INTRODUCTION

Chapter three summarizes the results of the study objectives and analysis plan. The baseline characteristics by TTI, HIV, HCV and HBV status and incidence rates of the blood donors are reported. The risk factors associated with TTI, HIV, HCV and HBV are summarized based on results from a univariate and multivariate binary logistic regression analysis. From 2005 through 2015, 227,442 donor records captured within the MBTS database were considered for this study. Of these, only 47,075 donors with their records met all the inclusion criteria and were analysed (Figure 3.1).

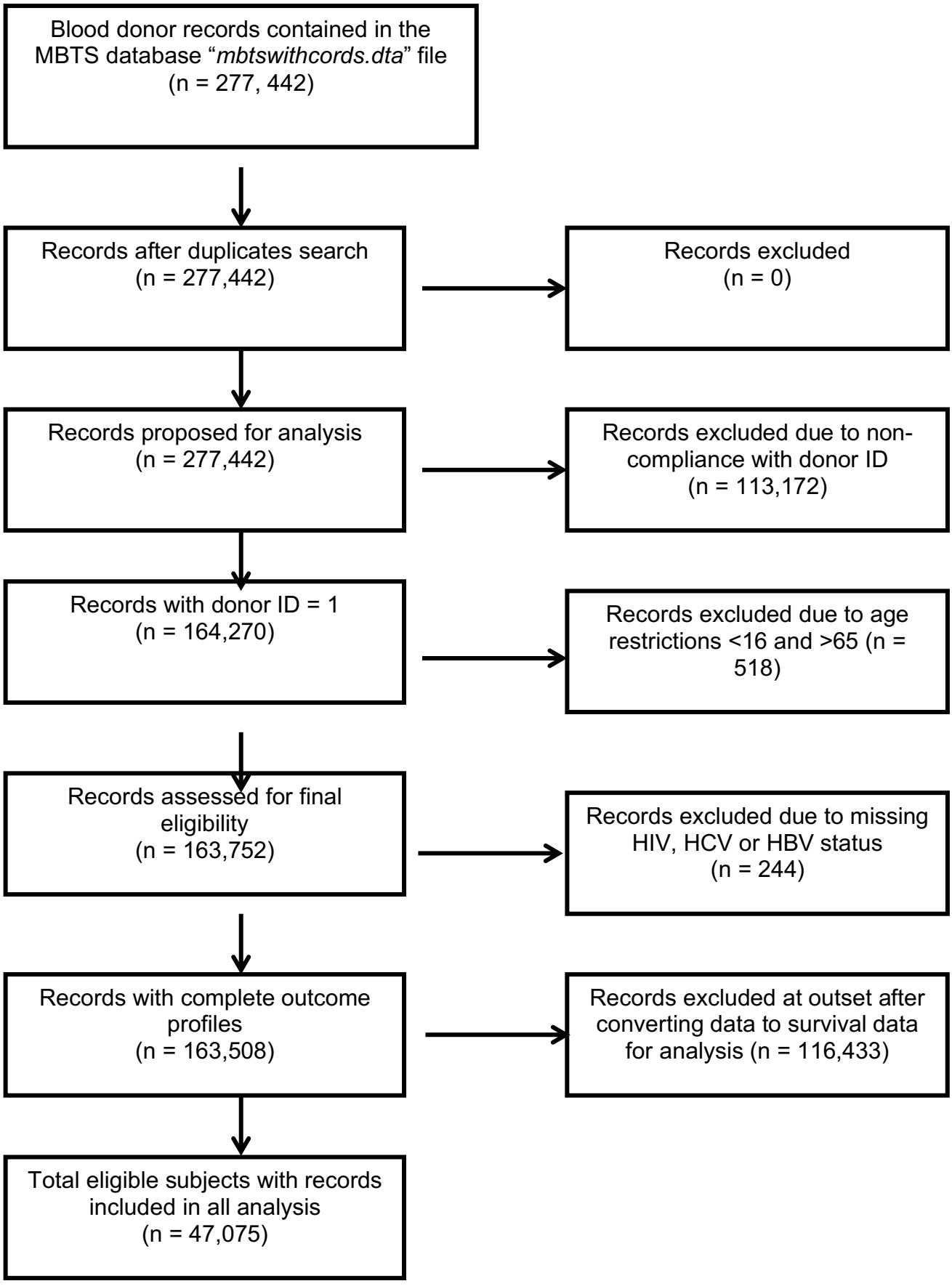


Figure 3:1: Flow chart diagram of blood donors enrolled in the study

3.2 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS

The study comprised of 47,075 blood donors. The median age was 22 years (IQR=18–22) shown in Table 3.1. The age grouping spanning 20–24 years constituted the highest number of donors 21,779 (46.26%) followed by the age group 16–19 years with 17,464 (37.10%) donors. Overall, 84.05% (n=39,568) of the donors were males compared to 7,507 (15,95%) females with 43,138 (91.64%) reported as not married. The majority 45,943 (97.60%) of donors were employed with the majority residing in the Southern 53.14% (n=25,014) and Central 32.59% (n=15,344) regions. A total of 23,941 (50.86%) donors had type O blood group, 42,390 (90.05%) reported having sex with multiple partners without condom use. Malaria infection was common in 20,126 (42.75%) of the donors while a minority 322 (0.68%) was positive for syphilis infection.

Table 3.1: Baseline characteristics of donor participants, by TTI status (N= 47,075)

Characteristic	N (%)	Infected (N=3,439)	Uninfected (N=43,636)	*p* value*
		n (%)	n (%)	
Age (years)	22 (18–22)*	22 (19–23)*	21 (18–22)*	**0.000**
Age Group (%)				**0.000**
16-19	17,464 (37.10)	1,101 (32.02)	16,363 (37.50)	
20-24	21,779 (46.26)	1,705 (49.58)	20,074 (46.00)	
25-29	4,343 (9.23)	352 (10.24)	3,991 (9.15)	
30-34	1,663 (3.53)	168 (4.89)	1,495 (3.43)	
35-39	833 (1.77)	64 (1.86)	769 (1.76)	
40-44	485 (1.03)	29 (0.84)	456 (1.05)	
45+	508 (1.08)	20 (0.58)	488 (1.12)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	
Sex (%)				**0.000**
Female	7,507 (15.95)	345 (10.03)	7,162 (16.41)	
Male	39,568 (84.05)	3,094 (89.97)	36,474 (83.59)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	
Marital Status (%)				**0.045**
Married	3,937 (8.36)	319 (9.28)	3,618 (8.29)	
Not Married	43,138 (91.64)	3,120 (90.72)	40,018 (91.71)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	
Employment Status (%)				**0.033**
Employed	45,943 (97.60)	3,334 (96.95)	42,609 (97.65)	
Unemployed	714 (1.52)	68 (1.98)	646 (1.48)	
Unknown	418 (0.89)	37 (1.08)	381 (0.87)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	
Region of Residence (%)				**0.000**
Central Region	15,344 (32.59)	1,153 (33.53)	14,191 (32.52)	
Northern Region	6,674 (14.18)	308 (8.96)	6,366 (14.59)	
Southern Region	25,014 (53.14)	1,975 (57.43)	23,039 (52.80)	
Unknown	43 (0.09)	3 (0.09)	40 (0.09)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	
ABO Blood Group (%)				0.301
A	10,524 (22.36)	820 (23.84)	9,704 (22.24)	
B	9,857 (20.94)	702 (20.41)	9,155 (20.98)	
AB	1,925 (4.09)	135 (3.93)	1,790 (4.10)	
O	23,941 (50.86)	1,723 (50.10)	22,218 (50.92)	
Missing	828 (1.76)	59 (1.72)	769 (1.76)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	

*Median (Interquartile Range); *p*-value= obtained by Pearson Chi-square for statistical differences within groups, significant at $p<0.05$. All significant values are in bold face

Table 3.1 (*Continued…*) Baseline characteristics of donor participants, by TTI status (N= 47,075)

Characteristic	N (%)	Infected (N=3,349)	Uninfected (N=43,636)	*p* value*
		n (%)	n (%)	
Sex with multiple partners without condom use (%)				**0.004**
No	4,685 (9.95)	391 (11.37)	4,294 (9.84)	
Yes	42,390 (90.05)	3,048 (88.63)	39,342 (90.16)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	
Other TTIs (%)				0.716
None	26,627 (56.56)	1,934 (56.24)	24,693 (56.59)	
Syphilis Infection	322 (0.68)	27 (0.79)	295 (0.68)	
Malaria Infection	20,126 (42.75)	1,478 (42.98)	18,648 (42.74)	
TOTAL	47,075 (100)	3,439 (100)	43,636 (100)	

* significant at $p<0.05$. All significant values are in bold face

3.2.1. BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY TTI STATUS

Figure 3.2 below shows non-normal age distribution of TTI positive donors.

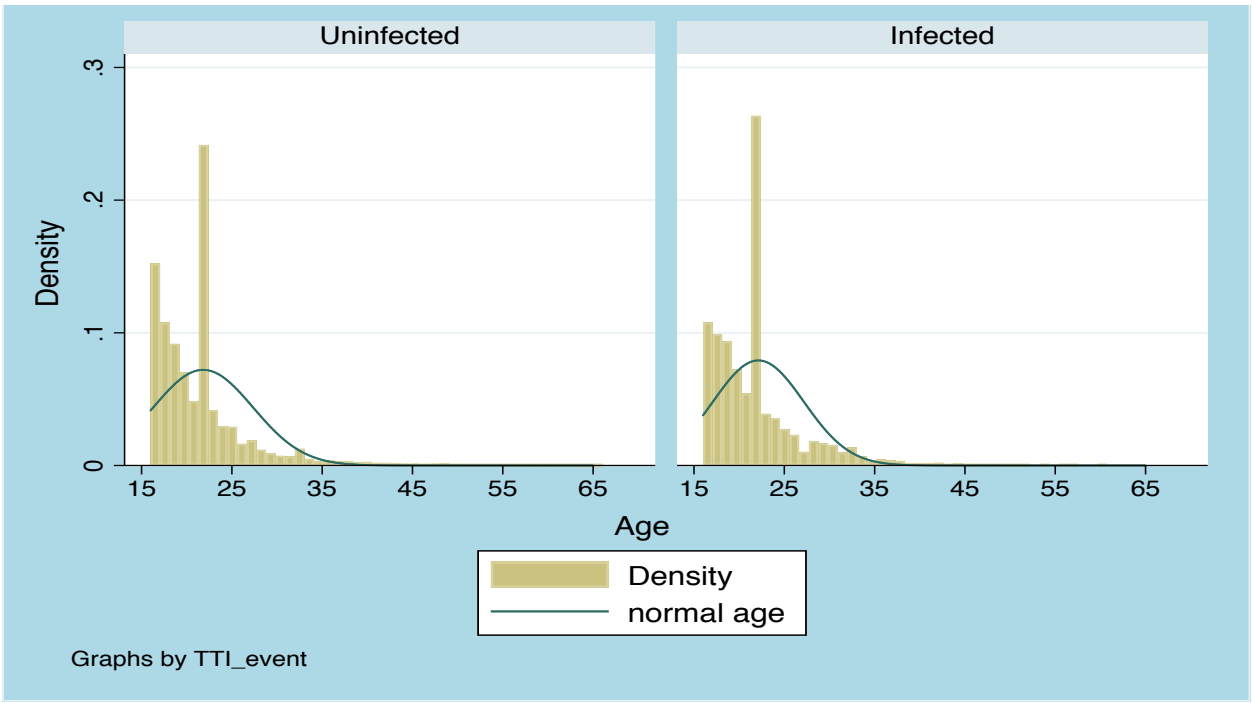


Figure 3.2: Distribution of donors' age by TTI status (N= 47,075)

Of the 47,075 registered donors, 3,439 (7.31%) were infected with TTI (Table 3.1). The median age for those infected was 22 years with IQR of 18–23 years. There was an overwhelmingly significant difference (p<0.0001) in the frequency of infection in donors of the different age groups. In particular, the frequency of TTI positivity was higher in donors aged 20–24 (49.58%), 16–19 (32.02%), 25–29 (10.24%), and 30–34 (4.89%). Among these, the frequency of infectivity was overwhelmingly significantly higher (p<0.0001) for male donors (89.97%) compared to females (10.03%) donors and for residents of the Southern (57.43%) and Central region (33.53%) compared to those from the Northern region (8.96%). Similarly, the frequency of TTI infectivity was significantly higher (p=0.045) for those not married (90.72%) compared to those married (9.28%). Sex with multiple partners without condom use was also shown to be significantly different (p<0.05) between those who did not engage in sex with multiple partners without condom use and those who engaged in sex with multiple partners without condom use. The frequency of infection was higher (88.63%) for donors who engaged in sex with multiple partners without condom use.

3.2.2 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY HIV STATUS

Of the 47,075 study participants, 818 (1.74%) were infected with HIV during the study period and 46,257 remained uninfected. The age distribution of donors followed a non-normal pattern with positive skewness (Figure 3.3). The median age for those infected was 22 years with IQR of 19–23 years. There was an overwhelmingly significant difference (p<0.0001) in the frequency of HIV infection in donors of the different age groups. In particular, the frequency of HIV positivity was higher in donors aged 20–24 (47.19%), 16–19 (30.44%), 25–29 (30.44%), and 30–34 years of age (5.26%). Among these, the

frequency of HIV infection was significantly different (p=0.008) for males (87.41%) compared to females (12.59) and for those not married (88.02%) compared to those married (11.98%). No HIV cases were reported among donors whose region of residence was unknown.

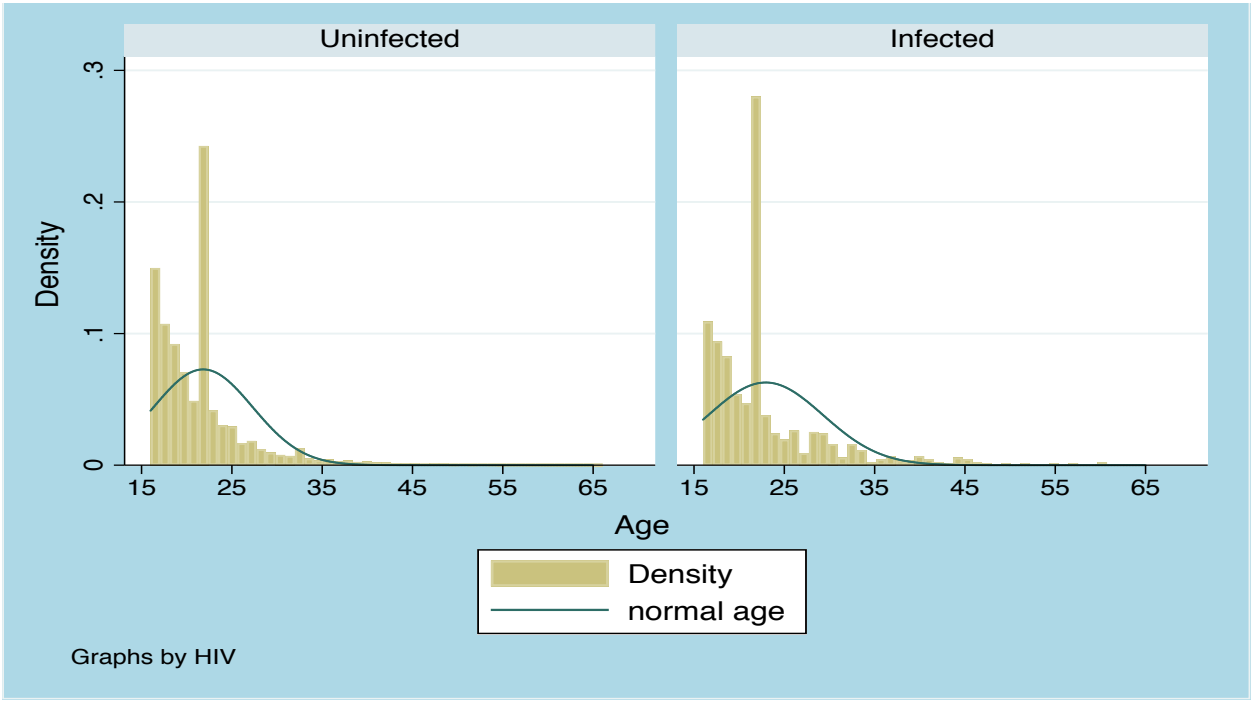


Figure 3.3: Distribution of donors' age by HIV status (N= 47,075)

The frequency of HIV infection was significantly higher (p=0.008) for participants who engaged in sex with multiple partners without condom use (n= 714; 87.29%) compared to those who had protected sex with multiple partners (n=104; 12.71%). Infection was highest in those co-infected with malaria (36.92%) compared to donors co-infected with syphilis (1.96%). This difference was overwhelmingly significant (p<0.0001).

