Opt-Out Model of HIV Screening- A Study in

Federal Capital Territory Abuja, Nigeria

Everistus Ibekwe

PhD 2019

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By

Everistus Ibekwe

A thesis submitted in partial fulfillment of the requirements of Manchester Metropolitan University for the degree of Doctor of Philosophy

2019

Acknowledgments

Abstract

Background: Nigeria is the most burdened with mother to child transmission (MTCT) of HIV, accounting for nearly one-third of the global prevalence in 2015. Advances in the treatment of MTCT of HIV with highly active antiretroviral therapy (HAART) suggest significant reductions in transmission rates from $\geq 30\%$ to $\leq 1\%$. HIV testing is the linchpin to the treatment, but low-test acceptance is still prevalent among pregnant women including those attending antenatal clinics (ANC). The World Health Organization (WHO) issued new guidelines for improving HIV testing in ANC; recommending provider-initiated routine testing approach, different from the current on-request client-led voluntary counselling and testing (VCT). However, the adoption of such a strategy requires settings' understanding of both the clinical and economic impact.

Objective: To evaluate the clinical and economic impact of routine offer of antenatal HIV testing for PMTCT in an urban health facility in North Central Nigeria.

Study design: A pre-post (before and after) non-randomized controlled study was conducted.

Methods: Midwife counsellors were trained to provide and recommend HIV testing to all the women attending ANC, using streamlined counselling. Data in ANC logbook was extracted and key outcomes during the 3-months client-initiated testing were compared with a 3-months record during the implementation of routine offer of HIV testing strategy.

Results: After the introduction of routine HIV testing, the proportion of pregnant women in the study site who underwent and learned their HIV status increased from 142(46.4%) to 292 (94.5%) and HIV-positive cases identified rose from 15 (10.1%) to 44(15%). HIV positive women receiving treatment intervention for PMTCT increased from 10(66%) to 44(100%).

Aggregate cost and cost per unit testing were £38183.50 and £20204.80 and £130.70 and £136 for routine and client-initiated approaches, respectively. Cases of HIV infection averted in children during routine testing were 34.32 compared with the client-initiated approach of 10.8. Additional cost per HIV averted was £398.42 while the incremental cost-effectiveness ratio (ICER) was £764.40.

Conclusion: Provider-initiated HIV testing was both clinically and economically effective. Routine testing led to a substantial increase in test acceptance and reductions in transmission rates at ICER value below the recommended threshold (ICER below three times the gross domestic product: $2,177.99 for Nigeria). In the context of policy goal in maximizing limited HIV resources, this study suggests that there may be considerable benefits in the provision of HCT, using routine testing strategy. The efficient adoption of the policy should be based on local contextual considerations such as the prevalence and availability of human resources.

Declaration

I, Everistus Ibekwe, declare that the content of this thesis is entirely my own and has not been presented for an award in another institution. Information obtained from other sources such as books or journal articles has been properly cited and referenced.

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Publications Ensuing from This Study

Journal Publications

Ibekwe, E., Haigh, C., Duncan, F. and Fatoye, F. (2017a) 'Clinical outcomes of routine opt-out antenatal human immunodeficiency virus screening: a systematic review.' *Journal of Clinical Nursing*, 26(3-4) pp. 341-355.

Ibekwe, E., Haigh, C., Duncan, F. and Fatoye, F. (2017b) 'Economic impact of routine opt-out antenatal human immune deficiency virus screening: A systematic review.' *Journal of Clinical Nursing*, 26(23-24) pp. 3832-3842.

Conference poster presentations

Ibekwe, E., Haigh, C. and Prof Francis Fatoye, F. (2017) Comparing Cost-Effectiveness of Strategies for Antenatal HIV Testing: VCT and Routine Testing in Urban Nigeria. *ISPOR 20th Annual European Congress, Glasgow, Scotland 4-8 November 2017*

Ibekwe E, Haigh C, Duncan F, Francis, F. Comparison of Economic Impact of Provider-initiated Antenatal HIV Screening: A Systematic Review. *ISPOR 22nd annual international meeting Boston, MA USA May 20-24, 2017.*

Ibekwe E, Haigh C, Duncan F, Francis, F. (2017) Routine Opt-Out Model of Antenatal HIV Screening: A Study in Urban City of Nigeria. *2017 Annual Research Conference Faculty Research in High Summer Conference (FRIHSC), Manchester Metropolitan Univ. 4-5 July 2017*

Glossary

ANC   **Antenatal Care**

AHI   **Acute HIV Infection**

AIDS   **Acquired Immune Deficiency Syndrome**

ART   **Antiretroviral Therapy**

ARV   **Antiretroviral**

BMI   **Body Mass Index**

CBA   **Cost Benefit Analysis**

CCR4-5   **Chemokine Receptor**

CDC   **Centres for Disease Control and Prevention**

CEA   **Cost Effectiveness Analysis**

CUA   **Cost Utility Analysis**

DHS   **Demographic and Health Survey**

DNA   **Deoxyribonucleic Acid**

EFV   Efevarin

FCT   Federal Capital Territory

FTC   Emtricitabine

EIA   Enzyme immunosorbent Assay

HAART   Highly active Anti-retroviral Therapy

HIV   Human Immune Deficiency Syndrome

ICER   Incremental Cost Effectiveness Ratio

LMICs   Low Middle Income Countries

MOH   Ministry of Health

MTCT   Mother to Child Transmission

NARHS   National HIV/AIDS and Reproductive Health Survey

NPC   National   Population Commission

O & G   Obstetrics and Gynaecology

PITC   Provider-Initiated Testing and Counselling

PMTCT   Prevention of Mother to Child Transmission

PSA   Probabilistic Sensitivity Analysis

RTD   Rapid Diagnostic Test

SBA   Skilled Birth Attendant

SERVICOM   Service Compact

SOP   Standard Operating Procedure

TB   Tuberculosis

TL   Thymus Lymphocyte

STDs   Sexually Transmitted Diseases

3TC   Lamivudine

TDF   Tenofovir Diproxil Fumarates

TTI   Transfusion Transmissible Infections

UNAIDS   Joint United Nations Programme on HIV/AIDS

UNESCO   United Nations Educational Scientific and Cultural Organization

UNICEF   United Nations Children's Fund

UK   United Kingdom

USA   United States of America

VCT   Voluntary Counselling and Testing

WHO   World Health Organization

Chapter 1 : Introduction

1.1 Introduction

This chapter will briefly describe the burden of mother to child transmission (MTCT) of the human immunodeficiency virus (HIV) at the global level and make special emphasis on Nigeria, the country where this study took place. A short description of factors militating against the scale-up of HIV testing as well as emerging and innovative ideas to overcome these problems are discussed. Additionally, the theoretical framework underpinning this research, including a description of the chapters in this thesis will also be discussed.

1.2. Background

There are now many recognized benefits derived from early detection of maternal HIV in pregnancy, using voluntary counselling and testing. Specifically, there are known health benefits to the mother and her child (Ahmed et al., 2013; Kieffer et al., 2014; Cowan et al., 2015; Kim et al., 2015). The woman receives lifesaving treatment (Rice-Davies, 2016), while the probability of transmission to her baby and uninfected sexual partners is greatly reduced to a relatively safe level of less than 1%. (Anglemyer et al., 2014; Austin et al., 2014)

These encouraging reports towards HIV screening in pregnancy have provoked discussion on the pragmatic approach for encouraging testing. Such a concept will be required to meet the ethical standards, in addition to being convenient, acceptable and contains appropriate patient information. The present trial study was designed to accomplish this gap by comparing two alternative models for offering HIV testing to pregnant women in an antenatal setting, using a non-randomized trial approach. For an intervention to be recognized as being better and more effective than the other it is important that the women who are infected with HIV be diagnosed as early as possible. Therefore, it is essential to understand how to increase test acceptance. The content and style of delivering patient information must be

adequately rich to enable women to make informed consent. Besides, it is important for the strategy to be cost-effective since adopting such intervention will ultimately be on the premise of value for money. Overall, establishing an acceptable program requires a better understanding of how women respond to the offer of the test relative to cost. Likewise, the level, content, and style of patient information need to be assessed.

1.3 Problem Statement

The epidemic of HIV/ AIDS remains one of the greatest public health challenges of the 21st century. Since the first confirmation of cases of mother to child transmission (MTCT) of (HIV) in the early 1980s, rigorous researches have led to an extensive knowledge of the global epidemiology of paediatric and prenatal HIV epidemic, plus the risk factors and mechanisms of MTCT. Surveillance data from the Joint United Nations Program on HIV/AIDS (UNAIDS) suggest high morbidity and mortality among children, particularly in sub-Saharan Africa. In 2015, an estimated 1.8 million children were living with HIV, of whom 1.6 million reside in the sub-Saharan African region alone, accounting for 87% of the global burden (UNICEF., 2016b). Likewise, in 2015, approximately 150,000 new HIV infections occurred among children under 15 years, of whom 120,000 (84%) reside in the sub-Saharan African region. Additionally, in 2015, almost all AIDS-related morbidity and mortality in under-15 took place in the 21 World Health Organization (WHO) Priority countries, accounting for 91,000 out of 110,000 deaths, which occurred in this population, worldwide (UNICEF., 2016b)). Most of the infected children (90%) acquired the virus perinatal from their infected mother (Nielsen-Saines et al., 2008; Vogler, 2014; Dinh et al., 2015; Moges et al., 2017) many of whom undiagnosed despite repeated visits to health care centres, including antenatal clinics during the pregnancy (Castilla et al., 2002; Wolbers et al., 2008).

Undiagnosed HIV infection in pregnant women has considerable implications for public health, as these individuals harbour unchecked replication of the virus, which increases the risk of transmission (Drake et al., 2014; Mnyani et al., 2014). In the absence of any intervention, an exposed baby born to an HIV-positive mother has 15-45% chances of acquiring the disease during pregnancy, labour, delivery, and breastfeeding (Branson et al., 2008; Nesheim et al., 2012). Transmission, however, can be reduced to less than 1% with the provision of potent antiretroviral therapy (ART) to the mother and her baby throughout the period when infection can occur (Birkhead et al., 2010b; Nesheim et al., 2012). Early identification of the virus in pregnancy empowers the woman to take necessary measures that benefit both her health and that of her unborn baby (Branson et al., 2008; FMoH Nigeria, 2011). This is because HIV testing and counselling (HTC) is a vital entry point to most other HIV intervention services, including treatment for prevention of mother to child transmission (PMTCT), care and support services. Early diagnosis of HIV also, necessitates rapid treatment, which is the cornerstone for minimizing the spread of the virus as well as halting immunosuppression: disease progression to advanced stages of acquired immune deficiency syndrome (AIDS) in the infected individuals (Cowan et al., 2015). In the absence of this, both transmission to others and the quality of life of the infected individual is seriously compromised. For the seronegative mother, this is an excellent opportunity to learn how to protect herself from becoming infected with the virus.

For a long time, HIV testing in Nigeria and in many parts of the world has been premised on 'client-initiated' voluntary counselling and testing, where individuals seek HIV testing of their own accord (World Health Organization., 2009; FMoH Nigeria., 2011). However, coverage of this model has generally been low. For instance, data from sub-Saharan Africa suggest that the median test acceptance were just 10% for women and 12% for men, notwithstanding the

crucial role of HIV testing (WHO., 2007). Studies from both industrialized and resource-constrained settings show that many opportunities to counsel and treat infected patients at health facility level are often missed. For instance, in 2017, in Nigeria, despite seeking services for other health care reasons and half of the women attending ANC, approximately one-third of the infected pregnant women learned their HIV status (Federal Ministry of Health (FMoH)., 2010; NACA, 2017). Report from the National Statistics suggests that over 70% of women in their reproductive age never received an HIV test (Nigeria, 2014), and as of 2016, only 30% of HIV infected women have a known HIV status (NACA, 2017). Thus, many HIV infected mothers are undiagnosed of their HIV status, even when they engaged in repeated visits to the health facility for other medical reasons. This problem contributes to the majority of the women being identified at late stages, if ever (Nigeria Federal Ministry of Health (FMoH), 2013).

In Federal Capital Territory (FCT) Abuja, where the rate of infection in pregnant mothers is high (**Oono** et al., 2015) (approximately double the national data (NACA, 2015a)), a recent study examined HIV activities in the city (Nigeria Federal Ministry of Health (FMoH), 2013). HIV testing strategy was identified as the reason for low testing and detection rates among HIV infected pregnant mothers. The researchers investigating the practice of testing in these ANC units found heterogeneity in both clinical practice and counselling information. The study reported that VCT protocols varied within and between health facilities: counselling information and skills varied considerably, midwife nurses rarely receive training and practice was inconsistent. Gourlay and colleagues (2013), identified long-standing health-system issues (ill-skilled and inadequate staffing, the cost associated with testing) and community-level factors (stigma, lack of partner support and fear of disclosure) as issues militating against testing. The researchers suggested that the potential of PMTCT programs such as HIV testing would remain elusive unless these barriers are tackled (Gourlay et al., 2013). "A well-

functioning, appropriate, and accessible voluntary counselling and testing service is a prerequisite for a successful programme of MTCT prevention"(Newell.,2001). The appropriate testing format would provide the right information that would encourage women to engage in HIV testing (Matovu and Makumbi., 2007; Menzies et al., 2009; FMoH Nigeria., 2011). This condition necessitates an urgent solution: to develop a structured protocol that is effective, acceptable and efficient.

Another concern is that many women do not receive HIV test even when there are chances to do so. Several studies report that opportunities to test women are often missed in settings where client-initiated HIV counselling and testing is the mainstream of screening (Anaya et al., 2008; Asiyanbola et al., 2016; NACA, 2017). This report was corroborated by data from NACA and UNAIDS, which suggests that less than 45% of test coverage. Hence, the diagnosis of pregnant mothers is often established late in the course of HIV infection (NACA, 2015a; NACA, 2015b; NACA, 2017). The empirical report shows that about one-third of these women are identified with HIV only when they are already in advanced stages of the disease (NACA, 2015). Report from National Agency for HIV/AIDS Prevention (NACA) in Nigeria suggests that 38.3% of women become immune-compromised within one year of HIV diagnosis while another 15% receive a diagnosis for AIDS after less than two years of testing (FMOH/NACA, 2015). Children born to these women face a disproportionately high risk of HIV acquisition, especially in countries such as Nigeria where approximately 30% of HIV positive pregnant women receive treatment for PMTCT (Branson et al., 2008; Becker et al., 2009).

Another conflict of opinion has centred on whether HIV testing should be offered with simplified information, in line with other ANC blood tests or whether comprehensive information should be used during the counselling session. Minimal or simplified information

would probably achieve high uptake and save cost (Chrystie et al., 1995b; Thornton et al., 1995; Strode et al., 2005), but may not give women sufficient time to internalise the implication of testing HIV positive (Rennie and Behets, 2006). Comprehensive information, on the other hand, is to ensure psychological readiness but may result in high cost regarding midwife time and may result in anxiety (Chrystie et al., 1995a; Prekker et al., 2015). Also, the relative merits of opt-in and opt-out have been an issue for debate. Whereas in opt-in, women elect to undergo testing on self-referral, often with active consent, opt-out requires that HIV test be offered as a battery of ANC tests to all women attending ANC and test is conducted unless the woman actively declines. The increasing availability and accessibility of antiretroviral treatment for prevention of mother to child transmission (PMTCT) are improving demand creation for HIV test and raising optimism for the benefits of antenatal HIV testing. Precisely, HIV infected women and their exposed babies can now access treatment for PMTCT without complexity. Apart from the emergence of simplified, single dose once a day combination antiretroviral therapy (ART), WHO now recommends 'test and treat' policy for HIV infected mothers (WHO., 2015a; McCreesh et al., 2017). As per this guideline, all HIV infected pregnant mothers are to be treated with ARV regardless of clinical staging or CD4 count. This optimistic development towards antenatal HIV screening had led to a request for an effective, affordable and suitable technique for HIV screening combined with appropriate patient information (Eisenman., 2001; Montoy et al., 2016).

In response to these problems, Centres for Disease Control (CDC) and World Health Organization (WHO) both in 2007, recommended the introduction of routine offer of HIV testing in all clinical settings, including ANC (Branson et al., 2008; Kennedy et al., 2013). However, Nigeria has not implemented this policy in part because of unanswered questions regarding the diagnostic yield of such an approach in this setting. The NACA's unwillingness

for the implementation of opt-out testing was premised on irregular evidence of its effectiveness in increasing women's HIV testing rate (FMOH/NACA., 2015). Subsequent trials in clinical units investigating test acceptance under routine testing suggest successful implementation and are associated with higher test acceptance rate but they show highly varied ranges from 29% to 99% (Merchant and Waxman., 2010; Lyons et al., 2013; White et al., 2011). The wide range in test acceptance suggests a full understanding of the testing program. This includes an understanding of how the test is offered, who does the offering, to whom, type of setting and the economic impact. Answering these questions will be vital in understanding how the patient responds to testing and assist the decision-maker in policy formulation.

The current study was designed to evaluate these strategies by comparing the effectiveness of two models for offering HIV testing to pregnant women in an antenatal health facility, using a non-randomized controlled trial. For an intervention to be effective, it is important that women who are living with HIV virus be diagnosed, therefore it is essential to identify how to increase uptake. Understanding an acceptable technique would require knowing how pregnant women respond to the offer of HIV tests. Besides, the level, style, and content need to be examined.

The Federal Capital Territory (FCT), Abuja is one of the cities in Nigeria with the highest HIV prevalence among pregnant women. While the national prevalence rate indicates 3.8%, The FCT, Abuja and four other states have prevalence above 8% (Nigeria National Agency for Control of Aids., 2012). However, prior to this trial, there was no universal testing policy in Nigeria, including Abuja and only a small proportion (less than 0.5%) who attended ANC with symptoms suggestive of AIDS were selectively offered HIV tests during antenatal. Few others

undergo testing on self-referral. In view of this high prevalence but lack of previous testing policy, FCT Abuja was critically ideal to conduct this trial.

1.4. Research objectives

1.4.1. Broad objective

This study seeks to make a comparative evaluation of two models for HIV testing: provider-initiated versus client-initiated testing, in terms of clinical and economic impacts, in an ANC setting in Nigeria. Following a lack of evidence-based data and paucity of studies in this area, the researcher construed it appropriate to elicit fundamental understanding through the conduction of an empirical study.

1.4.2 Specific Objectives.

The current trial aimed to determine whether two different approaches of the universal offer of testing (provider-initiated versus client-initiated), in terms of different levels of information giving, would result in significantly different:

i. Test acceptance rate.

II. Maternal case identification rate.

III. Rate of referrals for anti-retroviral treatment for PMTCT.

IV. Another important objective of this study was to evaluate the association between individual midwife's characteristics and test acceptance. The goal was to further understand the most effective and acceptable strategy for testing.