Table 3.2: Baseline characteristics of donor participants, by HIV status (N=47,075)

Characteristic	N (%)	Infected (N=818)	Uninfected (N=46,257)	*p* value*
		n (%)	n (%)	
Age (years)	22 (18-22)*	22 (19-23)*	22 (18-22)*	**0.000**
Age Group (%)				**0.000**
16-19	17,464 (37.10)	249 (30.44)	17,215 (37.22)	
20-24	21,779 (46.26)	386 (47.19)	21,393 (46.25)	
25-29	4,343 (9.23)	91 (11.12)	4,252 (9.19)	
30-34	1,663 (3.53)	43 (5.26)	1,620 (3.50)	
35-39	833 (1.77)	18 (2.20)	815 (1.76)	
40-44	485 (1.03)	18 (2.20)	467 (1.01)	
45+	508 (1.08)	13 (1.59)	495 (1.07)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	
Sex (%)				**0.008**
Female	7,507 (15.95)	103 (12.59)	7,404 (16.01)	
Male	39,568 (84.05)	715 (87.41)	38,853 (83.99)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	
Marital Status (%)				**0.000**
Married	3,937 (8.36)	98 (11.98)	3,839 (8.30)	
Not Married	43,138 (91.64)	720 (88.02)	42,418 (91.70)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	
Employment Status (%)				0.607
Employed	45,943 (97.60)	794 (97.07)	45,149 (97.60)	
Unemployed	714 (1.52)	15 (1.83)	699 (1.51)	
Unknown	418 (0.89)	9 (1.10)	409 (0.88)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	
Region of Residence (%)				**0.000**
Central Region	15,344 (32.59)	301(36.80)	15,043 (32.52)	
Northern Region	6,674 (14.18)	68 (8.31)	6,606 (14.28)	
Southern Region	25,014 (53.14)	449 (54.89)	24,565 (98.21)	
Unknown	43 (0.09)	0 (0.00)	43 (0.09)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	
ABO Blood Group (%)				0.247
A	10,524 (22.36)	204 (24.94)	10,320 (22.31)	
B	9,857 (20.94)	177(21.64)	9,680 (20.93)	
AB	1,925 (4.09)	36 (4.40)	1,889 (4.08)	
O	23,941 (50.86)	385 (47.07)	23,556 (50.92)	
Missing	828 (1.76)	16 (1.96)	812 (1.76)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	

*****Median (Interquartile Range); *p*-value= obtained by Pearson chi2 test to compare frequencies between groups, significant at $p<0.05$. All significant values are in bold face

Table 3.2 (*Continued…*) Baseline characteristics of donor participants, by HIV status (N= 47,075)

Characteristic	N (%)	Infected (N=3,349)	Uninfected (N=43,636)	*p* value*
		n (%)	n (%)	
Sex with multiple partners without condom use (%)				**0.008**
No	4,685 (9.95)	104 (12.71)	4,581 (9.90)	
Yes	42,390 (90.05)	714 (87.29)	41,676 (90.10)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	
Other TTIs (%)				**0.000**
None	26,627 (56.56)	500 (61.12)	26,127 (56.48)	
Syphilis Infection	322 (0.68)	16 (1.96)	306 (0.66)	
Malaria Infection	20,126 (42.75)	302 (36.92)	19,824 (42.86)	
TOTAL	47,075 (100)	818 (100)	46,257 (100)	

* significant at $p<0.05$. All significant values are in bold face

3.2.3 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY HCV STATUS

Figure 3.4 below shows a non-normal age distribution of HCV infected donors.

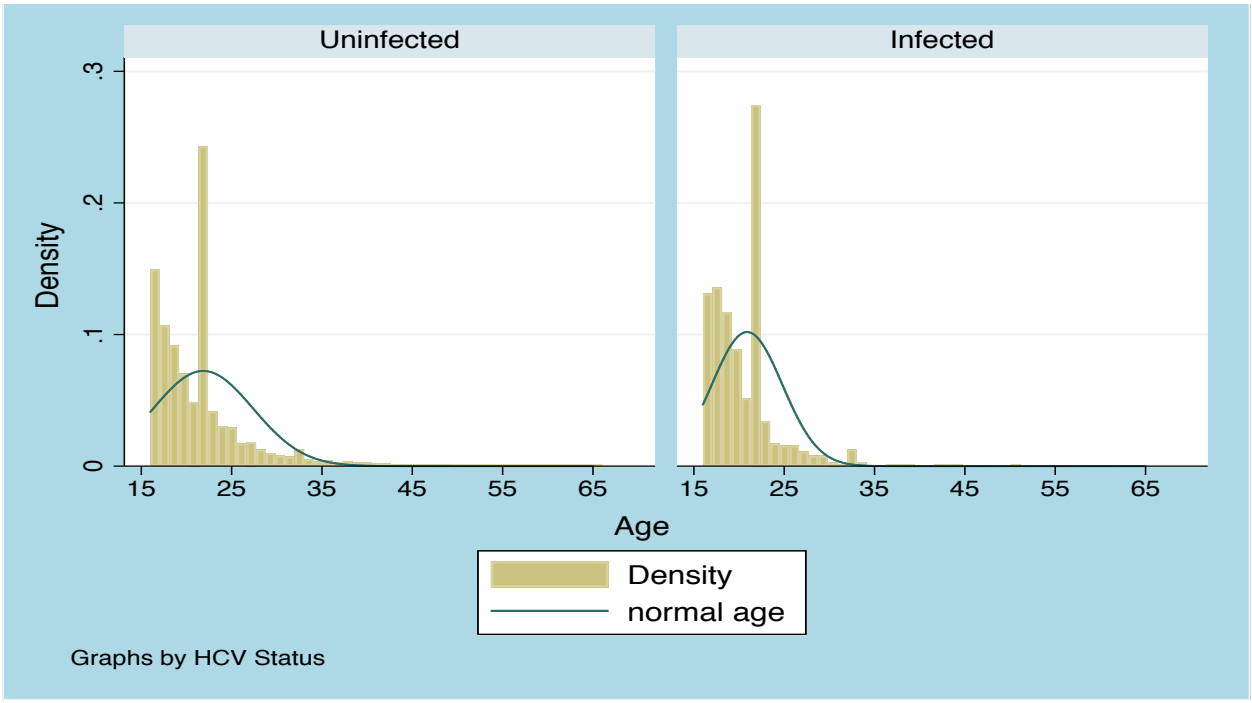


Figure 3:4: Distribution of donors' age by HCV status (N= 47,075)

Of the 47,075 study participants, 602 (1.28%) were infected with HCV during the study period and 46,473 remained uninfected (Table 3.3). The median age for those infected was 20 years (IQR=18-22 years). Among these, the frequency of HCV infection was overwhelmingly significantly different (p<0.0001) among donors in the different age groups. In particular, the frequency of HCV positivity was higher in donors aged 20–24 (49.67%) and 16–19 (40.86%). Infection was higher in males (90.53%) compared to females (9.47%). The frequency of HCV infectivity was also significantly different for those not married (94.52%) compared to those married (5.48%). Additionally, the frequency of infection was higher for blood type O (43.69%) and type A (25.91%) donors. Infection was highest in those co-infected with malaria (40.53%) compared to donors co-infected with syphilis (1.50%). This difference was significant (p=0.034).

Table 3.3: Baseline characteristics of donor participants, by HCV status (N=47,075)

Characteristic	N (%)	Infected (N=602)	Uninfected (N=46,473)	*p* value*
		n (%)	n (%)	
Age (years)	22 (18–22)*	20 (18–22)*	22 (18–22)*	0.070
Age Group (%)				**0.000**
16-19	17,464 (37.10)	246 (40.86)	17,218 (37.05)	
20-24	21,779 (46.26)	299 (49.67)	21,480 (46.22)	
25-29	4,343 (9.23)	37 (6.15)	4,306 (9.27)	
30-34	1,663 (3.53)	13 (2.16)	1,650 (3.55)	
35-39	833 (1.77)	3 (0.50)	830 (1.79)	
40-44	485 (1.03)	3 (0.50)	482 (1.04)	
45+	508 (0.23)	1 (0.17)	507 (1.09)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	
Sex (%)				**0.000**
Female	7,507 (15.95)	57 (9.47)	7,450 (16.03)	
Male	39,568 (84.05)	545 (90.53)	39,023 (83.97)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	
Marital Status (%)				**0.010**
Married	3,937 (8.36)	33 (5.48)	3,904 (8.40)	
Not Married	43,138 (91.64)	569 (94.52)	42,569 (91.60)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	
Employment Status (%)				0.686
Employed	45,943 (97.60)	591 (98.17)	45,352 (97.59)	
Unemployed	714 (1.52)	8 (1.33)	706 (1.52)	
Unknown	418 (0.89)	3 (0.50)	415 (0.89)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	
Region (%)				
Central Region	15,344 (32.59)	220 (36.54)	15,124 (32.54)	0.084
Northern Region	6,674 (14.18)	72 (11.96)	6,602 (14.21)	
Southern Region	25,014 (53.14)	309 (51.33)	24,705 (53.16)	
Unknown	43 (0.09)	1 (0.17)	42 (0.09)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	
ABO Blood Group (%)				**0.001**
A	10,524 (22.36)	156 (25.91)	10,368 (22.31)	
B	9,857 (20.94)	135 (22.43)	9,722 (20.92)	
AB	1,925 (4.09)	29 (4.82)	1,896 (4.08)	
O	23,941 (50.86)	263 (43.69)	23,678 (50.95)	
Missing	828 (1.76)	19 (3.16)	809 (1.74)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	

*****Median (Interquartile Range); *p*-value= obtained by Pearson chi2 or Fisher's exact test to compare frequencies between groups, significant at $p<0.05$. All significant values are in bold face

Table 3.3 (*Continued…*) Baseline characteristics of donor participants, by HCV status (N=47,075)

Characteristic	N (%)	Infected (N=602)	Uninfected (N=46,473)	*p* value*
		n (%)	n (%)	
Sex with multiple partners without condom use (%)				0.054
No	4,685 (9.95)	74 (12.29)	4,611 (9.92)	
Yes	42,390 (90.05)	528 (87.71)	41,862 (90.08)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	
Other TTIs (%)				**0.034**
None	26,627 (56.56)	349 (57.97)	26,278 (56.54)	
Syphilis Infection	322 (0.68)	9 (1.50)	313 (0.67)	
Malaria Infection	20,126 (42.75)	244 (40.53)	19,882 (42.78)	
TOTAL	47,075 (100)	602 (100)	46,473 (100)	

* significant at $p<0.05$. All significant values are in bold face

3.2.4 BASELINE CHARACTERISTICS OF DONOR PARTICIPANTS BY HBV STATUS

Figure 3.5 below shows a non-normal age distribution of donors with positive skewness.

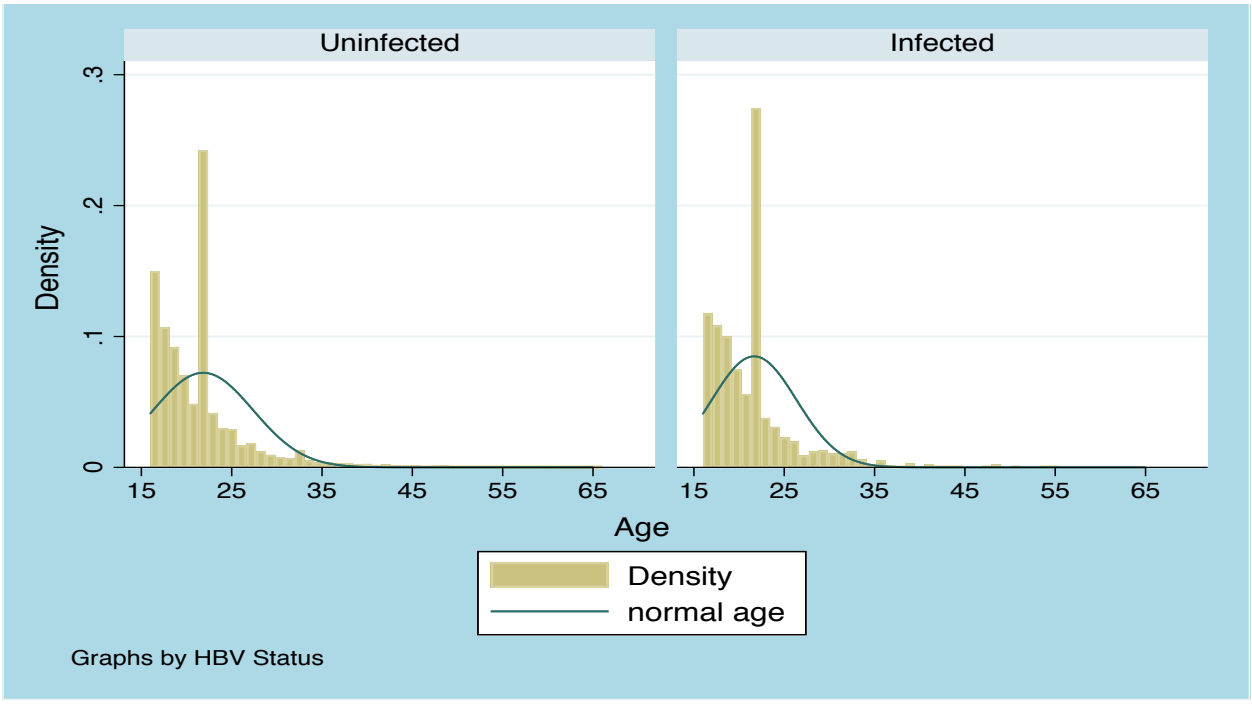


Figure 3.5: Distribution of donors' age by HBV status (N= 47,075)

Of the 47,075 registered donors, 1,238 (2.63%) were infected with HBV (Table 3.4). The median age for those infected was 22 years with an IQR of 19-22 years.