V. In addition, an equally important aim of the study was to evaluate the economic impact of the interventions based on cost-effectiveness measures as follows:

i. Cost per HIV test

ii. Cost per new HIV diagnosis detected

ii Costs per infections averted.

1.5. Reason for Conducting the Study in SHMC Health Facility.

1.5.1 Choice of Study Facility.

The SHMC is an important government health facility that is strategically located in FCT, which provides health services to the residents and the neighbouring states. It is a unique health centre in that it provides both general and specialist health services and accommodates all tribes of Nigeria by the quota system (significantly representing all the local culture of the country). The findings here are likely to represent the general behaviour in the larger Nigeria. SHMC is described as the epicentre of HIV/AIDS prevention, having been among the few initial centres that were established by the central government to offer services in this area.

1.6. Outline of the Thesis.

1.6.1 A Brief Introduction to the Chapters of the Thesis.

 There are ten chapters of this thesis containing the information as described below.

Chapter 1 is the introductory chapter, which presents an overview of the study, the problem statement, the goal of the research and outline of the thesis structure.

Chapter 2 presents an in-depth review of existing literature regarding the natural history, epidemiology and pathophysiology of HIV, particularly in women and children.

Discussion in Chapter 3 focused on issues surrounding testing, diagnosis and essential prenatal care for PMTCT.

Chapter 4 is the presentation of a published systematic review of this study focusing on the clinical impact entitled as follows:

I. Clinical outcomes of routine opt-out antenatal human immunodeficiency virus screening: a systematic review.

Besides, in chapter 5 is yet another published systematic review from the economic viewpoint of the study interventions, and entitled as follows:

"The economic impact of routine opt-out antenatal human immune deficiency virus screening: A systematic review".

Chapter 6 discusses in details the methodological approaches underpinning the fieldwork of the clinical aspect of this study, including the ethical considerations and analytical tools for the data. A pre-post clinical trial was conducted in an ANC setting based on the identified gaps from the literature review.

Chapter 7 outlines the economic dimension of the study methodological procedures and the different approaches to economic evaluation with special emphasis on cost-effectiveness analysis.

Chapter 8 reports the results of the research findings from both the clinical and economic aspects. Results were presented in statistical formats using absolute numbers tabulated on tables, graphs, and percentages, histograms, bar charts, and pie charts.

Chapter 9 discusses the findings of the study. Here, two sets of findings (the economic evaluation and the clinical impacts of the two interventions) are drawn together and wider conceptual analysis of the issues emerging from the research are developed and interpreted in the light of the literature. Also, in this chapter, a holistic deliberation on the implication of

the study findings with emphasis on not just the study setting but on how it adds to a wider body of knowledge are examined.

In chapter 10, the summary, conclusions, and recommendation are put forward and this encompasses the concluding thoughts that end the thesis.

1.7. Chapter Summary

1.7.1 **Conclusion**

Nigeria has the highest burden of vertical transmission of HIV in the world. Many children become infected through their undiagnosed mothers. Knowledge of positive serostatus is the only way women can access anti-retroviral treatment to reduce the chances of transmitting the virus to their unborn babies. However, opportunities to test women for HIV are often missed by health care providers. Many of these pregnant women visit the health facilities during pregnancy without receiving an offer for an HIV test. Approaches to offering an HIV test have evolved from client-initiated VCT to provider-initiated routine testing. The standard VCT approach has failed to attract enough women to know their HIV-status. Routine testing has been adjudged successful in some parts of the world and many women have learned their HIV status through this program with many of the infected women being successfully enrolled in the PMTCT program. Although WHO promotes this testing regime, however, a deeper understanding is needed before a widespread adoption in any given setting. The next chapter 2 will take a closer look at the global epidemiology and natural history of HIV, with a focus on HIV in women and children in Nigeria.

Chapter 2 : History and Epidemiology of HIV.

2.1 Introduction

This chapter will briefly discuss the origin, discovery, and epidemiology of HIV/AIDS focusing on children and highlighting the sub-Saharan African situation with emphasis on Nigeria. The chapter will also consider some of the cultural, economic and political situations in Nigeria, which may have some bearing on the spread of HIV.

2.2 Overview

The human immunodeficiency virus (HIV) is the organism that causes AIDS. In humans, the virus invades and replicates in white cells particularly the lymphocytes and macrophages, eroding the integrity of an individual's immune system. This culminates in depressed immunity and susceptibility to various opportunistic infections including the manifestation of certain malignancies, after several years of the infection. This organism is one of the most purulent and destructive epidemics, which the world has ever witnessed, making it one of the most public health challenges of the modern world (Ortblad et al., 2013). Although every part of the world felt the impact of the disease, the sub-Saharan African region is most affected, and the impact of HIV/AIDS is most severe in this region.

2.3 Historical Background

The origin of HIV has been a subject of academic debate since the first strain of the virus was recognized in humans in the early 1980s. There is now a growing wealth of information on the origin of the virus. HIV is classified as a lentivirus, species of virus that attacks the immune system of humans in a similar way the Simian Immunodeficiency Virus (SIV) destroys the immune system of Apes and monkeys (Worobey et al., 2010). Research findings suggest that SIV in chimpanzee crossed species to become HIV (Gao et al., 1999; Sharp and Hahn., 2010).

Although anecdotal findings suggest that the first cross-species of SIV to become HIV in humans took place in Kinshasa, the Democratic Republic of Congo in 1920 (Faria et al., 2014), there is, however, no concrete evidence to support this claim.

The first cases of acquired immune deficiency syndrome (AIDS) were established in America in 1981, among men who sleep with men (MSM), following the manifestation of recurrent cases of Kaposi sarcoma and pneumonia from infection with *pneumocystis carinii* (Hymes et al., 1981; Centers for Disease, 1981; Centers for Disease, 1982), both conditions were normally rare in humans. It was soon realised that the disease was not confined to MSM but had spread to other populations such as haemophiliacs and intravenous drug addicts. While scientist struggled to comprehend this condition, in 1983, Luc Montagnier, a research scientist and his colleagues at the Pasteur Institute in France announced the isolation of a rare virus known as Lymphadenopathy Associated Virus (LAV), which was suggested as a definitive cause of AIDS, in a Caucasian woman (Barré-Sinoussi et al., 1983; Barré-Sinoussi et al., 2004). Following this discovery, Roberto Gallo and his team at the National Cancer Institute in the USA also claimed to have isolated a new sub-group of the human T-cell leukaemia virus family designated HTLV-III in more than one-third of patients with AIDS (Centers for Disease,. 1982; Gallo and Montagnier, 2003; Worobey et al., 2010). It was later established that both viruses were the same and belonged to the same family, which is the etiologic (causative) agent of AIDS (Gallo and Montagnier., 2003).

In June 1983, AIDS-defining illnesses were identified in some children and subsequent researches confirmed that the children acquired the virus perinatal from their HIV infected mother (Centers for Disease., 1982). Centres for disease control also identified that other routes of infection are through sexual intercourse and contact with contaminated blood and

body fluids. Subsequently, in 1985, the first two AIDS cases in Nigeria were discovered in 1985 and reported at the International AIDS conference in 1986 (Kalipeni and Djukpen., 2007). One of these two cases was in an under-15 female child who tested positive for HIV after presenting with AIDS-related symptoms. Since then, Nigeria has witnessed a localized epidemic among high-risk groups (sex workers and men who sleep with men). Soon after this, the infection exploded into a generalized epidemic, spreading across both young and old through mostly heterosexual and MTCT modes of transmission. The surge in national rates, established through a survey of seroprevalence women attending antenatal clinics increased from 1.2% in 1999 to an unacceptable rate of 5.8% in 2001. The full detail of the epidemiology is discussed in the proceeding section of this chapter.

2.4 Pathophysiology

As stated above, HIV is believed to be a cross-species of SIV that entered the human population through wild chimpanzees and sooty Mangabeys (old World monkeys) that are domiciled in Africa (Sharp et al., 1995; Ayouba et al., 2013).

The HIV life cycle comprises six stages: binding and entry, reverse transcription, integration, replication, budding, and maturation. The HIV envelope proteins called gp120 and gp41 bind to CD4+ cell receptors and co-receptors on the surface of CD4+ cells ad macrophages.

During binding and entry, the chemokine receptors CCR5 and CXCR4 aid viral entry. T-cell tropic viruses need CXCR4 to bind, whereas macro-tropic strains of the virus utilize CCR5. R5 is the most common virus transmitted during acute infection but later during infection, it switches to X4 to become the most common virus. The existence of a homozygous inactive mutation of the CCR5 allele results in resistance to infection by the R5 virus. The assemblage of the proteins, the receptors and co-receptors fuse the HIV membrane with the CD4+ cell

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membrane, and the virus gains entry into the CD4+ cell and macrophage. The viral membrane and the envelope proteins remain outside of the CD4+ cell, whereas the core of the virus enters the CD4+ cell. CD4+ cell enzymes interact with the viral core to trigger the release of viral RNA and viral enzymes such as reverse transcriptase, integrase, and protease. Once the HIV RNA has gained entrance to the host cell, it is converted to DNA before fusing with the host DNA via the CD4+ cell. This process known as reverse transcriptase is mediated by the HIV enzyme reverse transcriptase. The product of this activity is a single strand of viral DNA from the viral RNA. Subsequently, the viral DNA undergoes replication into double-stranded HIV DNA. At this stage during integration, the viral DNA permeates the nucleus of the CD4+ cell and with the help of viral enzyme integrase, the viral DNA is introduced into the CD4+ cell's DNA. The CD4+ cell becomes the hub for the continuous synthesis of copies of the viral DNA. As new viruses are produced, they bud through the CD4+ cell membrane to infect other CD4+ cells, after they have undergone a maturation process.