Table 3.4: Baseline characteristics of donor participants, by HBV status (N=47,075)

Characteristic	*N*	Infected (N=1,238)	Uninfected (N=45,837)	*p* value*
		n (%)	n (%)	
Age (years)	22 (18–22)*	22 (19–22)*	22 (18–22)*	0.215
Age Group (%)				**0.005**
16-19	17,464 (37.10)	430 (34.73)	17,034 (37.16)	
20-24	21,779 (46.26)	626 (50.57)	21,153 (46.15)	
25-29	4,343 (9.23)	101 (8.16)	4,242 (9.25)	
30-34	1,663 (3.53)	52 (4.20)	1,611 (3.51)	
35-39	833 (1.77)	16 (1.29)	817 (1.78)	
40-44	485 (1.03)	6 (0.48)	479 (1.05)	
45+	508 (1.08)	7 (0.57)	501 (1.09)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	
Sex (%)				**0.000**
Female	7,507 (15.95)	134 (10.82)	7,373 (16.09)	
Male	39,568 (84.05)	1,104 (89.18)	38,464 (83.91)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	
Marital Status (%)				0.085
Married	3,937 (8.36)	87 (7.03)	3,850 (8.40)	
Not Married	43,138 (91.64)	1,151 (92.97)	41,987 (91.60)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	
Employment Status (%)				0.404
Employed	45,943 (97.60)	1,207 (97.50)	44,736 (97.60)	
Unemployed	714 (1.52)	23 (1.86)	691 (1.51)	
Unknown	418 (0.89)	8 (0.65)	410 (0.89)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	
Region of Residence (%)				
Central Region	15,344 (32.59)	484 (39.10)	14,860 (32.42)	**0.000**
Northern Region	6,674 (14.18)	133 (10.74)	6,541 (14.27)	
Southern Region	25,014 (53.14)	621 (50.16)	24,393 (53.22)	
Unknown	43 (0.09)	0 (0.00)	43 (0.09)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	
ABO Blood Group (%)				0.505
A	10,524 (22.36)	290 (23.42)	10,234 (22.33)	
B	9,857 (20.94)	246 (19.87)	9,611 (20.97)	
AB	1,925 (4.09)	47 (3.80)	1,878 (4.10)	
O	23,941 (50.86)	639 (51.62)	23,302 (50.84)	
Missing	828 (1.76)	16 (1.29)	812 (1.77)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	

*****Median (Interquartile Range); *p*-value= obtained by Pearson chi2 or Fischer's exact test to compare frequencies between groups, significant at $p<0.05$. All significant values are in bold face

Table 3.4 (*Continued…*) Baseline characteristics of donor participants, by HBV status (N=47,075)

Characteristic	*N*	Infected (N= 1,238)	Uninfected (N= 45,837)	*p* value*
		n (%)	n (%)	
Sex with multiple partners without condom use (%)				0.057
No	4,685 (9.95)	143 (11.55)	4,542 (9.91)	
Yes	42,390 (90.05)	1,095 (88.45)	41,295 (90.09)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	
Other TTIs (%)				**0.047**
None	26,627 (56.56)	713 (57.59)	25,914 (56.54)	
Syphilis Infection	322 (0.68)	15 (1.21)	307 (0.67)	
Malaria Infection	20,126 (42.75)	510 (41.20)	19,616 (42.80)	
TOTAL	47,075 (100)	1,238 (100)	45,837 (100)	

* significant at $p<0.05$. All significant values are in bold face

There was a significant difference ($p=0.005$) in the percentage of HBV infection in the different age groups. Of noteworthy, the frequency of HBV positivity was higher in donors aged 20–24 (50.57%), 16–19 (34.73%), 25–29 (8.16%), and 30–34 (4.20%). The frequency of HBV infection was overwhelmingly significantly different ($p<0.0001$) for male donors (89.18%) compared to females (10.82%) donors and for residents in the different residential regions; 50.16% for the Southern, 39.10% for the Central, and 10.74% for the Northern region. Infection was highest in those co-infected with malaria (41.20%) compared to donors co-infected with syphilis (1.21%). This difference was significant ($p=0.047$).

3.3 INCIDENCE OF TRANSFUSION TRANSMISSIBLE HIV, HCV AND HBV INFECTIONS

3.3.1 INCIDENCE OF TTI (HIV+, HCV+ or HBV+)

The Kaplan-Meier survival curve as shown below (Figure 3.6) suggests that the probability of survival was about 63% after 60 months of follow-up. Overall, the rate of TTI incidence among the study participants was 43.4 per 10,000.

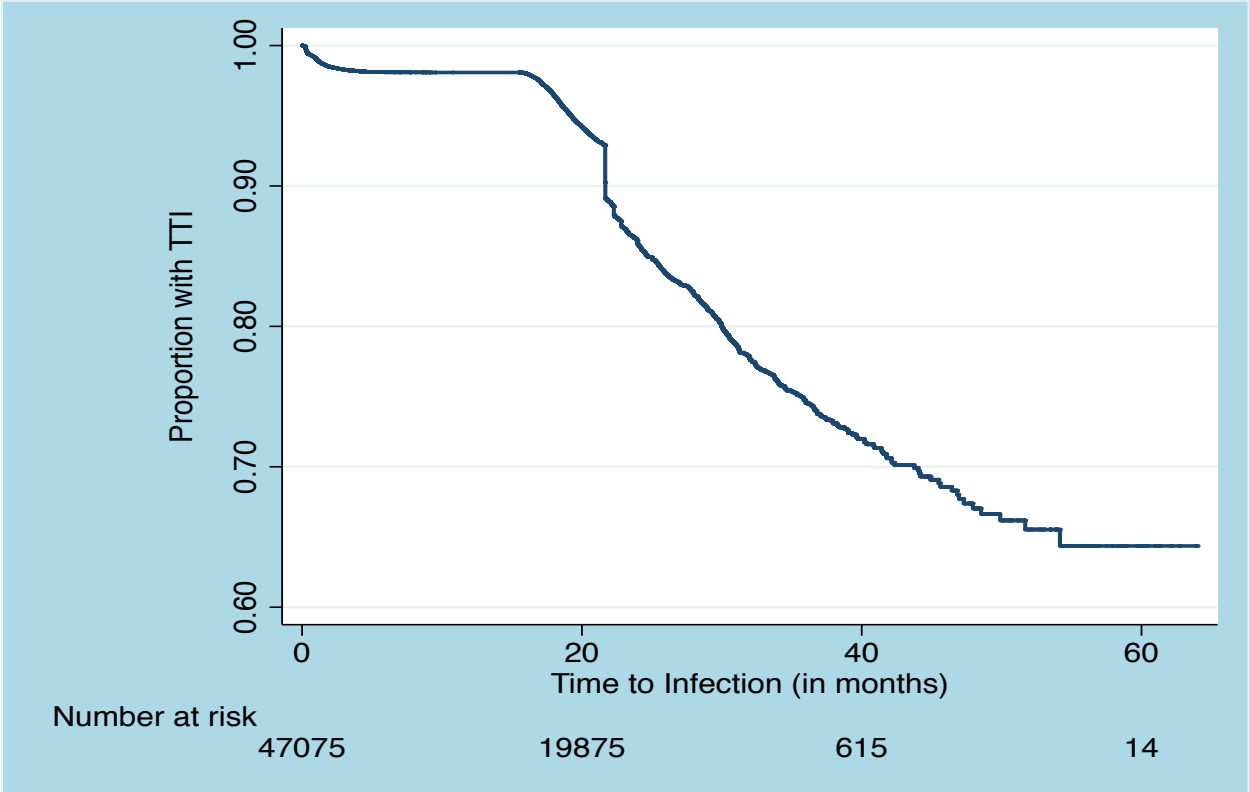


Figure 3.6: Overall Kaplan-Meier survival estimates of TTI (N= 47,075)

Basing on the Kaplan-Meier curve, the probability of survival was higher for females than for males (Figure 3.7). The results of the log rank test showed that the survival distributions for the two groups was overwhelmingly significantly different, with a log-rank Chi-square of 31.24 on one degree of freedom at $p<0.0001$. TTI incidence rate was higher among males (46.36 cases per 10,000; 95% CI= 44.76–48.03) compared to females (27.59 cases per 10,000; 95% CI= 24.83–30.66). TTI incidence was higher than expected among males (3,094 observed cases compared to the expected number of 2,983).

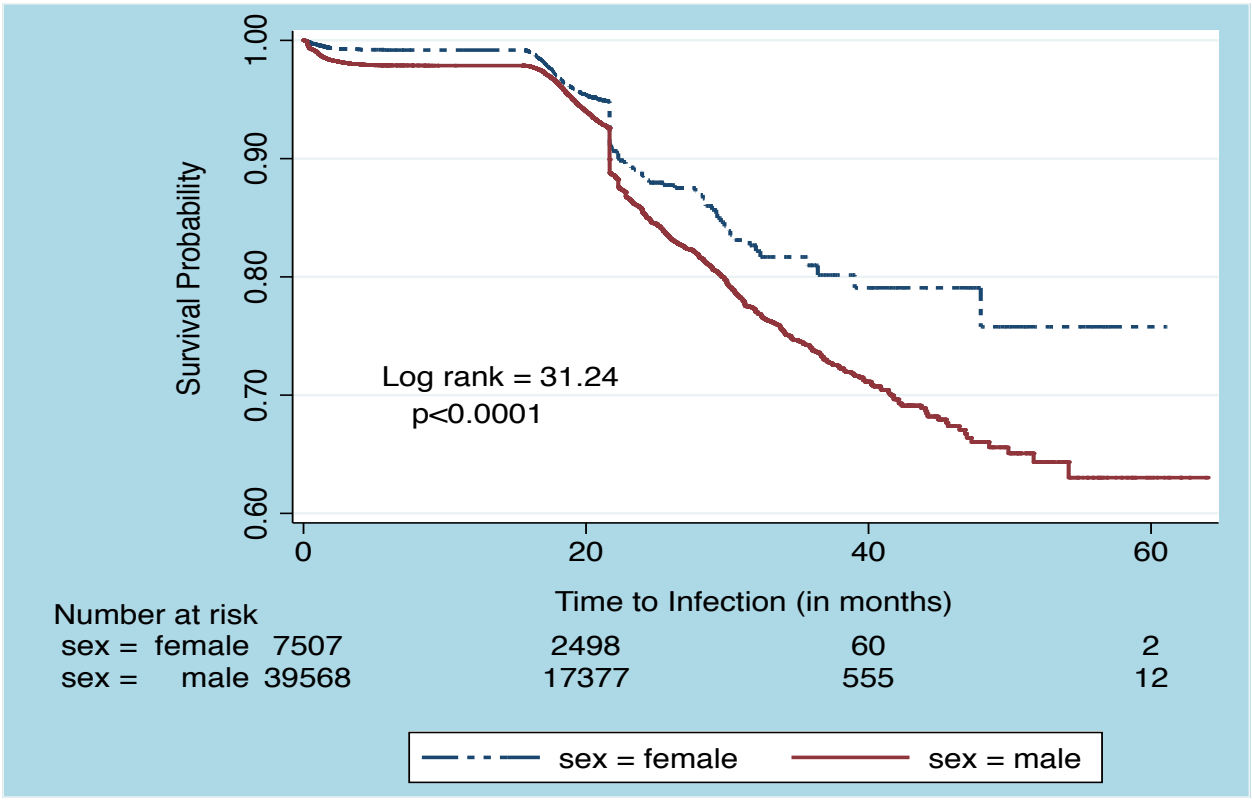


Figure 3.7: Kaplan-Meier survival estimates of TTI, by sex (N= 47,075)

Table 3.5 below summarizes the TTI incidence rates per 10,000 person years of exposure by level of each potential explanatory variable.

Table 3.5: TTI incidence rates by potential risk factors and confounders (N=47,075)

Characteristic	TTI Cases		PY	IR (95% CI) per 10,000 pyears	*p* value*
	Observed	Expected			
Overall	**3,439**		**79.24**	**43.40 (41.98-44.88)**	
Age Group					
16-19	1,101	536	27.28	40.35 (38.03- 42.81)	**0.000**
20-24	1,705	1,716	36.02	47.33 (45.14- 49.63)	
25-29	352	481	7.07	49.81 (44.87- 55.29)	
30-34	168	285	3.68	45.64 (39.23- 53.09)	
35-39	64	168	2.07	30.88 (24.17- 39.45)	
40-44	29	120	1.47	19.70 (13.69- 28.35)	
45+	20	131	1.64	12.22 (7.88- 18.94)	
Sex					
Female	345	455	12.50	27.59 (24.83- 30.66)	
Male	3,094	2983	66.73	46.36 (44.76- 48.03)	**0.000**
Marital Status					
Married	319	587	8.19	38.97 (34.92- 43.49)	
Not Married	3120	2,851	71.05	43.91 (42.40- 45.48)	**0.000**
Employment Status					
Employed	3,334	3,345	77.46	43.04 (41.61- 44.53)	
Unemployed	68	57	1.04	65.23 (51.43- 82.74)	**0.048**
Unknown	37		0.73	50.39 (36.51- 69.55)	
Region of Residence					
Central Region	1,153	1,190	26.12	44.14 (41.67- 46.77)	
Northern Region	308	500	12.80	24.06 (21.52- 26.90)	
Southern Region	1,975	1,744	40.24	49.09 (46.97- 51.30)	**0.000**
Unknown	3	3	0.08	37.55 (12.11-116.42)	
ABO Blood Group					
A	820	760	17.73	46.25 (43.19-49.52)	0.158
B	702	710	16.40	42.81 (39.76-46.10)	
AB	135	141	3.25	41.56 (35.11-49.20)	
O	1,723	1,761	40.29	42.76 (40.80-44.83)	
Missing	59	65	1.57	37.68 (29.20-48.63)	
Sex with multiple partners without condom use					
No	391	340	7.96	49.13 (44.50-54.25)	**0.004**
Yes	3,048	3098	71.28	42.76 (41.27-44.31)	
Other TTIs (%)					
None	1,934	2126	49.29	39.24 (37.53-41.03)	
Syphilis Infection	27	28	0.63	42.54 (29.17-62.03)	
Malaria Infection	1,478	1284	29.32	50.42 (47.91-53.05)	**0.000**

* significant at $p<0.05$. All significant values are in bold face; IR= Incidence rate; CI= Confidence intervals; PY= Person-years

Of the 3,439 TTI infected donors, The TTI incidence grew with increasing age until age 29, and then the rates fell to the lowest rate of 12.22 per 10,000. The rates were 40.35 per 10,000, 47.33 per 10,000, 49.81 cases per 10,000, and 45.64 per 10,000 among 16–19, 20–24, 25–29, and 30–24 age groups, respectively. However, the observed number of cases (n= 1,101) for ages 16–19 was overwhelming significantly different (p<0.00001) from the expected (n= 536) cases. TTI incidence also differed according to marital and employment status. Donors who were not married developed TTI at a rate of 43.91 per 10,000 per year with those married at a rate of 38.97 per 10,000 per year. The difference in the observed number of cases (n= 3,120) and the expected cases (n= 2,851) for unmarried donors was overwhelmingly significant (p<0.00001).

Unemployed donors developed TTI at a rate of 65.23 per 10,000 per year while the employed developed TTI at a rate of 43.04 per 10,000 per year. The observed number of cases (n= 68) was significantly different (p=0.0476) from the expected (n= 57). Similarly, donors residing in the Southern region developed TTI at a higher rate of 49.09 per 10,000 per year while residents of the Central and Northern regions developed TTI at a rate of 44.14 per 10,000 and 24.06 per 10,00 per year, respectively. The difference in the observed number of cases (n= 1,975) and the expected cases (n= 1,744) for donors in the Southern region was overwhelmingly significant (p<0.00001). Blood type B donors, and donors who engaged in unprotected sex with multiple partners developed TTI at a rate of 42.81 per 10,000, and 49.13 per 10,000 per year, respectively. The observed number of cases (n= 391) compared to the expected cases (n= 340) was significantly different (p=0.0041) for donors who had unprotected sex with multiple partners.

3.3.2 INCIDENCE OF HIV

The Kaplan-Meier survival curve as shown below (Figure 3.7) suggests that the probability of survival was about 84% after 60 months of follow-up. Overall, the rate of HIV incidence among the study participants was 10.32 per 10,000.

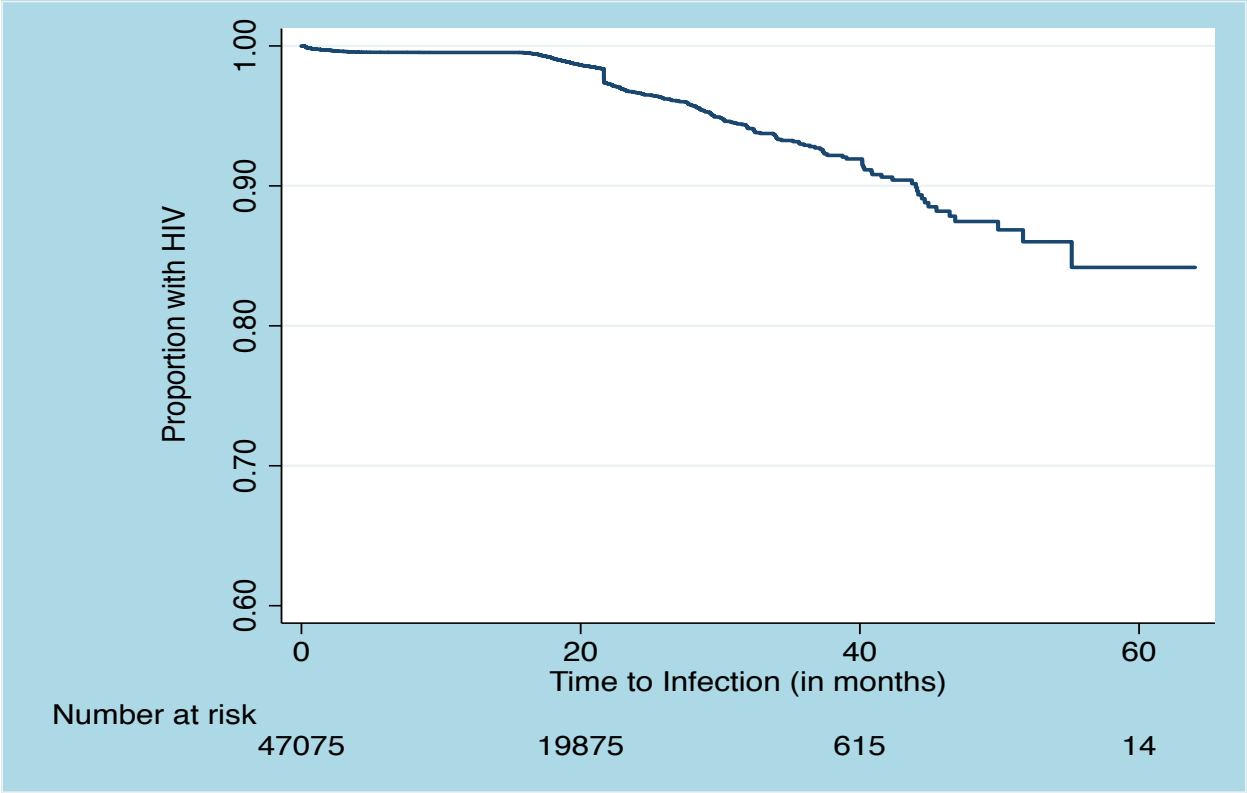


Figure 3.8: Overall Kaplan-Meier survival estimates of HIV (N= 47,075)

Based on the Kaplan-Meier curve, the probability of survival was higher for females than for males by the end of the follow-up period (Figure 3.9). The results of the log rank test showed that the survival distributions for the two groups was not statistically significantly different, log-rank Chi-square of 0.35 on one degree of freedom at p=0.5519. However, HIV incidence rate was higher than expected among males (715 observed cases compared to the expected number of 709.24).

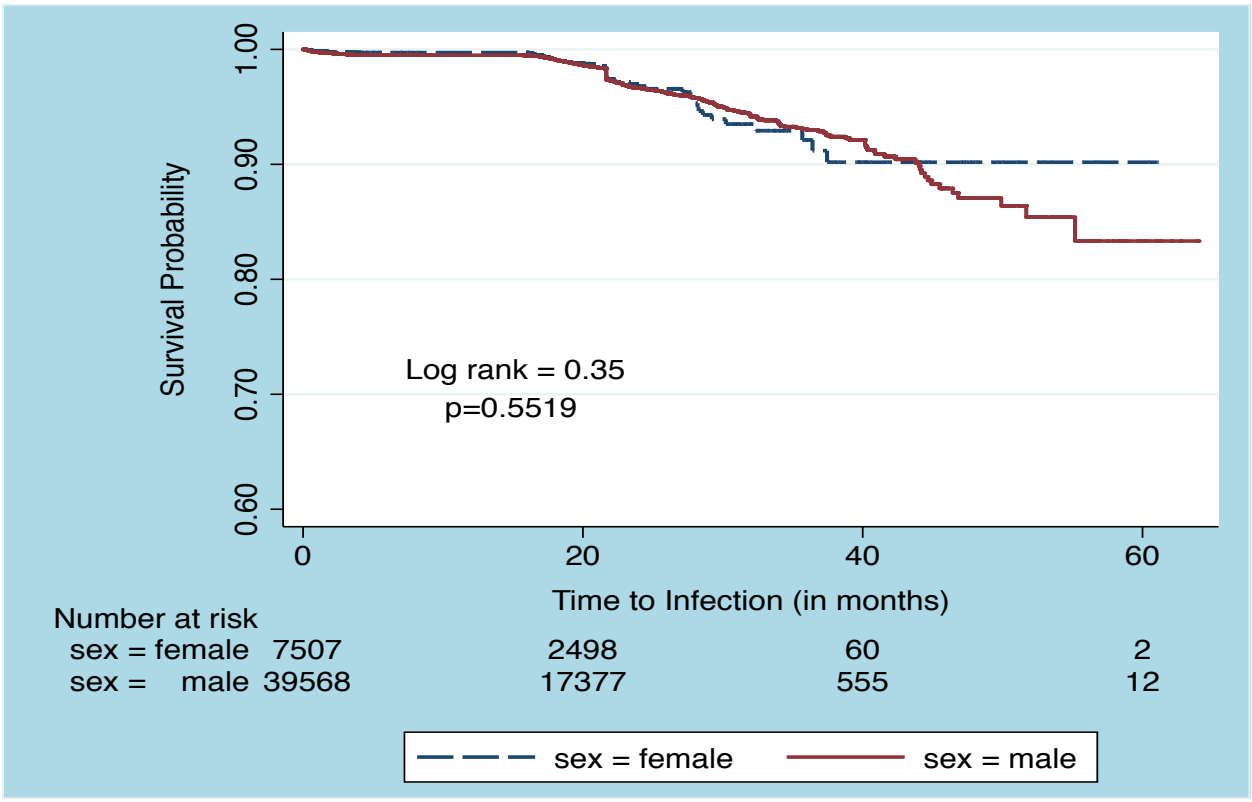


Figure 3.9: Overall Kaplan-Meier survival estimates of HIV, by sex (N= 47,075)

To investigate these further, other explanatory variables were considered. Table 3.6 below summarizes the HIV incidence rates per 10,000 person years of exposure by level of each potential explanatory variable. Of the 818 HIV infected donors, the HIV incidence rates were 91.26 per 10,000, 107.15 per 10,000, 128.77 cases per 10,000, 116.81 cases per 10,000, and 122.29 per 10,000 among 16–19, 20–24, 25–29, 30–24, and 40–44 age groups, respectively. However, the observed number of HIV cases (n= 249) for ages 16–19 was overwhelming significantly different from the expected (n= 127) cases (p<0.00001). HIV incidence also differed according to marital status. Donors who were not married developed HIV at a higher rate of 107.14 per 10,000 per year than those who were married (82.37 per 10,000 per year). The difference in the observed number of cases (n= 720) and the expected (n= 666) for unmarried donors was overwhelmingly significant (p<0.00001).

Table 3.6: HIV incidence rates by potential risk factors and confounders (N=47,075)

Characteristic	HIV Cases		PY	*IR (95% CI) per 10,000 pyears	*p* value*
	Observed	Expected			
Overall	**818**		**79.24**	**10.32 (09.64–011.06)**	
Age					
16-19	249	127	2.73	91.26 (80.60–103.33)	**0.000**
20-24	386	394	3.60	107.15 (96.98–118.39)	
25-29	91	105	0.71	128.77 (104.85–158.14)	
30-34	43	68	0.37	116.81 (86.63–157.50)	
35-39	18	42	0.21	86.85 (54.72–137.86)	
40-44	18	33	0.15	122.29 (77.05–194.09)	
45+	13	45	0.16	79.42 (46.12–136.78)	
Sex					
Female	103	108	1.25	82.37 (67.91–99.92)	
Male	715	709	6.67	107.14 (99.57–115.29)	0.552
Marital Status					
Married	98	151	0.82	119.73 (98.22–145.94)	
Not Married	720	666	7.11	101.33 (94.20–109.01)	**0.000**
Employment Status					
Employed	794	795	7.75	102.50 (95.62–109.89)	
Unemployed	15	12	0.10	143.90 (86.75–238.69)	0.662
Unknown	9	10	0.07	122.58 (63.78–235.59)	
Region of Residence					
Central Region	301	283	2.61	115.24 (102.93–129.02)	**0.000**
Northern Region	68	119	1.28	53.12 (41.88–67.37)	
Southern Region	449	413	4.02	111.59 (101.73–122.41)	**0.000**
Unknown	0	1	0.01	0.00	
ABO Blood Group					
A	204	180	1.77	115.06 (100.30–131.98)	0.184
B	177	169	1.64	107.94 (93.15–125.07)	
AB	36	33	0.32	110.83 (79.94–153.65)	
O	385	418	4.03	95.55 (86.46–105.58)	
Missing	16	15	0.16	102.18 (62.60–166.80)	
Sex with multiple partners without condom use					
No	104	80	0.80	130.68 (107.83–158.38)	**0.006**
Yes	714	737	7.13	100.17 (93.07–107.79)	
Other TTIs					
None	500	506	4.93	101.45 (92.94–110.74)	
Syphilis Infection	16	7	0.06	252.08 (154.44-411.48)	**0.003**
Malaria Infection	302	304	2.93	103.02 (92.03–115.31)	

* significant at $p<0.05$. All significant values are in bold face; IR= Incidence rate; CI= Confidence intervals; PY= Person-years

Similarly, donors residing in the Central region developed HIV at a higher rate of 115.24 per 10,000 per year compared to residents of the Southern regions who developed HIV at a rate of 111.59 per 10,000. The difference in the observed number of cases versus the expected cases for donors in the Southern (449 observed compared to 413 per 10,000 expected cases) and the Central (204 observed compared to 180 per 10,000 expected cases) regions was overwhelmingly significant (p<0.00001). Donors who engaged in unprotected sex with multiple partners developed TTI at a rate of 130.68 per 10,000 while the rate of infection in donors who did not engage in unprotected sex with multiple partners was 100.17 per 10,000 per year. The observed number of cases (n= 104) compared to the expected cases (n= 80) was significantly different (p=0.0056) for donors who had unprotected sex with multiple partners. Donors infected with syphilis developed HIV at a higher rate (252.08 per 10,000 per year) compared to the rate of HIV in malaria-infected individuals (103.02 per 10,000 per year). The difference in the observed (n=16) and the expected number of cases (n=7) for syphilis-infected donors was significant (p=0.0033).

3.3.3 INCIDENCE OF HCV

The Kaplan-Meier survival curve as shown below (Figure 3.10) suggests that the probability of survival was high at about 93% after 60 months of follow-up. Overall, the rate of HCV incidence among blood donors was 7.60 per 10,000 person-years.

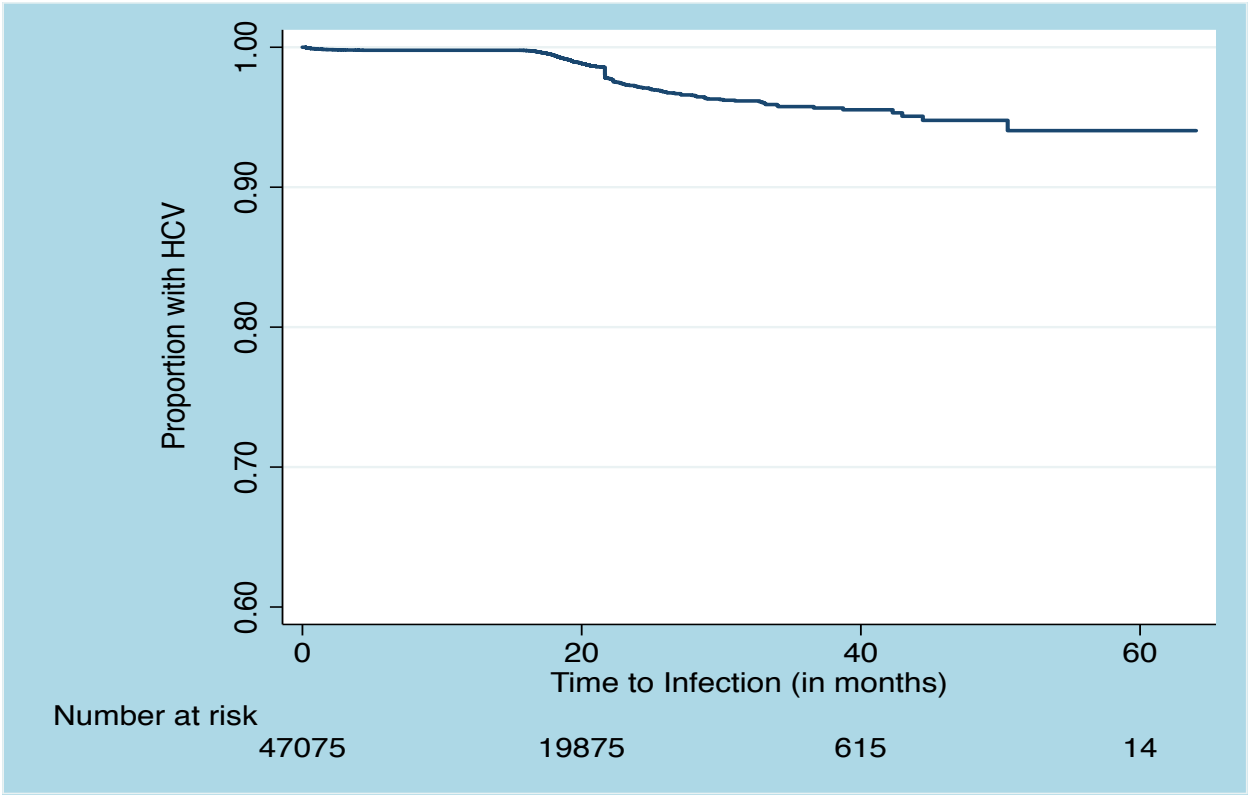


Figure 3.10: Overall Kaplan-Meier survival estimates of HCV (N= 47,075)

Based on the Kaplan-Meier curve, the probability of survival was higher for females than for males by the end of the follow-up period (Figure 3.11). The results of the log rank test showed that the survival distributions for the two groups was statistically significantly different, log-rank Chi-square of 6.84 on 1 degree of freedom at p=0.0089. The rate of infection was twice as high in males compared to females (IR= 8 per 10,000 person-years). HCV incidence rate was higher than expected among males (545 cases per 10,000 compared to the expected number of 523).

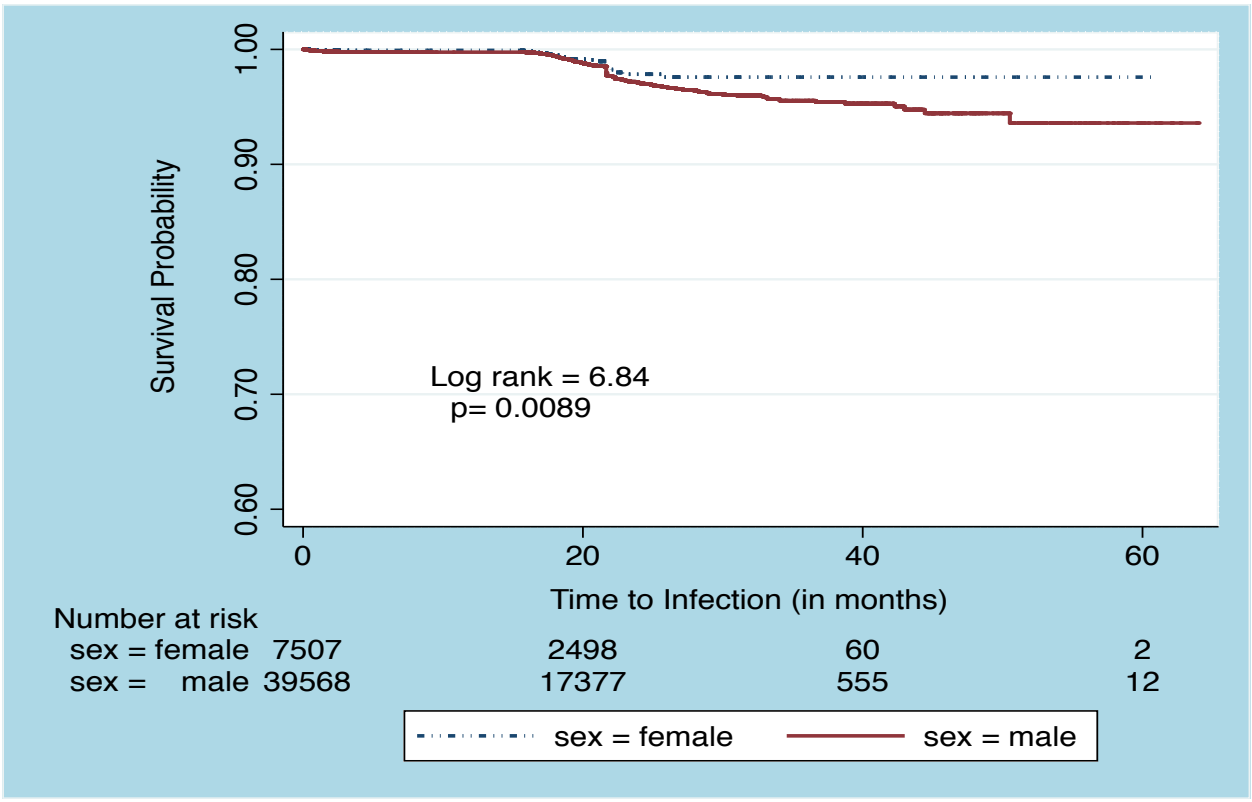


Figure 3.11: Kaplan-Meier survival estimates of HCV, by sex (N= 47,075)

Other explanatory variables were considered for further investigation and a summary of the HCV incidence rates per 10,000 person-years of exposure by level of each potential explanatory variable are as shown in Table 3.7 below. Of the 602 HCV infected persons, the incident rate decreased with increasing age. The incidence rate of HCV was 9.02 per 10,000 and 8.30 per 10,000 for age groups 16–19, and 20–24, respectively. However, the observed number of HCV cases (n= 246) for ages 16–19 was overwhelming significantly different from the expected (n= 83) cases (p<0.00001). HCV incidence also differed by marital status. Donors who were not married developed HCV at a rate of 8 per 10,000 per year while those who were married had an incident rate of 4.56 per 10,000 per year. The difference in the observed number of cases (n= 569) and the expected (n= 508) for unmarried donors was overwhelmingly significant (p<0.00001).