The HIV viral particles replicate rapidly and typically destroying or impairing the normal functions of the immune cell system involving the thymus lymphocytes (T-lymphocyte) in an infected individual. The hallmark of HIV infection is the systematic depletion of the cluster of differentiator T-cells (CD4 T-cells); the thymus, CD4+ progenitor cells in the bone marrow and peripheral lymphoid organs; as well as CD4+ cells within the nervous system, such as microglia. (Maartens et al., 2014). The depletion of CD4$^+$ cells results in the appearance of opportunistic infections and sometimes the occurrence of neoplastic processes.

Acute HIV infection or acute retroviral syndrome is the initial stage of HIV infection, and it typically manifests within 2 to 6 weeks after contracting the virus. During this period, there is high viral load and the peripheral CD4+ cells count is rapidly destroyed but rarely drop below
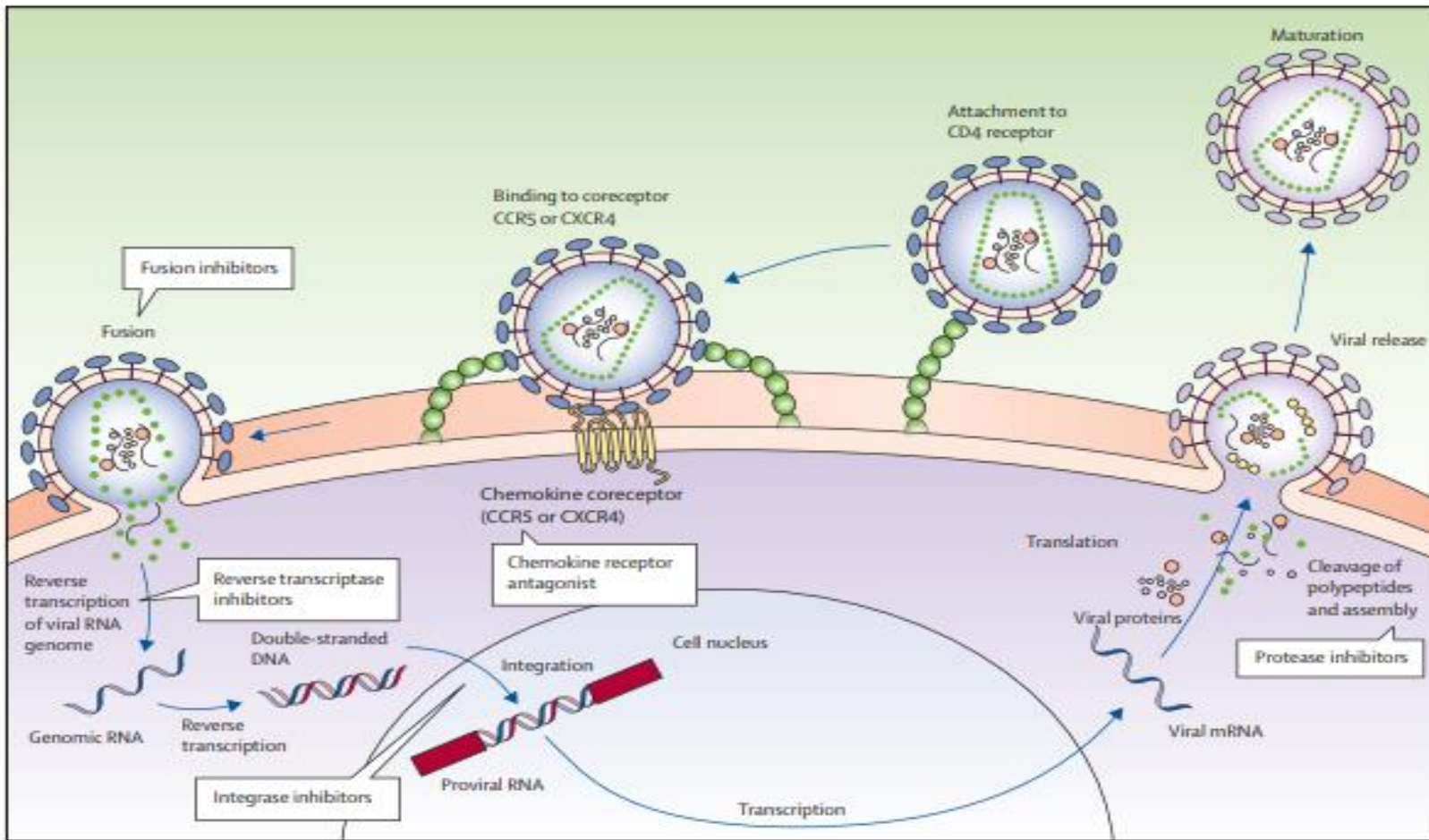
Figure 2-1 Diagrammatic representation of HIV life cycle displaying points of actions of viral/host cell interaction. Source:(Simpson, 2014)

less than 200 cells/μL. CD4+ cells in the lymph nodes and the thymus are the main target of the virus during this stage, making it difficult for the thymus to produce T-lymphocytes, thus rendering the immune system vulnerable. Unlike adults, children have high lymphocyte counts. Figure 2.1 above depicts the pathophysiology of HIV.

2.5 Routes of HIV Transmission and Risk of Acquisition

2.5.1 Outline of Transmission Routes

Principally, there are three major routes of HIV infection, consisting of sexual contact, parenteral and mother to child transmission, also known as vertical transmission. Most people who have been infected with the virus, since the onset of the epidemic, with exception to few individuals, became infected through one of these routes of transmission (de Silva et al., 2010). Parental transmission of HIV occurs through infected blood and blood-related products, contaminated sharp objects and HIV infected organs (Kuhar et al., 2013). Studies suggest that while parenteral mode may significantly contribute to infection in parts of the Western World such as the United States and the United Kingdom, this is not a major route of infection in Africa (Berkley, 1991; Pybus et al., 2003).

2.5.2 Sexual Transmission

HIV can also be transmitted from person to person through body fluids (Levy, 2009; Aberg et al., 2009). Sexual routes of transmission are by far the most common mode of HIV infection globally (De Cock et al., 2012; Haase, 2010). Although the initial cases of HIV were among the homosexual men living in the United States of America (USA) and Europe (Antoniou et al., 2012; Laga and Piot, 2012), heterosexual route is predominantly the route of transmission in sub-Saharan Africa (Chirenje et al., 2010)-the region with the highest global burden. The higher proportion of women than men also live with HIV (Celentano and Beyrer, 2008; J. A.

Higgins et al., 2010), perhaps, due to anatomical and biological reasons (Del Castillo et al., 2010), and in Africa, due to social and cultural conditions (Malta et al., 2010) such as gender inequality and polygamy (Reniers and Tfaily, 2012).

The risk of HIV transmission in one episode of sexual intercourse varies considerably and depends on multi-factorial conditions, including the type of sexual act being practiced (Boily, 2009; Patel et al., 2014). Broadly, unprotected anal intercourse has a higher risk of HIV acquisition than unprotected vaginal intercourse (Baggaley et al., 2010). Women have a twofold risk of acquiring HIV infection from an infected partner compared with a man's relative risk of transmission from an infected female during a sexual encounter. Aggregate analysis of studies across countries found that vaginal intercourse with a chronically HIV infected man with no ARV treatment carries a 0.08% risk of transmitting the virus to the woman in every unprotected sexual encounter (Boily, 2009). Likewise, studies showed that the chances of heterosexual penile-vaginal transmission of HIV are approximately two or more times more efficient compared with female to male transmission risk, involving vaginal-penile acts (Baggaley et al., 2010). This means that the risk of HIV acquisition is higher for an uninfected female who indulges in vaginal-penile sex with an infected man than it is for an uninfected male involved with an infected woman in the same vaginal-penile intercourse. The risk increases significantly for females during defloration or first bout of a sexual encounter in life due to some biological factors (Bouvet et al., 1989; UNAIDS, 2016e).

In the case of anal intercourse, the risk of transmitting the virus from an HIV-positive insertive partner (top) to the receptive partner (bottom) is about 0.82% per sexual session against 0.06% risk for uninfected insertive partner acquiring the virus from the infected receptive partner. In the United States, for example, most new HIV infections that occurred in 2010

were among gay or Men who have sex with men (MSM), followed by heterosexual African American women (Craig, 2016). Despite representing 4% of the male population in the united states, male-to-male sex accounted for over three-fourth (78%) of new HIV infections in men, and almost two-thirds (63%) of all new infections in the general population, whereas heterosexual mode represented an estimated 25% of the infection (Craig, 2016).

In southern and eastern Africa, most infections (60-90%) occur among heterosexual individuals who engage in multiple sex partners (Gouws et al., 2012). Likewise, in Nigeria, heterosexual sex is the primary route of HIV transmission, accounting for an estimated 80% of the burden (NACA, 2015a). Because a substantial number of infections are among unsuspecting individuals who are in a stable, mutually faithful, but discordant relationship, diagnosis is made in late stages. Most of whom engage in unprotected sex because of their erroneous perception of low risk of exposure and the need to become pregnant (NACA, 2015a). A considerable number of these pregnancies result in mother to child transmission of HIV, which is indeed a key route of transmission in children in Nigeria. Other drivers of the epidemic are inter-generational sex, inefficient and ineffective sexually transmitted infections (STI's) clinic and inadequate health centres (NACA, 2015a).

2.5.3 Mother to Child Transmission of HIV

Mother to child transmission of HIV (MTCT) also known as the vertical transmission is the transfer of HIV from an HIV-infected mother to her child in utero, labour, delivery or through breast milk (Shetty, 2013; Mayaux et al., 1997). Worldwide, HIV is transmitted to children through this important and common route (Del Castillo et al., 2010). Vertical transmission of HIV accounts for approximately 90% of infections in children, globally (Coutsoudis et al., 2010; Lima et al., 2014) and is the second most important route of transmission in the African

continent (Kuhn et al., 2008). Other modes of transmission, such as transfusion of blood and child abuse still exist, though rare. Women of childbearing age; particularly pregnant mothers have witnessed high infection rates, resulting in a correspondingly high HIV epidemic in children (Gourlay et al., 2013).

Foetus become infected with HIV when the virus in their infected mother cross the placental barrier, the relative risk of acquisition during this period is 5-10% (Lehman and Farquhar, 2007). Similarly, the risk of transmission is heightened to rates between 10-20% when the foetus is exposed to the mother's cervical secretions or blood during intrapartum. Breastfeeding the child also carries a risk of transmission ranging between 10-20%. Overall, in the absence of effective pregnancy intervention, an HIV infected mother has a 30-45% chance of passing the virus to her baby (Lehman and Farquhar, 2007).

2.6 Risk Factors for Mother to Child Transmission of HIV

2.6.1 Driving Factors

The susceptibility to MTCT of HIV depends on three broad conditions, which are:

I. How infectious the virus is, for instance, because HIV-2 has slower disease progression and lower viral load, this variant has a lower transmission rate of 0-4% compared with HIV-1 with a transmission rate of 20-45% (Burgard et al., 2010).

II. The efficiency of the route of transmission.

III. The vulnerability of the baby.

2.6.2 Maternal Risk Factors

Typically, the risk of vertical transmission is multi-factorial. Several studies have demonstrated that women with advanced stages of HIV or AIDS defining-illnesses have the

most potential of transmitting the virus, both in-utero and during breastfeeding (Burgard et al., 2010; Ngwende et al., 2013; da Cruz Gouveia et al., 2013; Drake et al., 2014). An exposed baby can acquire the infection in-utero via maternal blood (During trans-placental haemorrhage) or during intrapartum (contact with cervicovaginal secretions delivery). HIV-particle levels in cervical fluid, most notably during intrapartum, are most associated with heightened transmission risk. Ngwende & colleagues (2012) reported that maternal viral load, AIDS-defining illnesses (Maternal immune status) and mode of delivery are the main determinant factors associated with an increased risk of HIV transmission to the foetus during pregnancy, labour or breastfeeding. Studies suggest that most infants (approximately 50-80%) become infected during the time of birth if the maternal HIV viral load is unsuppressed (Mofenson, 1997; Reshi and Lone, 2010).

Additionally, the maternal acquisition of HIV during pregnancy increases the risk of MTCT of HIV to the unborn baby (Drake et al., 2014). Naturally, in the first few weeks of HIV acquisition, the viral load spike to very high levels and so women with primary HIV infection during pregnancy are significantly at greater risk of transmitting the virus to their unborn-baby (Birkhead et al., 2010b). Secondly, an HIV-positive woman can also transmit the virus to her unborn baby during the stages of pregnancy, particularly during the third trimester if there is treatment interruption (Tubiana et al., 2010). However, early initiation and uninterrupted use of ARV drugs during this period significantly lower the risk of MTCT (Burgard et al., 2010; Warszawski et al., 2008). Trial studies suggest that longer treatment with ARV during the pregnancy without any form of ARV interruption is strongly associated with lower MTCT rates (Tubiana et al., 2010; Gonfa and Gebre-Selassie, 2014). This is because the risk of transmission is higher preceding treatment or before viral suppression is achieved, including when there is a treatment interruption gap due to the resurgence of high viral load. Thirdly, HIV-positive

women, who become ill, acquire sexually transmitted diseases (STI's), bacterial vaginosis and other situations that result in inflammation of the placenta or the foetal membrane are associated with a higher risk of MTCT (Wawer et al., 1999; Marx et al., 2010). Illness during pregnancy induces the risk factors associated with HIV transmissions such as a transient rise in viral load, an increase in immune activation and a rise in the cluster of differentiation (CD4) target cells. Other maternal factors to consider are genetic influences (Singh and Spector, 2009) as well as behavioural factors, such as smoking, the health of sexual partners, and intravenous drug use (Ellington et al., 2011).

2.6.3 Obstetrics Risk Factors

Mandelbrot and colleagues (1999), The International Perinatal HIV Group (1999), Mark and colleagues (2012) in trial-based studies investigated the association between vertical transmission and mode of delivery. The studies found that Vaginal delivery is a predictor of MTCT with a higher risk of vertical transmission of HIV from an HIV infected mother due to contact with vaginal secretions and other body fluids along the birth canal (Tubiana et al., 2010). This risk increases with prolonged contact with the contaminated body fluid in cases of premature rupture of the membrane and prolonged labour. Landesman and colleagues (2008) also reported that prolonged rupture of the membrane, contact with cervicovirginal fluid and blood during labour and delivery are all associated with a significant risk of MTCT. Findings from a large register of HIV exposed twins indicate that the first delivered twin has less risk of infection compared to the second-born twin (Goedert et al., 1991; Scavalli et al., 2007). Randomized controlled trials in Europe (Parazzini et al., 1999; Thompson et al., 2015) and a combined large American-European meta-analysis (Read and Int Perinatal, 1999) showed a reduction in risk at rates exceeding 50% associated with the caesarean section before the onset of labour and certainly prior to membrane rupture. Subsequent studies

confirmed the effect of caesarean section in reducing MTCT of HIV in cases with low or high

viral load and in women receiving ART (Brocklehurst, 2000; John et al., 2001). The intervention

is cost-effective for PMTCT even in a wide range of circumstances (Mrus et al., 2000).

However, delivery through caesarean section is often not possible in parts of the world with

the highest-burden of MTCT and even in settings where the procedure is possible, the

amplified risk of infectious morbidity has to be borne in mind (Landesman et al., 1996; Newell,

2001).

2.6.4 Infant Associated Risk

Table 2.1 below, presents the factors that accentuate the likelihood of HIV transmission from

the mother to the child. The risk factors associated with an infant's susceptibility to increased

perinatal HIV infection include premature birth, low birth weight, presence of lesions on the

skin and mucous membrane (oral thrush) and actual breastfeeding the child (Aagaard-Tillery

et al., 2006; Lopez et al., 2012).

In a meta-analysis, Xiao & colleagues (2015) found that HIV seropositive mothers are at

greater risk of delivering low birth weight or preterm babies compared with uninfected ones.

Preterm birth and low birth weight threaten the overall healthy growth and maturation of the

foetus, including disruption of the vital early brain development, increased risk of infection

and death (Xiao et al., 2015). Neonates with skin and mucous membrane lesion such as thrush

have a significant risk of acquiring HIV through contact with the mother's bodily fluid. Skin

lesions make it easier for the virus to gain access to the infant's body. Breast milk carries the

risk of HIV transmission in children born to HIV infected mothers who breastfeed their babies.

The probability that a child will acquire HIV through breastfeeding is approximately 14% for

mothers with known HIV and 29% for the women who become infected during the period of

lactation (Dunn et al., 1992; John-Stewart et al., 2004).

Table 2-1 Factors associated with risk of mother to child transmission of HIV, level of association, and impact on transmission (Newell, 2001)

Risk factor	Strength of association	Impact[a]
Maternal		
RNA viral load	Strong	Large
AIDS	Strong	Small to medium
Immune deficiency	Strong	Medium
Genetic	Weak	Small
Other sexually transmitted infections	Medium	Small to medium
Chorioamnionitis	Medium	Small
Vitamin A deficiency	Medium	Small
Obstetric		
Mode of delivery	Strong	Large
Duration of membrane rupture	Strong	Large
RNA in vagina/cervix	Medium	Medium
Invasive procedures	Strong	Small
Paediatric		
Prematurity	Strong	Medium
Breastfeeding	Strong	Large
Breast health	Strong	Small
Genetic	Weak	Small

[a] The impact of a risk factor is not only determined by the strength of the association with the risk of transmission but also by the frequency of the factor in a population.

This highlights the need for primary prevention of HIV acquisition in breastfeeding mothers. Data from a randomized trial in which women were allocated in two groups (breastfeeding or artificial feeding) confirmed the additional absolute risk of MTCT 16% through breastfeeding, during a two-year follow-up (Nduati et al., 2000). In this study, breastfeeding nearly doubled the overall rate of vertical acquisition of HIV.

In one study, exclusive breastfeeding was reported as very essential for infants in the first six months of life (Arifeen et al., 2001). The study also suggested an additional benefit of protecting the mother against pregnancy. However, in the era of prenatal HIV infection, optimal breastfeeding requires adequate information and support for the infected mother who elects to exclusively breastfeed her child. This is to ensure that she understands the issues surrounding exclusive breastfeeding and the techniques required to achieve the optimal goal (Cope and Allison, 2008). Largely, exclusive breastfeeding is the preferred option compared with mixed feeding due to the overall health benefits. Besides, while transmission through breastfeeding does not negate a reduction in the risk of transmission attained through ARV treatment in pregnancy, breastfeeding does reduce the general efficacy of ARV Peripartum interventions. In a Kenyan (Mbori-Ngacha et al., 2001) and Botswana (Thior et al., 2006) trials, mortality was higher for children born to HIV positive women using exclusive breastfeeding than those using formula feeding 11% against 9% and 7.6% against 3.7%, respectively. Although the characteristics of the women in both arms were relatively the same (plasma viral load, CD4 count), the rate of intrauterine transmission was higher in the breastfeeding group and they probably experienced advanced stages of HIV. Exclusively breastfeeding a child for 6months carries a 5 to 20% risk of MTCT and mixed feeding may increase the risk (Coovadia et al., 2007).