Table 3.7: HCV incidence rates by potential risk factors and confounders (N=47,075)

Characteristic	HCV Cases		PY	*IR (95% CI) per 10,000 pyears	*p* value*
	Observed	Expected			
Overall	**602**		**79.24**	**7.60 (7.01–8.23)**	
Age					
16-19	246	83	27.28	9.02 (7.96–1.0e+01)	**0.000**
20-24	299	326	36.02	8.30 (7.41–9.30)	
25-29	37	86	7.07	5.24 (3.79–7.23)	
30-34	13	45	3.68	3.53 (2.05–6.08)	
35-39	3	24	2.07	1.45 (0.47–4.49)	
40-44	3	16	1.47	2.04 (0.66–6.32)	
45+	1	18	1.64	0.61 (0.09–4.34)	
Sex					
Female	57	78	12.50	4.56 (3.52–5.91)	
Male	545	523	66.73	8.17 (7.51–8.88)	**0.009**
Marital Status					
Married	33	93	8.19	4.03 (2.87–5.67)	
Not Married	569	508	71.05	8.00 (7.38–8.69)	**0.000**
Employment Status					
Employed	591	585	77.46	7.63 (7.04–8.27)	0.265
Unemployed	8	9	1.04	7.67 (3.84–15.35)	
Unknown	3	3	0.73	4.09 (1.32–12.67)	
Region of Residence					
Central Region	220	208	26.12	8.42 (7.38–9.61)	0.294
Northern Region	72	87	12.80	5.62 (4.46–7.09)	
Southern Region	309	304	40.24	7.68 (6.87–8.59)	0.294
Unknown	1	0	0.08	12.52 (1.76–88.85)	
ABO Blood Group					
A	156	133	17.73	8.80 (7.52–10.29)	**0.002**
B	135	124	16.40	8.23 (6.95–9.75)	**0.002**
AB	29	24	3.25	8.93 (6.20–12.85)	**0.002**
O	263	308	40.29	6.53 (5.78–7.37)	
Missing	19	11	1.57	12.13 (7.74–19.02)	**0.002**
Sex with multiple partners without condom use					
No	74	60	7.96	9.30 (7.40–11.68)	0.061
Yes	528	541	71.28	7.41 (6.80–8.07)	
Other TTIs					
None	349	373	49.29	7.08 (6.38–7.86)	
Syphilis Infection	9	5	0.63	14.18 (7.38–27.25)	**0.037**
Malaria Infection	244	223	29.32	8.32 (7.34–9.44)	

* significant at $p<0.05$. All significant values are in bold face; IR= Incidence rate; CI= Confidence intervals

Similarly, donors with blood type A, B and AB developed HCV at a rate of 8.80 per 10,000 per year, 8.23 per 10,000 per year, 8.93 per 10,000 per year, respectively. The difference in the observed number of cases versus the expected cases for blood type A donors (156 observed compared to 133 per 10,000 expected cases), blood type B (135 observed compared to 124 per 10,000 expected cases), and blood type AB (29 observed compared to 24 per 10,000 expected cases) was significant (p=0.0017). Donors infected with syphilis developed HCV at a higher rate (14.18 per 10,000 per year) compared to the rate of HCV in malaria-infected individuals (8.32 per 10,000 per year). The difference in the observed (n=9) and the expected number of cases (n=5) for syphilis-infected donors was significant (p=0.0374).

3.3.4 INCIDENCE OF HBV

A Kaplan Meier (KM) curve was used to summarize the overall survival of blood donors based on their HBV status. Among the 47,075 donors included in the study, 1,238 became infected with HBV. The Kaplan-Meier survival curve as shown below (Figure 3.12) suggests that about the probability of survival was high at about 83% after 60 months of follow-up. Overall, the rate of HBV incidence among blood donors was 15.62 per 10,000 person-years.

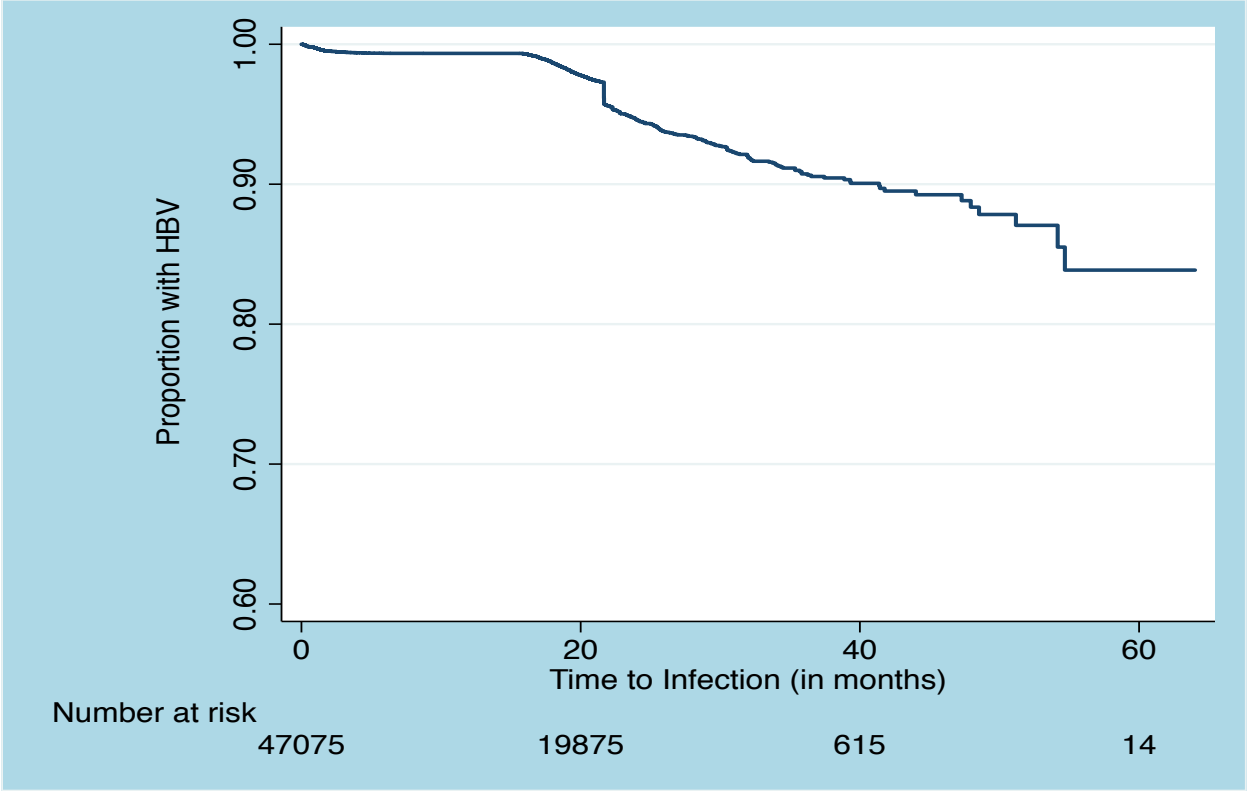


Figure 3.12: Overall Kaplan-Meier survival estimates of HBV (N= 47,075)

Figure 3.13 below demonstrates that there were differences among survivor curves of sex categories with the probability of survival higher for females than for males by the end of follow-up period. The results of the log rank test showed that the survival distributions for the two groups was statistically significantly different, log-rank Chi-square of 6.84 on 1 degree of freedom at p=0.0089. HBV incidence rate was higher than expected among males (1,104 cases compared to the expected number of 1,072).

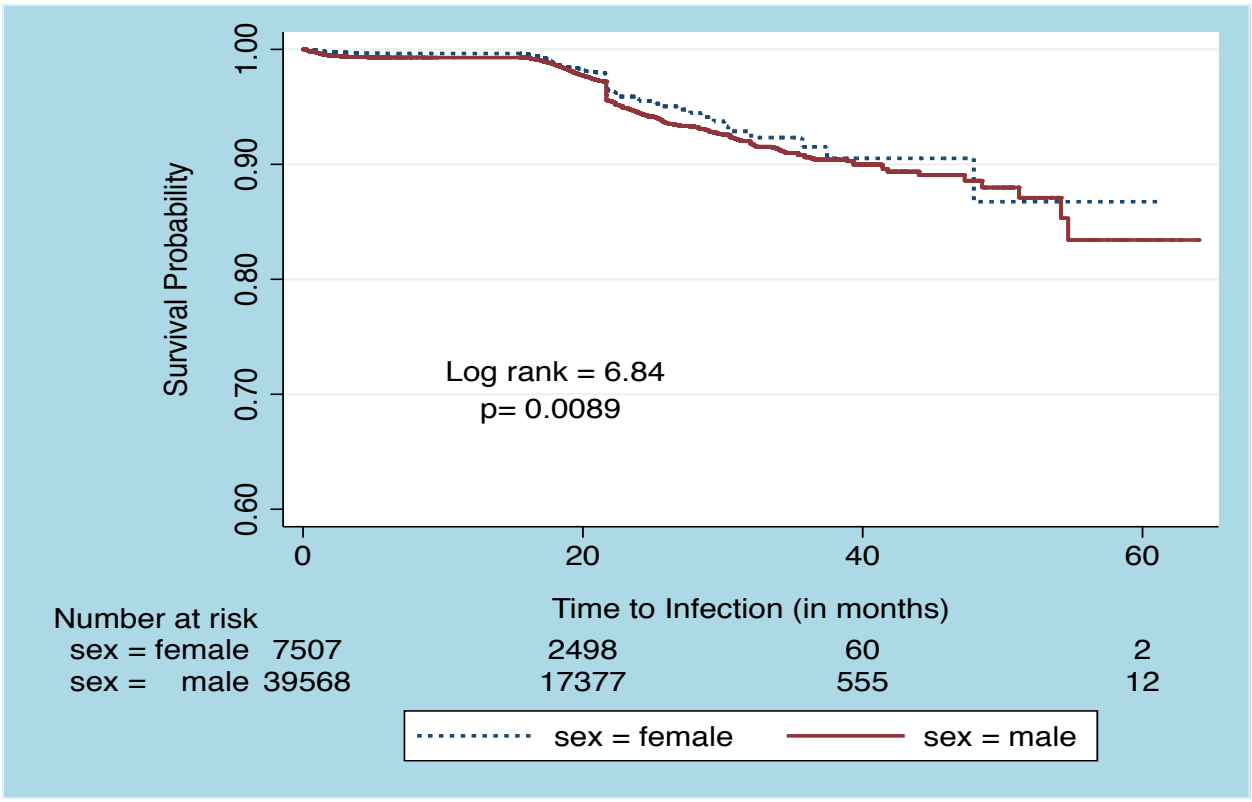


Figure 3.13: Kaplan-Meier survival estimates of HBV, by sex (N= 47,075)

Other explanatory variables were considered for further investigation and a summary of the HBV incidence rates per 10,000 person years of exposure by level of each potential explanatory variable are as shown in Table 3.8 below. Of the 1,238 HBV infected persons, the incidence rate of HBV was 15.76 per 10,000, 17.38 per 10,000, 14.29 per 10,000, and 14.13 per 10,000 for age groups 16–19, 20–24, 25–29, and 30–34, respectively. However, the observed number of HBV cases (n= 430) for ages 16–19 was overwhelming significantly different from the expected (n= 193) cases (p<0.00001).

Table 3.8: HBV incidence rates by potential risk factors and confounders (N=47,075)

Characteristic	HBV Cases		PY	*IR (95% CI) per 10,000 pyears	*p* value*
	Observed	Expected			
Overall	**1,238**		**79.24**	**15.62 (14.78–16.52)**	
Age Group					
16-19	430	193	27.28	15.76 (14.34–17.32)	**0.000**
20-24	626	643	36.02	17.38 (16.07–18.79)	
25-29	10	170	07.07	14.29 (11.76–17.37)	
30-34	52	95	03.68	14.13 (10.76–18.54)	
35-39	16	54	02.07	07.72 (04.73–12.60)	
40-44	6	37	01.47	04.08 (01.83–09.07)	
45+	7	43	01.64	04.28 (02.04–08.97)	
Sex					
Female	134	165	12.50	10.72 (09.05–12.69)	
Male	1,104	1072	66.73	16.54 (15.60–17.55)	**0.009**
Marital Status					
Married	87	198	08.19	10.63 (08.61–13.11)	
Not Married	1,151	1,039	71.05	16.20 (15.29–17.16)	0**.000**
Employment Status					
Employed	1,207	1,204	77.46	15.58 (14.73–16.49)	0.127
Unemployed	23	18	01.04	22.06 (14.66–33.20)	0.127
Unknown	8	14	00.73	10.90 (05.45–21.79)	
Region of Residence					
Central Region	484	427	26.12	18.53 (16.95–20.25)	**0.000**
Northern Region	133	181	12.80	10.39 (08.77–12.31)	
Southern Region	621	627	40.24	15.43 (14.27–16.70)	
Unknown	0	1	00.08	00.00	
ABO Blood Group					
A	290	273	17.73	16.36 (14.57–18.35)	0.389
B	246	256	16.40	15.00 (13.24–16.99)	
AB	47	51	03.25	14.47 (10.87–19.26)	
O	639	633	40.29	15.86 (14.68–17.14)	0.389
Missing	16	23	01.57	10.22 (06.26–16.68)	
Sex with multiple partners without condom use					
No	143	123	07.65	17.97 (15.25–21.16)	0.060
Yes	1,095	1114	71.28	15.36 (14.47–16.30)	
Other TTIs					
None	713	766	49.29	14.47 (13.44–15.57)	
Syphilis Infection	15	10	00.63	23.63 (14.25–39.20)	**0.004**
Malaria Infection	510	460	29.32	17.40 (15.95–18.97)	**0.004**

* significant at $p<0.05$. All significant values are in bold face; IR= Incidence rate; CI= Confidence intervals; PY= Person-years

HBV incidence also differed by marital status. Donors who were not married developed HBV at a rate of 16.20 per 10,000 per year while those who were married had an incident rate of 10.63 per 10,000 per year. The difference in the observed number of cases (n= 1,151) and the expected (n= 1,238) for unmarried donors was overwhelmingly significant (p<0.00001). Similarly, donors residing in the Central region developed HBV at a higher rate of 18.53 per 10,000 per year compared to residents of the Southern regions who developed HBV at a rate of 15.43 per 10,000. The difference in the observed number of cases versus the expected cases for donors in the Central region (484 observed compared to 427 per 10,000 expected cases) was highly significant (p=0.0001). Donors infected with syphilis developed HBV at a higher rate (23.63 per 10,000 per year) compared to the rate of HBV in malaria-infected individuals (17.40 per 10,000 per year). The difference in the observed (n= 15) and the expected number of cases (n= 10) for syphilis-infected donors was significant (p=0.0040).