2.7 Epidemiology of HIV

2.7.1 Global Burden

Since the first case was reported in 1981, the virus has spread wildly across the world, particularly in the Sub-Saharan Africa region. Globally, the number of people living with HIV rose from around 8 million in 1990 to approximately 36.7 million at the end of 2016 (Wang et al., 2016), whom 2.1 million were children. New HIV infections in 2016 were estimated at 1.8 million people. Overall, according to WHO, more than 72 million people have so far been infected with HIV and 35 million have died from AIDS-related diseases since the start of the epidemic. The global prevalence has also levelled at 0.8% since 2001 (Wang et al., 2016). Almost all individuals living with HIV reside in low-middle-income countries (LMIC). Sub-Saharan Africa is the hardest-hit region with approximately 25.6 million people living with the virus, including 66% of new HIV infections that occurred in 2016. Women of childbearing, essentially pregnant women have witnessed high infection rates resulting in a correspondingly high HIV epidemic among children who predominantly acquire the virus through their infected mother during the periods of pregnancy or breast-feeding (Gourlay et al., 2013). The changes in the number of new HIV infections in men compared with women are more marked at younger ages. For instance, in 2016, new HIV infections among young women aged 15-24 were 44% more than the male counterpart (Joint United Nations Program on HIV/AIDS (UNAIDS), 2017). In the majority of LMICs with a high magnitude of HIV prevalence, young women remain at unacceptably high risk of contracting HIV. For instance, in sub-Saharan Africa, particularly eastern and southern regions, young women between the ages of 15-24 accounted for 26% of new HIV infection in 2016 even though this group makes up only 10% of the entire population.
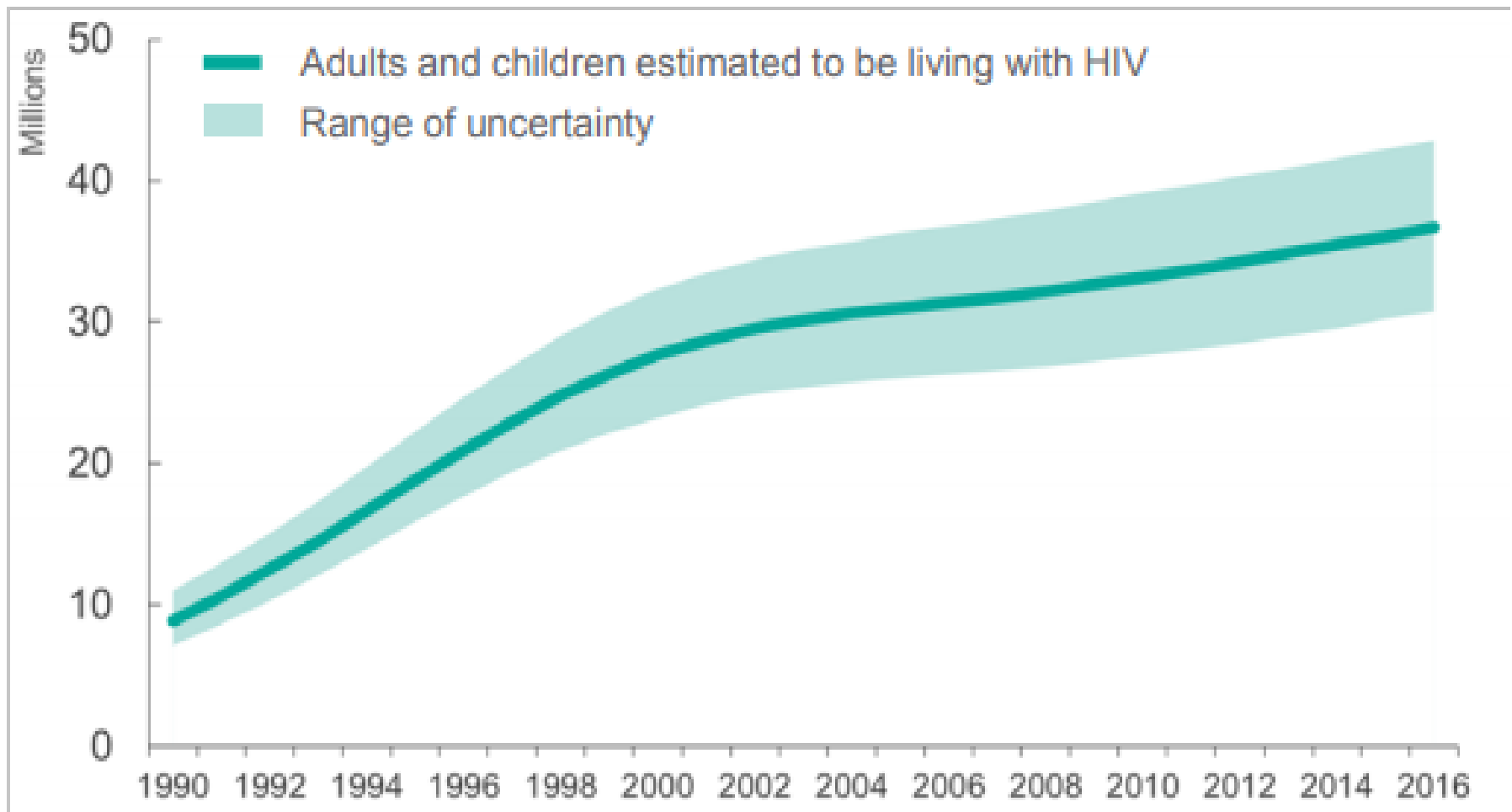
Figure 2-2 Global trend of people (Adults and children) living with HIV from 1990 to 2016 (Joint United Nations Program on HIV/AIDS (UNAIDS), 2017)

Table 2-2 Synopsis of HIV prevalence among different population groups in 2016 (UNAIDS, 2017b)

Summary of the global HIV epidemic (2016)

Number of people living with HIV in 2016		
Total	36.7 million	[30.8 million – 42.9 million]
Adults	34.5 million	[28.8 million – 40.2 million]
Women	17.8 million	[15.4 million – 20.3 million]
Men	16.7 million	[14.0 million – 19.5 million]
Children (<15 years)	2.1 million	[1.7 million – 2.6 million]

People newly infected with HIV in 2016		
Total	1.8 million	[1.6 million – 2.1 million]
Adults	1.7 million	[1.4 million – 1.9 million]
Children (<15 years)	160 000	[100 000 – 220 000]

AIDS deaths in 2016		
Total	1.0 million	[830 000 – 1.2 million]
Adults	890 000	[740 000 – 1.1 million]
Children (<15 years)	120 000	[79 000 – 160 000]

Source: UNAIDS/WHO estimates.

World Health Organization

Likewise, young women residing in western and central Africa and the Caribbean respectively are responsible for 22% and 17% of new HIV infections that occurred globally in 2016. Figure 2.2 above depicts the global trend of HIV from 1990 to 2016 (Joint United Nations Program on HIV/AIDS (UNAIDS), 2017), while table 2.2 shows the current global burden according to sex and age.

2.7.2. Epidemiology of HIV in children.

Over the past three decades, since the first cases of HIV were reported in 1981, the number of children living with the virus has increased remarkably, particularly in LMICs. This is because the number of HIV infected women of childbearing age has risen. Young adult women account for more than half of the 56% of women who make-up adult HIV infection in Africa (UNAIDS, 2017b). Primary HIV infection in pregnant women drives the paediatric epidemic. In 2016, The WHO estimated that globally, approximately 438 HIV infections in children occurred every day or an estimated 160,000 new infections annually, 90% of whom reside in sub-Saharan Africa (Joint United Nations Program on HIV/AIDS (UNAIDS), 2017). Approximately 110,000 of these children died of AIDS-related diseases (UNAIDS, 2016b). Most of them acquire the infection *in utero,* at the time of birth (Peripartum) or through breastfeeding.

Although Sub-Saharan Africa is home to an estimated 12% of the world population, the region accounts for 71% and 74% of global burden and HIV related deaths respectively (UNAIDS., 2016a). Almost all the children infected with HIV live in Africa where HIV/AIDS is a leading cause of death among under-15 (UNICEF., 2016a).

 Nigeria is arguably the most burdened nation with the HIV epidemic in the world. First, it has the second-largest infection in the world and second, it has one of the highest new infections
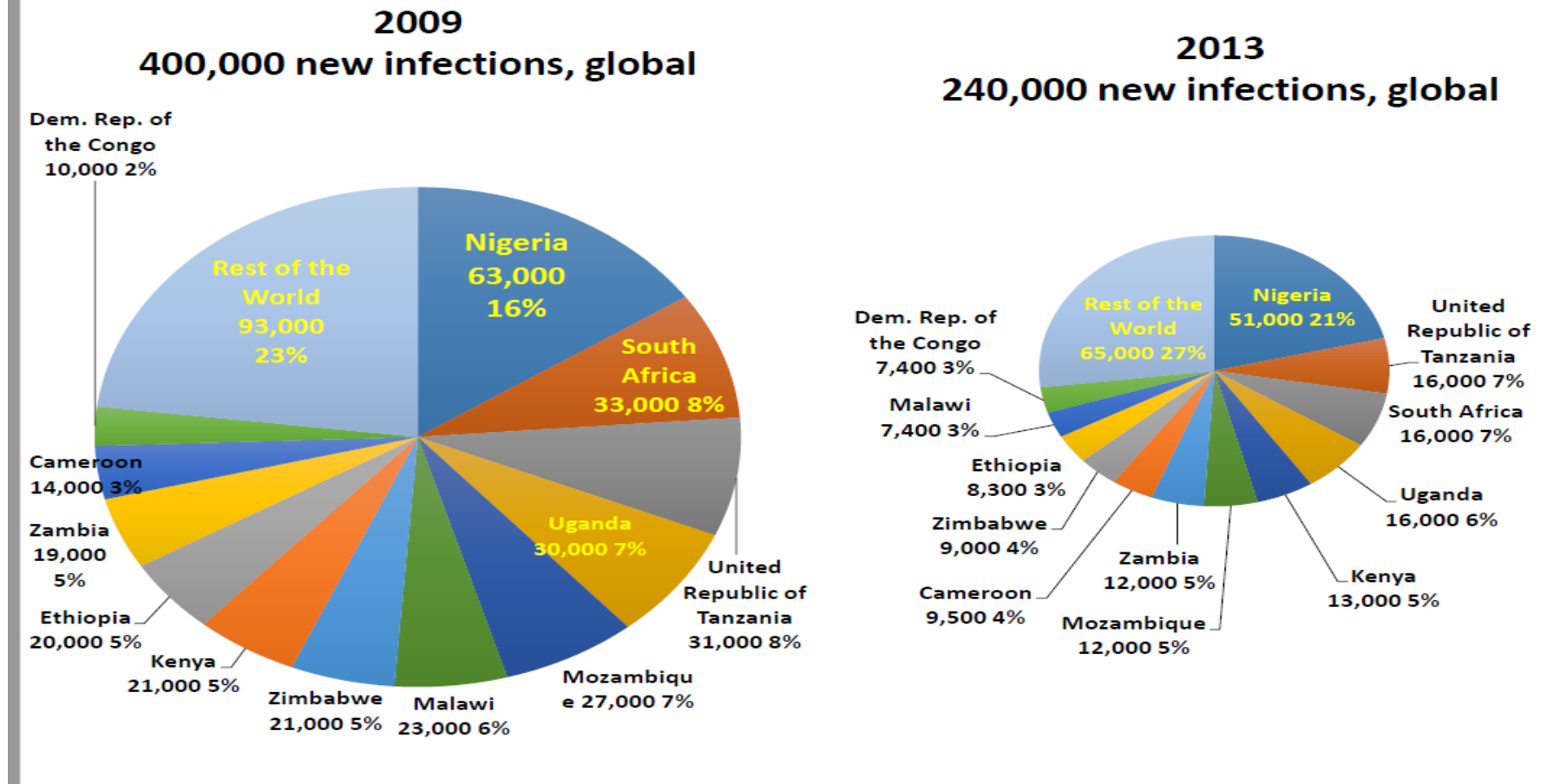
Figure 2-3 Burden of new HIV infections among under-14 children in most affected countries.

Estimated number and percentage of children aged 0—14 living with HIV, West and Central Africa, 2016

- CONGO 6,000 1%
- CENTRAL AFRICAN REPUBLIC 9,200 2%
- BENIN 6,300 1%
- NIGER 5,800 1%
- COUNTRIES WITH LESS THAN 5,000 CHILDREN LIVING WITH HIV 26,000 5%
- BURKINA FASO 10,000 2%
- GUINEA 10,000 2%
- CHAD 11,000 2%
- TOGO 12,000 2%
- MALI 14,000 2%
- GHANA 32,000 6%
- COTE DIVOIRE 36,000 7%
- CAMEROON 46,000 9%
- DEMOCRATIC REPUBLIC OF THE CONGO 48,000 9%
- NIGERIA 270,000 49%

Regional Total: 540,000

Figure 2-4 Distribution of the burden of MTCT in west and central Africa (UNAIDS., 2017a)

in Sub-Saharan Africa (FMOH/NACA., 2015). Precisely, Nigeria is home to 3.2 million people who are currently living with HIV and bore 60% of new HIV infections that occurred in sub-Saharan Africa in 2016, amounting to 220,000 (Joint United Nations Program on HIV/AIDS (UNAIDS)., 2017). Similarly, in 2016, Nigeria has 270,000 children living with HIV-the largest in one country, accounting for approximately 15% of the global burden and nearly half of the west and central Africa burden. Besides, 37,000 new infections in children occurred in the same year. Likewise, morbidity and mortality from AIDS-defining illnesses have not yet been abated: an estimated 160,000 under-15 children have so far died from AIDS-related illnesses. Figures 2.3 and 2.4 above present the global and regional trends of HIV spread.

With over a third of MTCT cases from the twenty-one Priority countries occurring in Nigeria alone and less than 30% of pregnant women living with HIV accessing ARV treatment, Nigeria is not yet on the path to achieving the Global Plan targets for PMTCT (UNAIDS., 2016b). Furthermore, of the 23,000 new infections that occurred in 2014, the national data also estimated that over 174,000 adults and children died from HIV/AIDS related-diseases (NACA, 2015a). Currently, Nigeria is the only country among the WHO classified high priority nations, which has not adopted the modified PMTCT management guidelines that stipulate, offer of lifelong HIV treatment to all pregnant and breastfeeding mothers. While other countries in sub-Saharan Africa with a high prevalence of MTCT, for example, South Africa and Botswana, have begun to witness considerable declines, there has not been any significant sign of abate in the nearest future, in the case of Nigeria, unless urgent steps are taken (UNAIDS., 2016b). In 2015, six of the priority countries, of course, without Nigeria, achieved the Global Plan of guaranteeing that 90% or more pregnant women living with HIV receive antiretroviral drugs for PMTCT (UNAIDS., 2017b). Jointly, countries have reduced new HIV infections in children from 270,000 in 2009 to 110,000 in 2015 (UNAIDS., 2016b). However, Nigeria still bears the

largest number of infected children at 41,000, almost the size of the next eight hardest-hit countries put together (UNAIDS., 2016b). Excluding Nigeria, the remaining twenty priority countries have reduced nearly two-third of the MTCT incidence rate (UNAIDS., 2016b).

Overall, the epidemic of HIV/AIDS has persisted in Nigeria since the first case was identified in 1986, with the national HIV seroprevalence trend continuously rising from 1.8 in 1991, 5.8 in 2001, 4.4 in 2005 and 4.6 in 2008 (NACA., 2015b). As of 2008, whereas 271,151 new HIV infections occurred in adults and 68,864 in children over 2.87 million Nigerians were already living with the virus.

The National HIV/AIDS and Reproductive Health Survey (NARHS) also reported a prevalence rate of 3.2% and 3.4 % in the general population in 2012 and 2013 respectively (Nigeria Federal Ministry of Health (FMoH)., 2013). Currently, the prevalence rate has slightly dropped to 3.1% in 2015 (UNAIDS, 2016f). However, there is a stark zonal disparity in the epidemiology of HIV in Nigeria as well as wide differences between urban and rural areas. For instance, whereas rates in Rivers state are as high as 15.2%, the rates in Ekiti state are 0.2% or lower (Nigeria Federal Ministry of Health (FMoH)., 2013). Although recent estimates suggest a gradual decline in new HIV infections, the proportion of women living with the virus has continued to exceed their male counterpart, Table 2.2. A combination of factors ranging from biological differences between men and women, complex social, cultural, and environmental factors may exacerbate women's vulnerability to HIV infection. For example, young women engage in partnerships with men older than they do, while young men form relationships with women of comparable age groups. Conversely, young adult men engage in multiple relationships than female (Gregson et al., 2002)

Table 2-3 Estimated new HIV infections in Nigeria (Nigeria Federal Ministry of Health (FMoH), 2013)

Year	Female	Male	Total
2009	157,976	1130,893	288,869
2010	154,973	128,616	283589
2011	149,864	124504	274,368
2012	130,497	109,209	239,706
2013	120,003	100,390	220,393

2.8 Care for Perinatal HIV Exposed New-Borns

2.8.1 Programmatic tools

PMTCT programs are a cascade of interventions put in place to minimize the risk of HIV transmission from an infected woman to her baby. Effective PMTCT services require women and their children to profusely access this continuum of care including ANC services and HIV testing, ART treatment for HIV infected women and their exposed infant, safe delivery practices and appropriate infant feeding option as well as early infant diagnosis and appropriate medical care for all the exposed babies (Padian et al., 2011).

2.8.2 Natural Course of HIV in Children

Although most HIV exposed children do not become infected with the virus, untreated HIV infection in infants deteriorates rapidly leading to high morbidity and mortality. As mentioned earlier in this chapter, multiple factors increase the risk of neonatal HIV acquisition. Data from studies around the world suggest that 65% of vertical transmission of HIV occurs during intrapartum (Landesman et al., 1996; Magder et al., 2005; Townsend et al., 2008; Birkhead et al., 2010a) if there are no PMTCT services (Davis et al., 2013). In the early 1990s, the probability of children with vertically transmitted HIV developing AIDS at age 3 was about 50%, and 90 percent mortality rate by age 10 (Pliner et al., 1998; Dollfus et al., 2010). However, less than a decade later, the proportion of AIDS cases in children declined to more than two-third, mainly because of innovative approaches in the management of perinatal exposure through PMTCT interventions Coovadia et al., 2012). Presently, the risk of transmission can vary from 1% to 33% relative to maternal disease conditions and interventions in place (Mofenson., 2002; Cotter et al., 2012).