3.4 COX PROPORTIONAL HAZARDS REGRESSION ANALYSIS

A Cox proportional hazard model was conducted to determine the factors associated with the risk of TTI, HIV, HCV, and HBV. Estimation of Cox proportional hazard model parameters was done using Breslow method approach. The results of fitting the Cox proportional model is as shown (Appendix VI). The variables found to be significantly associated with TTI on univariate analysis at p<0.2 were age group, sex, marital status, occupation, region, ABO blood group, safe sex with multiple partners and other TTIs. A total of 47,075 blood donors with complete data were included in multivariable analysis. As shown (Appendix VII), age group, male, unemployment, Southern region, and malaria infection were significantly associated with the risk of TTI. Males compared to females

(aHR= 1.57; 95% CI 1.36 – 1.70), unemployed donors compared to those employed (aHR=1.31, 95%CI 1.03 – 1.67), donors residing in the Southern region compared to those living in the Central region (aHR=1.08, 95%CI 1.00 – 1.16), and individuals co-infected with malaria (aHR=1.44, 95% CI 1.24 – 1.54) were independently associated with increased risk of disease adjusting for the other variables.

3.4.1 TESTING PROPORTIONAL HAZARD ASSUMPTION

The assumption of proportionality of the Cox proportional hazards regression model was checked using the Grambsch-Therneau test on the Schoenfeld and scaled Schoenfeld residuals. The results (Appendix VIII) showed that the variables marital status, employment status, and region met the proportional hazard assumption with *p*-value> 0.05. Meanwhile, the variables age category, sex, and other TTIs with *p*-value<0.05 did not fulfil the proportional hazard assumption. The results of the global test showed overwhelming evidence ($p<0.00001$) that the proportionality assumption is violated. Based on the results of the Grambsch-Therneau test using Schoenfeld and scaled Schoenfeld residuals, with an overall violation of the assumption of proportional hazards, the factors associated with TTI, HIV, HCV and HBV were subsequently determined using binary logistic regression analysis for reasons explained under section 2.8.4.

3.5 LOGISTIC REGRESSION ANALYSIS

3.5.1 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF TTI

A logistic regression was performed to ascertain the factors associated with TTI (Table 3.9) in a cohort of 47,075 blood donors in Malawi through the period of 2005 to 2015.

Table 3.9: Predictors of incident TTI in blood donors: univariate model (N= 47,075)

Characteristic	Univariate Analysis	
	Unadjusted Odds Ratio (95% CI)	*p* value*
Age Group		
16–19	1.64 (1.05–2.59)	**0.031**
20–24	2.07 (1.32–3.25)	**0.001**
25–29	2.15 (1.36–3.41)	**0.001**
30–34	2.74 (1.71–4.41)	**0.000**
35–39	2.03 (1.21–3.40)	**0.007**
40–44	1.55 (0.87–2.78)	0.140
45+	REF	
Sex		
Female	REF	
Male	1.76 (1.57–1.97)	**0.000**
Marital Status		
Married	1.13 (1.00–1.28)	**0.045**
Not Married	REF	
Employment Status		
Employed	REF	
Unemployed	1.35 (1.05–1.73)	**0.021**
Unknown	1.24 (0.88–1.74)	0.212
Region of Residence		
Central Region	REF	
Northern Region	0.60 (0.52–0.68)	**0.000**
Southern Region	1.06 (0.98–1.14)	0.164
Unknown	0.92 (0.29–2.99)	0.894
ABO Blood Group		
A	REF	
B	0.91 (0.82–1.01)	0.069
AB	0.89 (0.74–1.08)	0.238
O	0.92 (0.84–1.00)	0.052
Missing	0.91 (0.69–1.19)	0.490
Sex with multiple partners without condom use		
No	REF	
Yes	0.85 (0.76–0.95)	**0.004**
Other TTIs		
None	REF	
Syphilis Infection	1.17 (0.79–1.74)	0.441
Malaria Infection	1.01 (0.94–1.09)	0.741

*significant at $p<0.05$. All significant values are in bold face

In the univariate (unadjusted) logistic regression model, age group, sex, marital status, employment status, region of residence, and sex with multiple partners without condom use were significantly associated with the odds of disease. As shown (Table 3.9), the odds of TTI in males were 76% higher (OR= 1.76; 95% CI= 1.57 – 1.97) than the odds of disease in females. When compared to donors aged 45 years and older, individuals in the age groups 16–19, 20–24, 25–29, 30–34, and 35–39 had increased odds of developing TTI (OR= 1.64, 95% CI= 1.04 – 2.58; OR= 2.07, 95% CI= 1.32 – 3.25; OR= 2.15, 95% CI= 1.36 – 3.41, OR= 2.74, 95% CI= 1.71 – 4.41; and OR= 2.03, 95% CI= 1.21 – 3.40, respectively).

The odds of disease in the married population of donors was 1.13 times as likely as the odds of disease among those not married (OR= 1.13; 95% CI= 1.00 – 1.27). Donors unemployed had higher odds of TTI (OR= 1.35, 95% CI= 1.05 – 1.73) compared to those employed. On the other hand, living in the Northern region and practicing safe sex with multiple partners was protective of the disease (OR= 0.60, 95% CI= 0.52 – 0.68; OR= 0.85, 95% CI= 0.76 – 0.95, respectively) compared to living in the Central region and practicing unsafe sex with multiple partners.

3.5.2 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF TTI

In the multivariate logistic regression model, age group, sex, marital status, employment status, region, and sex with multiple partners without condom use, which were significant at $p<0.2$ in the univariate analysis were assessed. All the variables in the chosen model were assessed for possible effect modification. Only factors found to be significantly associated with development of TTI ($p<0.05$) are represented in the final model (Table

3.10). As observed, the odds of TTI were higher in males compared to females (OR= 1.65; 95% CI= 1.46 – 1.84), adjusting for age group, marital status, region, ABO blood group and the interaction between marital status and protected sex with multiple partners. When compared with donors aged 45 years and older, individuals in the age groups 16–19, 20–24, 25–29, 30–34, and 35–39 had increased odds of developing TTI (aOR= 1.82, 95% CI= 1.15 – 2.89; aOR= 2.15, 95% CI= 1.36 – 3.41; aOR= 2.13, 95% CI= 1.33 – 3.39; aOR= 2.69, 95% CI= 1.67 – 4.34; and aOR= 2.00, 95% CI= 1.19 – 3.35, respectively) keeping the other variables constant.

Compared with donors who did not engage in unprotected sex with multiple partners, donors who were married and engaged in unprotected sex with multiple partners had a 2–fold increased risk of TTI adjusting for age group, sex, region and ABO blood group. Donors in the Northern region compared to those in the Central region (OR= 0.65; 95% CI= 0.57 – 0.74) and blood type O individuals compared to type A (OR= 0.91; 95% CI= 0.84 – 1.00) had significantly reduced odds of TTI. There was a statistically significant interaction between marital status and sex with multiple partners without condom use (p< 0.0001).

Table 3.10: Predictors of incident TTI in blood donors: multivariate model* (N= 47,075)

Characteristic	Multivariate Analysis	
	Adjusted Odds Ratio (95% CI)	***p* value***
Age Group		
16–19	1.82 (1.15–2.89)	**0.011**
20–24	2.15 (1.36–3.41)	**0.001**
25–29	2.13 (1.33–3.39)	**0.002**
30–34	2.69 (1.67–4.34)	**0.000**
35–39	2.00 (1.19–3.35)	**0.008**
40–44	1.54 (0.86–2.76)	0.148
45+	REF	
Sex		
Female	REF	
Male	1.65 (1.47–1.85)	**0.000**
Marital Status		
Married	1.92 (1.38–2.68)	**0.000**
Not Married	REF	
Region of Residence		
Central Region	REF	
Northern Region	0.64 (0.57–0.73)	**0.000**
Southern Region	1.08 (1.00–1.16)	**0.049**
Unknown	0.97 (0.30–3.16)	0.963
ABO Blood Group		
A	REF	
B	0.90 (0.81–1.00)	0.062
AB	0.89 (0.74–1.08)	0.228
O	0.91 (0.84–1.00)	**0.039**
Missing	0.96 (0.73–1.27)	0.793
maritalstatus#riskyess		
Married#Yes	0.47 (0.34–0.66)	**0.000**
Not Married#Yes	0.92 (0.82–1.03)	0.163

***** Model adjusted for the variables shown; significant at $p<0.05$. All significant values are in bold face

The final model showed no evidence of misspecification (specification error $p= 0.699$) with an overall good fit (Pearson Chi square $p= 0.9838$; Hosmer-Lemeshow goodness-of-fit $p= 0.3435$). All variables in the final model showed no evidence of multi-collinearity as the VIF and tolerance levels for all significant predictors of TTI were within the norm. Removing the observations with large Pearson and deviance residuals did not significantly impact the

regression model. Employment status, sex with multiple partners without condom use, and other TTIs were not independent risk factors for TTI.

3.5.3 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HIV

No observations were reported for donors whose region of residence was unknown so the region category “unknown” was excluded from the regression analysis. Hence a binary logistic regression was performed to ascertain the factors associated with HIV in cohort of 47,032 blood donors in Malawi through the period of 2005 to 2015 (Table 3.11). In the univariate (unadjusted) logistic regression model, age group, sex, marital status, region of residence, sex with multiple partners without condom use, and other TTIs were significantly associated (p<0.2) with HIV. As shown (Table 3.11), donors aged 16–19 had reduced odds of HIV (OR= 0.55; 95% CI=0.31 – 0.96). The odds of HIV in males were 0.32 times more likely than the odds of disease in females (OR= 1.32; 95% CI= 1.07 – 1.63). Compared with those not married, the odds of disease were 50% more likely in donors who were married (OR=1.50; 95% CI=1.21 – 1.86).

While infection with syphilis was associated with a 2.7–fold increased odd of HIV (OR=2.74; 95% CI=1.64 – 4.56), donors who were infected with malaria were less likely to develop the disease compared to those uninfected (OR=0.79; 95% CI=0.69 – 0.92). The odds of disease were 0.49 times less likely for individuals from the Northern region compared to those from the Central region (OR=0.51; 95% CI=0.39 – 0.67). Similarly, Individuals who had protected sex with multiple partners had reduced odds of HIV compared to those who had unprotected sex with multiple partners (OR= 0.75; 95% CI= 0.61 – 0.93). Additionally, although ABO blood group was not independently associated

with HIV, the odds of disease was 17% less likely in blood type O individuals compared to type A donors (OR= 0.83; 95% CI= 0.61 – 0.93).

Table 3.11: Predictors for incident HIV in blood donors: univariate model (N= 47,032)

Characteristic	Univariate Analysis	
	Unadjusted Odds Ratio (95% CI)	*p* value*
Age Group		
16–19	0.55 (0.76–3.90)	**0.037**
20–24	0.68 (1.06–1.46)	0.183
25–29	0.81 (1.16–1.89)	0.486
30–34	1.01 (1.32–2.55)	0.987
35–39	0.84 (0.94–2.47)	0.627
40–44	1.46 (1.64–4.33)	0.307
45+	REF	
Sex		
Female	REF	
Male	1.32 (1.07–1.63)	**0.008**
Marital Status		
Married	1.50 (1.21–1.86)	**0.000**
Not Married	REF	
Employment Status		
Employed	REF	
Unemployed	1.22 (0.73–2.05)	0.449
Unknown	1.25 (0.64–2.43)	0.505
Region of Residence		
Central Region	REF	
Northern Region	0.51 (0.39–0.67)	**0.000**
Southern Region	0.91 (0.79–1.06)	0.229
Unknown	1 (empty)	
ABO Blood Group		
A	REF	
B	0.92 (0.75–1.13)	0.447
AB	0.96 (0.67–1.38)	0.840
O	0.83 (0.70–0.98)	**0.028**
Missing	1.00 (0.60–1.67)	0.988
Sex with multiple partners without condom use		
No	REF	
Yes	0.75 (0.61–0.93)	**0.008**
Other TTIs		
None	REF	
Syphilis Infection	2.74 (1.64–4.56)	**0.000**
Malaria Infection	0.80 (0.69–0.92)	**0.002**

* significant at $p<0.05$. All significant values are in bold face

3.5.4 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HIV

In the multivariate logistic regression model, age group, sex, marital status, occupation, region, and sex with multiple partners without condom use, which were significant at $p<0.2$ in the univariate analysis were assessed. All the variables in the chosen model were assessed for possible effect modification. Only factors found to be significantly associated with development of HIV ($p<0.05$) are represented in the final model (Table 3.12). Adjusting the data to account for differences between the infected donors, it was observed that the independent predictors of were male sex (associated with a 1.25–fold increased odds of HIV; 95% CI= 1.02 – 1.54), married (associated with 1.49–fold increased odds of HIV; 95% CI= 1.21 – 1.85), and syphilis co-infection (2.62–fold increased odds of HIV; 95% CI= 1.57 – 4.38). Keeping the other variables constant, living in the Northern region compared to living in the Central region (aOR= 0.58, 95% CI= 0.44 – 0.76), blood type O (aOR= 0.83, 95% CI= 0.70 – 0.99), engaging in safe sex (aOR= 0.78, 95% CI= 0.63 – 0.96), and infection with malaria (aOR= 0.85, 95% CI= 0.73 – 0.99), conferred protection against HIV. Age group and employment status were not predictors of HIV. No possible interaction effect between the variables was observed.

The final logistic regression model with sex, marital status, region, ABO blood group type O, sex with multiple partners without condom use, and other TTIs showed no evidence of misspecification (specification error $p= 0.944$) with an overall good fit (Pearson Chi square $p= 0.9110$; Hosmer-Lemeshow goodness-of-fit $p= 0.8998$). All variables in the final model showed no evidence of multicollinearity as the VIF and tolerance levels for all significant predictors of HIV were within the norm. Removing the observations with large Pearson and deviance residuals did not significantly impact the regression model.

Table 3.12: Predictors for incident HIV in blood donors: multivariate model* (N= 47,032)

Characteristic	Multivariate Analysis	
	Adjusted Odds Ratio (95% CI)	*p* value*
Sex		
Female	REF	
Male	1.25 (1.02–1.54)	**0.035**
Marital Status		
Married	1.49 (1.21–1.85)	**0.000**
Not Married	REF	
Region of Residence		
Central Region	REF	
Northern Region	0.58 (0.44–0.76)	**0.000**
Southern Region	0.96 (0.82–1.11)	0.566
Unknown	1 (empty)	
ABO Blood Group		
A	REF	
B	0.93 (0.76–1.14)	0.462
AB	0.97 (0.68–1.39)	0.872
O	0.83 (0.70–0.99)	**0.034**
Missing	1.03 (0.62–1.73)	0.897
Sex with multiple partners without condom use		
No	REF	
Yes	0.78 (0.63–0.96)	**0.020**
Other TTIs		
None	REF	
Syphilis Infection	2.62 (1.57–4.38)	**0.000**
Malaria Infection	0.85 (0.73–0.99)	**0.031**

* Model adjusted for the variables shown; significant at $p<0.05$. All significant values are in bold face

3.5.5 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HCV

A binary logistic regression was performed to ascertain the factors associated with HCV in cohort of 47,075 blood donors in Malawi through the period of 2005 to 2015. In the univariate logistic regression model, age group, sex, marital status, region of residence, ABO blood group, sex with multiple partners without condom use, and other TTIs were significantly associated with the risk of HCV at $p<0.2$. As shown (Table 3.13), donors aged 16–19 had increased odds of HCV (OR= 7.24; 95% CI=1.01 – 51.73). The odds of HCV in

males were 0.83 times more likely than the odds of disease in females (OR= 1.83; 95% CI= 1.39 – 2.40).

Table 3.13: Predictors of incident HCV in blood donors: univariate model (N= 47,075)

Characteristic	Univariate Analysis	
	Unadjusted Odds Ratio (95% CI)	*p* value*
Age Group		
16-19	7.24 (1.01–51.73)	**0.048**
20-24	7.06 (0. 99–50.36)	0.051
25-29	4.36 (0.60–31.82)	0.183
30-34	3.99 (0.52–30.61)	0.600
35-39	1.83 (0.19–07.66)	0.320
40-44	3.16 (0.33–30.44)	
50+	REF	
Sex		
Female	REF	
Male	1.83 (1.39–2.40)	**0.000**
Marital Status		
Married	0.63 (0.44–0.90)	**0.011**
Not Married	REF	
Employment Status		
Employed	REF	
Unemployed	0.87 (0.43–1.75)	0.696
Unknown	0.55 (0.18–1.73)	0.310
Region of Residence		
Central Region	REF	
Northern Region	0.75 (0.57–0.98)	**0.035**
Southern Region	0.86 (0.72–1.02)	0.089
Unknown	1.64 (0.22–11.95)	0.627
ABO Blood Group		
A	REF	
B	0.92 (0.73–1.16)	0.498
AB	1.02 (0.68–1.52)	0.936
O	0.74 (0.60–0.90)	**0.003**
Missing	1.56 (0.96–2.53)	0.070
Sex with multiple partners without condom use		
No	REF	
Yes	0.79 (0.62–1.00)	0.054
Other TTIs		
None	REF	
Syphilis Infection	2.17 (1.11–4.24)	**0.024**
Malaria Infection	0.92 (0.78–1.09)	0.347

*significant at $p<0.05$. All significant values are in bold face

Compared with those not married, the odds of disease were 37% less likely in donors who were married (OR=0.63; 95% CI=0.44 – 0.90). Similarly, the odds of disease were 0.75 times as likely for individuals from the Northern region as the odds of disease for those from the Central region (OR=0.75; 95% CI=0.57 – 0.98). Additionally, the odds of disease were 26% less likely in blood type O individuals compared to type A donors (OR= 0.74; 95% CI= 0.60 – 0.90). Infection with syphilis was associated with a 2–fold increased odd of HCV (OR=2.17; 95% CI=1.11 – 4.24) compared to those uninfected.

3.5.6 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HCV

In the multivariate logistic regression model, age group, sex, marital status, region of residence, ABO blood group, sex with multiple partners without condom use, and other TTIs, which were significant (p<0.2) in the univariate model were assessed. All the variables in the chosen model were assessed for possible effect modification. Only factors found to be significantly associated with incident HCV (p<0.05) are represented in the final model (Table 3.14). Adjusting the data to account for differences between the infected donors, it was observed that the independent predictors of incident HCV were age groups 16–19 (associated with a 7.91–fold increased odds of HCV; 95% CI= 1.11 – 56.54) and 20–24 (associated with a 7.22–fold increased odds of HCV; 95% CI= 1.01 – 51.50), male sex (associated with a 1.90–fold increased odds of HCV; 95% CI= 1.44 – 2.51), and syphilis infection (2.03–fold increased odds of HCV; 95% CI= 1.04 – 3.98). Keeping the other variables constant, living in the Northern region compared to living in the Central region (aOR= 0.74, 95% CI= 0.56 – 0.98), and blood type O compared to type A (aOR= 0.75, 95% CI= 0.61 – 0.91) conferred protection against HCV. Marital status, employment

status and sex with multiple partners without condom use were not predictors of HCV. No possible interaction effect between the variables was observed.

Table 3.14: Predictors of incident HCV in blood donors: multivariate model* (N= 47,075)

Characteristic	Multivariate Analysis	
	Adjusted Odds Ratio (95% CI)	*p* value*
Age Group		
16-19	7.91 (1.11–56.54)	**0.039**
20-24	7.22 (1.01–51.50)	**0.049**
25-29	4.34 (0.59–31.74)	0.148
30-34	3.99 (0.52–30.57)	0.183
35-39	1.85 (0.19–17.84)	0.595
40-44	3.14 (0.33–30.34)	0.322
45+	REF	
Sex		
Female	REF	
Male	1.90 (1.44–02.51)	**0.000**
Region of Residence		
Central Region	REF	
Northern Region	0.74 (0.56–00.98)	**0.036**
Southern Region	0.86 (0.72–01.03)	0.093
Unknown	1.64 (0.22–12.00)	0.629
ABO Blood Group		
A	REF	
B	0.93 (0.73–1.17)	0.521
AB	1.02 (0.68–1.52)	0.938
O	0.75 (0.61–0.91)	**0.004**
Missing	1.56 (0.96–2.53)	0.070
Other TTIs		
None	REF	
Syphilis Infection	2.03 (1.04–3.98)	**0.039**
Malaria Infection	1.01 (0.85–1.19)	0.947

***** Model adjusted for the variables shown; significant at $p<0.05$. All significant values are in bold face

The final model showed no evidence of misspecification (specification error $p= 0.630$) with an overall good fit (Pearson Chi square $p= 0.9991$; Hosmer-Lemeshow goodness-of-fit $p= 0.9781$). All variables in the final model showed no evidence of multi-collinearity as the VIF and tolerance levels for all significant predictors of HCV were within the norm. Removing

observations with large Pearson and deviance residuals as well as possible influential points did not significantly impact the regression model.

3.5.7 UNIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HBV

No observations were reported for donors whose region of residence was unknown so the region category “unknown” was excluded from the regression analysis. Hence a binary logistic regression was performed to ascertain the factors associated with HBV in cohort of 47,032 blood donors in Malawi through the period of 2005 to 2015 (Table 3.15). In the unadjusted logistic regression model, age group, sex, marital status, region of residence, sex with multiple partners without condom use, and other TTIs were significantly associated with the odds of HBV infection. As shown (Table 3.15) donors aged 30–34 were more likely to become infected with HBV (OR= 2.30; 95% CI= 1.04–5.09) compared to donors aged 45 and above. The odds of HBV in males were 0.58 times more likely (OR= 1.58; 95% CI= 1.32–1.89) than the odds of disease in females. Similarly, the odds of HBV for individuals co-infected with syphilis were 78% more likely than the odds of HBV in those uninfected (OR=1.78; 95% CI=1.05–3.01). On the other hand, donors living in the Northern and Southern regions compared to those living in the Central region were less likely to develop HBV (OR= 0.62, 95% CI= 0.51 – 0.76; OR= 0.78; 95% CI= 0.69 – 0.88).

Table 3.15: Predictors of incident HBV in blood donors: univariate model (N= 47,032)

Characteristic	Univariate Analysis	
	Unadjusted Odds Ratio (95% CI)	*p*-value*
Age Group		
16-19	1.80 (0.85–3.81)	0.127
20-24	2.11 (1.00–4.46)	0.051
25-29	1.70 (0.78–3.67)	0.179
30-34	2.30 (1.04–5.09)	**0.040**
35-39	1.39 (0.57–3.41)	0.468
40-44	0.89 (0.30–2.67)	0.837
45+	REF	
Sex		
Female	REF	
Male	1.58 (1.32–1.89)	**0.000**
Marital Status		
Married	0.82 (0.66–1.03)	0.086
Not Married	REF	
Employment Status		
Employed	REF	
Unemployed	1.23 (0.81–1.88)	0.325
Unknown	0.72 (0.36–1.46)	0.368
Region of Residence		
Central Region	REF	
Northern Region	0.62 (0.51–0.76)	**0.000**
Southern Region	0.78 (0.69–0.88)	**0.000**
Unknown	1 (empty)	
ABO Blood Group		
A	REF	
B	0.90 (0.76–1.07)	0.242
AB	0.88 (0.65–1.21)	0.434
O	0.97 (0.84–1.11)	0.634
Missing	0.69 (0.42–1.16)	0.161
Sex with multiple partners without condom use		
No	REF	
Yes	0.84 (0.71–1.01)	0.057
Other TTIs		
None	REF	
Syphilis Infection	1.78 (1.05–3.01)	**0.031**
Malaria Infection	0.95 (0.84–1.06)	0.339

* significant at $p<0.05$. All significant values are in bold face

3.5.8 MULTIVARIATE LOGISTIC REGRESSION MODEL FOR RISK FACTORS OF HBV

In the multivariate logistic regression model, age group, sex, marital status, region of residence, sex with multiple partners without condom use, and other TTIs, which were significant (p<0.2) in the univariate model were assessed. All the variables in the chosen model were assessed for possible effect modification. The possible effect of age group on sex, marital status, region, sex with multiple partners without condom use, and other TTIs was explored. Also, the possible effect of sex on marital status, region, sex with multiple partners without condom use, and other TTIs was investigated. Additionally, the possible interaction effect of marital status on region, sex with multiple partners without condom use, and other TTIs was explored. Furthermore, the possible effect of region on sex with multiple partners without condom use, and other TTIs was explored. Lastly, the interaction effect of sex with multiple partners without condom use on other TTIs was accessed. Only factors found to be significantly associated with incident HBV (p<0.05) are represented in the final model (Table 3.16).

Adjusting the data to account for differences between the infected donors, it was observed that the independent predictors of HBV were age groups 20–24 (associated with a 2.14–fold increased odds of incident HBV; 95% CI= 1.01 – 4.53) and 30–34 (associated with a 2.26–fold increased odds of incident HBV; 95% CI= 1.02 – 5.01), male sex (associated with a 1.53–fold increased odds of incident HBV; 95% CI= 1.27 – 1.84) and syphilis infection (1.71–fold increased odds of incident HBV; 95% CI= 1.01 – 2.89). Keeping the other variables constant, living in the Northern and Southern regions compared to living in the Central region conferred protection against HBV (aOR= 0.64, 95% CI= 0.53 – 0.79; aOR= 0.79; 95% CI= 0.70 – 0.89, respectively). Employment status, ABO blood group and

protected sex with multiple partners were not predictors of incident HBV. No possible interaction effect between the variables was observed.

Table 3.16: Predictors of incident HBV in blood donors: multivariate model* (N= 47,032)

Characteristic	Multivariate Analysis	
	Adjusted Odds Ratio (95% CI)	*p* value*
Age Group		
16-19	1.94 (0.91–4.12)	0.084
20-24	2.14 (1.01–4.53)	**0.047**
25-29	1.67 (0.77–3.60)	0.196
30-34	2.26 (1.02–5.01)	**0.045**
35-39	1.38 (0.56–3.38)	0.481
40-44	0.88 (0.29–2.64)	0.821
45+	REF	
Sex		
Female	REF	
Male	1.53 (1.27–1.84)	**0.000**
Region of Residence		
Central Region	REF	
Northern Region	0.64 (0.53–0.79)	**0.000**
Southern Region	0.79 (0.70–0.89)	**0.000**
Unknown	1 (empty)	
Other TTIs		
None	REF	
Syphilis Infection	1.71 (1.01–2.89)	**0.045**
Malaria Infection	1.02 (0.90–1.15)	0.759

* Model adjusted for the variables shown; significant at $p<0.05$. All significant values are in bold face

The final model showed no evidence of misspecification (specification error $p= 0.612$) with an overall good fit (Pearson Chi square p= 0.0869; Hosmer-Lemeshow goodness-of-fit $p= 0.7458$). No evidence of multi-collinearity was observed as the VIF and tolerance levels for all significant predictors of HBV were within the normal range. Removing observations with large Pearson and deviance residuals as well as possible influential points did not significantly improve the model fit.

CHAPTER FOUR: DISCUSSIONS, CONCLUSIONS AND RECOMMENDATIONS

4.1 INTRODUCTION

Blood safety and availability continues to be of serious concern in Malawi due to the increased frequency of blood–borne viral and other communicable diseases like HIV, HBV, HCV and syphilis. Although epidemiological data published in recent years suggest that significant progress has been made in countries where WHO national surveillance protocols have been implemented, the risk of TTIs remains a major crisis in Malawi. Therefore, the continued monitoring of incidence trends of TTIs markers in the donor population as a valuable pointer for evaluating the effectives of present intervention strategies and impact on blood supply and safe transfusions is vital. This chapter summarizes the findings of this study in line with the main objectives to determine the incidence and factors associated with incident transfusion transmissible HIV, HCV and HBV infections in blood donors in Malawi. Data for predetermined potential risk factors were recorded at baseline from 47,075 donors recruited throughout the study period who met all the inclusion criteria. The study limitations and strengths are also discussed.

4.2 SUMMARY OF MAIN FINDINGS

The overall incidence rate of TTI in the blood donors was 43 per 10,000 with a higher incident rate at 15 per 10,000 in HBV-infected donors followed by HIV with 10 per 10,000 and HCV with 7 per 10,000. The observed TTI incidence was significantly higher than expected among donors aged 16–19 (IR= 40 per 10,000), males (IR= 46 per 10,000),

unmarried donors (IR= 43 per 10,000), unemployed (IR= 65 per 10,000), Southern region (IR= 49 per 10,000), unprotected sex with multiple partners (IR= 49 per 10,000), and malaria-positive donors (IR= 50 per 10,000). Similarly, the observed HIV, HBV and HCV incidence was higher than expected among donors aged 16–19, donors not married, and co-infected with syphilis.

Age groups 16–19, 20–24, 25–29, 30–34, 35–39, male sex, and married status were found to be significantly associated with TTI incidence after adjusting for other factors. Employment status, ABO blood group, sex with multiple partners without condom use, and other TTIs on the other hand, were not found to be significantly associated with TTI incidence. Age group 20–24 was commonly significantly associated with incident HCV and HBV in the multivariate models. Adjusting for the other variables, male sex and syphilis co-infection remained common risk factors for incident HIV, HCV and HBV infections. Keeping sex, region of residence, ABO blood group, sex with multiple partners without condom use and other TTIs constant, married status was an overwhelmingly significant risk factor for HIV.

Safe and adequate blood supply is essential in improving health care. However, the risk of TTIs remains of serious concern toward the safety of blood transfusion programs in countries with limited resources (48, 49). Thus, current data on the incidence of TTIs among blood donors, especially in settings with a high burden like Malawi, would advise policy makers to formulate strategies to plan, implement, and evaluate routines. To our knowledge, this study is first to comprehensively look into the incidence and risk factors of TTIs in blood donors in Malawi. In this study, the majority of blood donors were males, which is consistent with the findings of previous studies in Africa (50-52). The male

majority may be justified by the general belief that men are healthier than women, and thus are better candidates for blood donation (53). According to Tagny and Owusu-Ofori (4), another plausible reason for this disproportionate male-to-female ratio can be, in part, some physiological status of women such as menstruation, pregnancy and breast-feeding, which occasionally, may prohibit the female gender from donating blood.

The incidence of TTI markers in the donor population in the assessed age groups was different. This result is in line with findings from other studies (26, 54). The frequency of TTI markers was substantially higher in the age groups 16–19, 20–24, 25–29, 30–34, and 35–39. Donors aged 40 and above had the lowest TTI frequency. The findings indicate that youths constitute a major population of blood donors. This might be explained by the fact that in a developing country like Malawi, the young represent the biggest fraction of the population compared to the older age. Looking at the age structure of the country, 16–24 and 25–54 years represent 20.58% and 27.41% of the population, respectively (55). These age groups fulfil the selection criteria for blood donation compared to the older age groups. Also, behavioural characteristics unique to these age categories may explain the high incidence of TTI in these age groups.

Regional disparity in TTI incidence was also observed; donors from the Central and Southern regions had higher incidence compared to the northerners. This may be attributed to cultural norms such as initiation ceremonies and rituals that have been associated with a high rate of unprotected sex, multiple and concurrent sex partners, and being married, all which have been shown to be potential drives for HIV infection (41, 56). Also, regional variations in the proportion of people living in informal settlements in these

regions were high, which could also contribute to a high rate of unprotected sex with multiple partners and a subsequent increase in incident TTI.

The frequency of transfusion transmissible HIV, HCV and HBV markers in this study was also found to be significantly associated with sex with a higher incidence reported in male donors. In a study by Mohammed and Bekele (57) conducted at Eastern Ethiopia, a similar association was observed (11.6% males compared to 3.8% females). In their study, Ataro et al. (52) noted a higher TTI prevalence among male donors (7.46%) compared to a 4.76% in female donors. According to them, “this might be due to some risk behaviours such as outside socialization, multiple sex relationships frequently observed in males, and fewer males donating blood, which translates to fewer female screening compared to males” (52). Siraj et al. (54) attributes this unbalanced male-to-female incident TTI ratio to behavioural, religious and socio-cultural drivers of high-risk sexual behaviour that are typically found in conventional societies. Another possible explanation as proposed by Tenthani et al. (58) is that in Malawi, females are better diagnosed due to antenatal care. As a result, more female blood donors may be conscious of their seronegative status for some of the TTIs.

The most dominant marker for TTI through the study duration was HBV (2.63%). The reported incidence is comparable to what was reported in Eritrea (54) but lower than results obtained from other studies (59, 60). In SSA, HBV among blood donors in high and this has been attributed to the generally high prevalence (8%) and endemicity of this pathogen in the region (61). These results support the fact that HBV in the general population is high (62). Similarly remarkably is the finding that incident HBV exhibited a statistically significant association with age groups 20–24 and 30–34, male sex, region of residence and syphilis infection. Behavioural, cultural and socio-economic disparities

associated with belonging to these groupings may explain the detected variation. In particular, the significant association of incident HBV and HCV in donors aged 20–24 years may be linked to early sexual activity, early marriage, among others in this age group.

According to our findings, the overall incidence of HIV among blood donors was 1.74%. The proportion is much lower compared to other studies conducted elsewhere in Africa (52, 59, 63-65). However, it was higher than the 1.37% obtained in Nigeria (66), 0.014 % in Libya (67), 0.6% in Eritrea (54), and 0.00% Egypt (68).

Overall, HCV incidence was 1.28%, which was higher than findings from previous findings within Southern Africa (69, 70). Although our finding compares favourably to a study by in Biadgo et al. (49) in North West Ethiopia, the incidence is lower when compared to the observed 1.5% in Tanzania (71), 0.32% in Ethiopia (72), 4.8% in Cameroon (51), and 3.4% in Sudan (73). This result agrees with the common knowledge that HCV poses less risk to blood transfusion in Southern parts of Africa by virtue of its low prevalence (61).

4.4. LIMITATIONS OF THE STUDY

A few limitations are noteworthy; firstly, this study was retrospective in design and therefore the analysis relied solely on the data collection, recording, and the screening systems used by the blood bank. Secondly, because it's retrospective in nature, a range of potential co-morbidities that might be associated with TTIs was not evaluated. The use of serological tests for HCV screening as opposed to nucleic acid testing (NAT) may have accounted for the low incidence in the population due to possible false negative results,

which is mostly common in immunocompromised individuals, and the presence of a 45–68 window period. Therefore, this result may have underestimated the frequency of TTIs among donors in the donor population (54, 74).

4.5. STRENGTHS OF THE STUDY

Despite the limitations, the sample size used for this study was large enough providing enough statistical power enabling us to highlight the incidence and risk factors of major TTIs in the Malawian donor population.

4.6. CONCLUSION

On the basis of this report, the following key findings are concluded:

1. The overall incidence of TTIs in the Malawian blood donor population was low. Nonetheless, the risk of TTIs remains a problem.
2. The incidence of TTI was more frequent in the younger age groups who constitute the majority of blood donors. An increased trend in the rate of TTI was observed with increasing age up to age 29. HCV incidence on the other hand decreased with increasing age.
3. The most common TTIs was HBV followed by HIV and HCV.
4. The risk of TTI was less likely for donors residing in the Northern region who constituted a minority of the donor population.
5. The risk factors for TTIs were age, particularly in the younger age groups; male sex and married status.

6. Syphilis was a common risk factor for HIV, HCV and HBV

4.7. RECOMMENDATIONS

In the light of the above findings, the following key recommendations are made:

1. Implement more stringent donor selection and blood screening procedures to improve the safety of blood supply.
2. Expand the donor age. Majority of blood donors in Malawi are young men between the ages 16–25 years. This may in part, explain why the country struggles to meet its annual blood need. Therefore, the MBTS should institute mechanisms to widen the donor age group by massively recruiting more people of older ages.
3. Recruit more females, unmarried people, and more donors from the Northern region for blood donation to ensure the safety of donated blood and increase blood volume supply thereby combating the ongoing crisis of blood shortage.
4. Continue monitoring the incidence of TTI markers in the donor population through use of more contextualised screening questionnaires and the use of NAT in addition to serological tests.
5. Future research can be done to estimate the volume of blood lost due to the incidence of TTIs in the donor population.

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APPENDICES

APPENDIX I: Plagiarism Declaration Form

WITS School of Public Health

Plagiarism declaration for written work: Master of Science in Epidemiology

I **DR CONSTANCE N. WOSE KINGE** (Student number: **1918187**) am a postgraduate student registered

for degree / Programme **MSC EPIDEMIOLOGY (EPIDEMIOLOGY & BIOSTATISTICS)** in the Wits School of Public Health.

I am submitting my written work for assessment for the module:

RESEARCH REPORT COMH 7177 (course name and code).

I hereby declare the following:

- I am aware that plagiarism is the use of someone else's work without their permission and/or without acknowledging the original source).
- I am aware that plagiarism is wrong.
- I confirm that the work submitted for assessment for the above course is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature: _____ Date: **17/10/2019**

APPENDIX II: MBTS Data Dictionary

Variable name	Variable label	Variable values
Donorno	donor number	
Packno	pack number	
olddonorno	old donor number	
Sex	Sex	0=female, 1=male
marital	marital status	0=single, 1=married, 2=separated, 3=widowed, 4= divorced
occupation	Occupation	
City	City	
noofdonations	number of donations	
Status	status of donor	0=A (active), 1=PD(permanent deferral), 2=TD(temporal deferral)
location	location of donation	
dateofbirth	date of birth of donor	
lastdonationdate	last donation date	
ttitestdate	tti test date	
abotestdate	blood group testdate	
Rh	rhesus factor	0=negative, 1=positive
Hiv	hiv status	0=negative, 1=positive, 2=discordant
hivinitest	hiv initial test result	0=negative, 1=positive, 2=indeterminate
hivaddtest	hiv additional test result	0=negative, 1=positive
hbv	hbv	0=negative, 1=positive
hcv	hcv	0=negative, 1=positive
syphilis	Syphilis	0=negative, 1=positive
pms	Pms	0=negative, 1=positive
abo	blood group	0=A, 1=B, 2=AB, 3=O
pcough	Pcough	0=no, 1=yes
anaemia	Anaemia	0=no, 1=yes
diabetes	Diabetes	0=no, 1=yes
weightloss	weight loss	0=no, 1=yes
sglands	sglands	0=no, 1=yes
nsweat	night sweat	0=no, 1=yes
Bp	Bp	0=no, 1=yes
Tb	Tb	0=no, 1=yes
heartdisease	heart disease	0=no, 1=yes
nosebleed	nose bleed	0=no, 1=yes
dizziness	Dizziness	0=no, 1=yes
kdisease	Kdisease	0=no, 1=yes
skinrashes	Skinrashes	0=no, 1=yes
sleepingsickness	sleeping sickness	0=no, 1=yes
epilepsy	epilepsy	0=no, 1=yes
std	Std	0=no, 1=yes
unexplainedfevers	unexplained fevers	0=no, 1=yes
diarrhoea	diarrhea	0=no, 1=yes
cancer	cancer	0=no, 1=yes
stomachulcers	stomach ulcers	0=no, 1=yes
jaundice	Jaundice	0=no, 1=yes
capsules	jaundice	0=no, 1=yes
aspirin	aspirin	0=no, 1=yes
vaccination	Vaccination	0=no, 1=yes
other	Other	0=no, 1=yes
surgical	Surgical	0=no, 1=yes
shingles	Shingles	0=no, 1=yes
malaria	Malaria	0=no, 1=yes
asthma	Asthma	0=no, 1=yes
skinpiercing	skin piercing	0=no, 1=yes
tattoos	Tattoos	0=no, 1=yes

bloodtransfunsion	blood transfusion	0=no, 1=yes
injection	Injection	0=no, 1=yes
acunctures	Acunctures	0=no, 1=yes
risk	Risk	0=no, 1=yes
pregnant	Pregnant	0=no, 1=yes
breastfeeding	breastfeeding	0=no, 1=yes
menstrualproblems	menstrualproblems	0=no, 1=yes
district	District	
school_nam	School name	
x_coordina	X- coordinate	
y_coordina	y_coordinate	
longitude	Longitude	
latitude	longitude	
districtcode	district code	
facilitycode	facility code	
facilityname	facility name	
zone	zone	
factype	facility type	
mga	managing authority	
Ftype	facility type	

APPENDIX III: Permission to use the MBTS Dataset

MALAWI BLOOD TRANSFUSION SERVICE

P.O. Box 2681
BLANTYRE
MALAWI
Tel: +265 (0) 1 870 522 / 699; 1 874 666
Fax: +265 (0) 1 870 770
E-mail: mbtsinfo@mbtsmalawi.com

LILONGWE BRANCH
P.O. Box 1699
LILONGWE
Tel: +265 (0) 1 753 828
Fax: +265 (0) 1 753 835
Web: www.mbtsmalawi.com

MZUZU BRANCH
P.O. Box 1242
MZUZU
Tel: +265 (0) 1 310 702 / 677
Fax: +265 (0) 1 310 680

BALAKA SATELLITE DEPOT
P.O. Box 56
BALAKA
Tel: +265 (0) 1 522 001 / 637
Fax: +265 (0) 1 552 668

Our ref: mbts/admin/ns/11/18

November 19, 2018

Prof. Clement Penny
Chairperson: Human Research Ethics Committee (Medical)
University of the Witwatersrand
29 Princess of Wales Terrace
Parktown
Johannesburg, 2193
South Africa

Dear Prof. Penny

RE: LETTER OF SUPPORT – ETHICS APPLICATION FOR M.SC. DISSERTATION TITLED "INCIDENCE AND DETERMINANTS OF TRANSFUSION-TRASNMISSIBLE INFECTIONS IN VOLUNTARY BLOOD DONORS IN MALAWI, 2005-2015"

This letter serves to support the ethics application to the University of the Witwatersrand, Human Research Ethics Committee (Medical) for the above-mentioned Masters dissertation by Constance N. Wose Kinge (Student Number 1918187).

Her research project is secondary analysis of data obtained from the Malawi Blood Transfusion Service (MBTS), which is routinely collected program data. Therefore, no informed consent, data collection, further laboratory tests will be required on her part with no risks or benefits to the donors. Permission to use the MBTS data has been granted and our members of staff, Dr. S Njolomole and Dr. M'baya are co-investigators of the study.

Her research seeks to determine the incidence and associated factors of transfusion-transmissible HIV, hepatitis C and B viral infections in blood donors in Malawi, and will be conducted at the School of Public Health, University of the Witwatersrand.

If you have any questions, please don't hesitate to contact the office at +265 88 820 5342 or email mbayab@mbtsmalawi.com

Yours Sincerely

Mrs N. Nsamala
CHIEF EXECUTIVE OFFICER

All correspondence to be addressed to the Chief Executive Officer, P.O. Box 2681, Blantyre

APPENDIX IV: Wits HREC Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Constance Wose Kinge et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M181008

NAME: (Principal Investigator)	Constance Wose Kinge et al
DEPARTMENT:	School of Public Health
PROJECT TITLE:	Incidence and Determinants of Transfusion Transmissible Infections in Voluntary Blood Donors in Malawi, 2005-2015
DATE CONSIDERED:	26/10/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Charles Chasela
APPROVED BY:	Doctor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	10/01/2019

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

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **October** and will therefore be due in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

07/02/2019
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX VI: Approval of Research Title

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

27 September 2018
Person No: 1918187
PAG

Dr CN Wose Kinge
G04 Knockando Residence
21 Rock Ridge Road
Parktown
2193
South Africa

Dear Dr Constance Wose Kinge

Master of Science in Epidemiology: Approval of Title

We have pleasure in advising that your proposal entitled *Incidence and Determinants of Transfusion-Transmissible Infections in Voluntary Blood Donors in Malawi, 2005 - 2015* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX VI: Cox proportional regression model for factors associated with TTI: univariate model (N=47,075)

Characteristic	Univariate Analysis	
	Unadjusted Hazard Ratio (95% CI)	***p*-value**
Age Group		
16-19	REF	
20-24	0.28 (0.25-0.31)	**0.000**
25-29	0.11 (0.09-0.13)	**0.000**
30-34	0.03 (0.02-0.04)	**0.000**
35-39	0.01 (0.00-0.01)	**0.000**
40-44	0.00 (0.00-0.01)	**0.000**
45-49	0.00 (0.00-0.00)	**0.000**
45+	0.00 (0.00-0.00)	**0.000**
Sex		
Female	REF	
Male	1.37 (1.23-1.53)	**0.000**
Marital Status		
Married	0.45 (0.47-0.51)	**0.000**
Others	REF	
Employment Status		
Employed	REF	
Unemployed	1.33 (1.05-1.69)	**0.019**
Unknown	0.89 (0.64-1.23)	
Region of Residence		
Central Region	REF	
Northern Region	0.64 (0.56-0.72)	**0.000**
Southern Region	1.17 (1.09-1.26)	**0.000**
Unknown	0.79 (0.25-2.45)	0.684
ABO Blood Group		
A	REF	
B	0.92 (0.83-1.01)	0.086
AB	0.88 (0.74-1.06)	0.176
O	0.91 (0.83-0.99)	**0.021**
Missing	0.84 (0.65-1.09)	0.197
Sex with multiple partners without condom use		
No	REF	
Yes	0.86 (0.77-0.95)	**0.004**
Other TTIs		
None	REF	
Syphilis Infection	1.03 (0.71-1.51)	0.863
Malaria Infection	1.27 (1.18-1.35)	**0.000**
maritalstatus#riskyess		
Married #Yes		
Others#Yes		

* *p*-value from the Pearson Chi-squared test

APPENDIX VII: Cox proportional regression model for factors associated with TTI: multivariate model* (N=47,075)

Characteristic	Multivariate Analysis	
	Adjusted Hazard Ratio (95% CI)	*p*-value
Age Group		
16-19	REF	
20-24	0.27 (0.24-0.30)	**0.000**
25-29	0.10 (0.08-0.12)	**0.000**
30-34	0.03 (0.02-0.04)	**0.000**
35-39	0.01 (0.00-0.01)	**0.000**
40-44	0.00 (0.00-0.01)	**0.000**
45-49	0.00 (0.00-0.00)	**0.000**
45+	0.00 (0.00-0.00)	**0.000**
Sex		
Female	REF	
Male	1.52 (1.36-1.70)	**0.000**
Marital Status		
Married	1.54 (1.14-2.10)	**0.006**
Not Married	REF	
Employment Status		
Employed	REF	
Unemployed	1.31 (1.03-1.67)	**0.028**
Unknown	1.04 (0.75-1.43)	0.830
Region of Residence		
Central Region	REF	
Northern Region	0.50 (0.44-0.57)	**0.000**
Southern Region	1.08 (1.00-1.16)	**0.049**
Unknown	0.83 (0.27-2.58)	0.746
Other TTIs		
Syphilis Infection	1.11 (0.76-1.62)	0.590
Malaria Infection	1.44 (1.34-1.54)	**0.000**
maritalstatus#riskyess		
Married #Yes	0.53 (0.39-0.72)	**0.006**
Others#Yes	0.93 (0.83-1.04)	0.188

* Model adjusted for the variables shown

APPENDIX VIII: Test of Proportional Hazards Assumption

Variable	rho	chi2	Df	Prob>chi2
Agegroup	**-0. 63479**	**3908.98**	**1**	**0.0000**
Sex	**-0. 04949**	**8.41**	**1**	**0.0037**
Marital Status	0. 01508	0.79	1	0.3730
Employment Status	-0. 02419	1.90	1	0.1678
Region of Residence	-0. 02709	2.71	1	0.0994
Other TTIs	**-0. 20953**	**147.26**	**1**	**0.0000**
1b.maritalstatus#yes	-0. 00635	0.14	1	0.7099
2.maritalstatus#yes	-0. 00695	0.17	1	0.6834
Global test		4312.62	8	**0.0000**

APPENDIX IX: Turnitin Report

1918187:CWK-_MSC_REPORT_18102019-correction.pdf

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