The recommended approach for adult HIV management includes early identification of HIV, administration of ART with subsequent suppression of viral load to undetectable levels as well as prevention and protection from opportunistic infections (Brocklehurst., 2000; Nesheim et al., 2012). Although in theory, the practice of viral load suppression is ideal for both infants' and adults' HIV management, however management of HIV in children is a rapidly evolving domain with limited information (Krist and Crawford-Faucher, 2002). Many consensus panels and WHO have established fundamental guidelines for PMTCT of HIV while WHO and her partner organizations such as CDC regularly update these guidelines (Glick., 1994; Abrams et al., 2000; Easterbrook et al., 2014).

HIV infection in children differs somewhat from adult infection, thus, presenting two forms of new-born infection. The first form has the same pattern with adult infection, which shows a prolonged course and progressive staging that leads to AIDS over a span of one decade- typically eight to ten years. The second form is associated with a more aggressive and fast- paced deterioration of health with early manifestation of AIDS. This condition is characterized by an increased risk of opportunistic infection and early mortality in most cases (Krist and Crawford-Faucher., 2002).

Children are also uniquely different in the manner they respond to HIV infection. Early infection accentuates the risk of developing AIDS. Here, the timing of the acquisition plays an important role. Early infection is one that occurred in utero as opposed to infections that took place intrapartum or postpartum; and this population test positive to viral HIV particle within 48 hours of birth and also experience increased risk of degeneration secondary to HIV/AIDS (Bryson et al., 1992; Magder et al., 2005). In a French study that evaluated HIV infection in perinatally exposed infants, those with hepatosplenomegaly, lymphadenopathy, lower than 30% CD_4 count or a positive DNA polymerase chain reaction (PCR) test within few weeks of life were all associated with increased progression to AIDS (Krist and Crawford-Faucher., 2002). Furthermore, another clinical trial showed that high viral load in infants who also have low CD_4 count increased the relative risk of death in HIV infected children (Mofenson et al., 1997).

2.9 Core Intervention for HIV Exposed and Infected Children

2.9.1 ARV Treatment

All infants exposed to maternal HIV are recommended to commence antiretroviral (ARV) treatment as soon as possible to minimize the prenatal acquisition of the virus (Abrams et al.,

2000; Lallemant et al., 2004; Money et al., 2014). Starting from eight hours after birth, these neonates should receive 2mg/kg of zidovudine six-hourly or daily nevirapine for not less than six weeks. The landmark research, which reported the benefits of prophylactic treatment of vertically exposed new-borns, was the Paediatric AIDS Clinical Trial Group Protocol (ACTG 076) (Connor et al., 1995; McSherry et al., 1999). In the report, maternal treatment with appropriate ARV combination therapy during pregnancy and labour combined with the treatment of neonates with zidovudine/nevirapine remarkably reduced the relative risk of vertical HIV acquisition by 66 percent. In comparison, infants and their mothers who did not receive ARV treatment had 25 percent likelihoods of transmission while mother and infant pair who received the complete course of the ARV treatment had an 8.3 percent risk of transmission.

Another study evaluated the effectiveness of nevirapine for PMTCT (Guay et al., 1999). In the study, HIV infected pregnant women were treated with 200mg of an oral dose of nevirapine at the onset of labour and their infants received 2mg per kg nevirapine in a single dose within 72 hours of birth. This measure was reported to have a minimized perinatal transmission rate of 47%. The study was conducted in Uganda, a breastfeeding setting where most infants (98%) are breastfed. All the participating women in the study were antiretroviral naïve. Due to the benefits of nevirapine as demonstrated in the study conducted in Uganda-an African nation, consideration for more beneficial regimen (zidovudine versus nevirapine) for the infant should be based on the clinical scenario, of which specialty consultation should be sought regarding this decision.

 Ideally, an HIV-positive mother should receive ARV combination drug regimen of tenofovir disoproxil fumarate (TDF) plus lamivudine (3TC) or emtricitabine (FTC) plus efevarin (EFV).

TDF + 3TC (or FTC) + EFV combination is treatment of choice for pregnant treatment of ARV naïve women. The associated side effect of these treatments on infants is that of anaemia, which peaks at six weeks of life and eventually resolves on its own by twelve weeks of age without requiring treatment. The follow-up data from ACTG 076 did not report any long-term adverse effects of the treatment in pregnancy (Culnane et al., 1999; Nozyce et al., 2014).

2.9.2 Follow-Up HIV Testing for the HIV Exposed New-Borns.

In general, early identification of HIV infection is crucial to the successful management of cases, including the new-borns. In the early days of the epidemic, the only and widely available tests for HIV were the enzyme-linked immunosorbent assay (ELISA) and the Western blot, both can only detect HIV-specific immunoglobulin antibodies IgG. However, testing new-borns with these techniques have some challenges because the mother's IgG can cross the placental barrier and enter the new-born, remaining in the circulation and masking the serostatus of the child for up to 18months (Praharaj, 2006).

Currently, techniques for directly detecting HIV have emerged (Pilcher et al., 2010; Pilcher et al., 2013). Unlike the antibody based-screening tests, the HIV DNA polymerase chain reaction (PCR), p-24 core antigen level, as well as HIV RNA, are all capable of early detection of neonatal HIV infection. However, the widely recommended technique for testing infants born to HIV infected mothers is the HIV-DNA PCR. This approach has a sensitivity of 93.2 percent and specificity of 94.9 percent, even though the accuracy is somewhat lower for neonates (Nesheim et al., 1997; Ciaranello et al., 2011). In the first month of birth, HIV-DNA PCR has a positive predictive value of 55.8 percent for infants with low-risk exposure. This value appreciates to 83.2 percent from the second month. Although the HIV culture test has comparable results output with HIV-DNA PCR, the former is more expensive, and results are

not readily available until after two weeks (McIntosh et al., 1994; Lambert et al., 2003). The p-24 core antigen level is also useful; however, this technique has low specificity and false-positive results are higher than other techniques (Marianne Burgard et al., 1992; Nesheim et al., 1997; Ciaranello et al., 2011). The HIV-RNA level is handy in follow-up monitoring of known HIV-positive patients, but this is not generally recommended for testing infants due to its low sensitivity. HIV-DNA PCR should be performed on all HIV exposed infants, usually within 48 hours of delivery. The test should be repeated two-monthly until the child becomes six months. Care must be taken not to test the baby's cord blood during the first test as this may be contaminated with maternal blood and may result in inaccurate results. Two positive virology HIV test results from separate blood of the same patient are confirmatory HIV-positive test results (Fearon, 2005; Garcia-Prats et al., 2012). Two consecutive negative virology test results at ages one month and four have 95 percent chances that the infant is uninfected with HIV. Additionally, a negative ELISA result at eighteen months of age, when the mother's antibodies would have weaned out, rules out infection in exposed babies.

HIV infected infants should receive CD_4 test to evaluate their immune level, and a full blood count (FBC) to assess the side effect of the medications (Abrams et al., 2000; Ikeda et al., 2007). These tests should be regularly repeated every 3-4 months. The absolute CD_4 count level varies according to age but the percentage value does not; therefore, CD_4 percentage is a preferred measurement for evaluating infant's immune level (Rouet et al., 2006; Githinji et al., 2011).

2.9.3 Prophylactic Treatment for Pneumocystis Carinii Pneumonia

Pneumocystis carinii pneumonia is a common occurrence in HIV-infected children in their early life. The organism is a yeast-like fungus implicated in causing pneumonia with a

debilitating effect often resulting in the fatality of the infected children (Simonds et al., 1993). It is usually the first indicator of perinatal HIV infection. Children who are between the ages of 3-6 months are at the highest risk of infection (Gona et al., 2006). HIV infected children who are younger than one year can also experience the infection regardless of their CD_4 and lymphocyte counts (Simonds et al., 1995; Gona et al., 2006). It is recommended that all HIV exposed children should receive prophylactic treatment for *Pneumocystis carinii* pneumonia, six weeks after birth and continuing until HIV infection has been ruled out (Thea et al., 1996; Crozier, 2011). Trimethoprim-sulfamethoxazole (Bactrim, Septra) is a standard treatment for the etiologic agent of pneumocystis carinii pneumonia. Other medications such as dapsone and atovaquone can also be used as an alternative treatment. Owing to the side effect of the treatment, FBC should be performed before treatment and continuous monthly monitoring thereafter.

Ideally, the treatment should commence immediately after the 6weeks ART prophylactic treatment. Because no cases of Pneumocystis carinii pneumonia has ever been reported in ages lower than 4-weeks, treatment at this period is not encouraged (Masur et al., 2002). Moreover, drug interaction can exacerbate anaemia in children, hence the need to delay treatment until the recommended period. The prophylactic treatment Pneumocystis carinii pneumonia should be discontinued once the HIV test result confirms that the child is uninfected. However, for an HIV infected child, the treatment should continue regardless of the CD_4 count level until the age of 12months at which CD_4 count plays a determining role in the treatment.

2.9.4 Screening for Tuberculosis

One of the commonest opportunistic infections in an HIV infected person is tuberculosis (TB). The re-emergence of TB has coincided with the HIV epidemic and HIV exposed infants are susceptible to TB infection. All HIV infected women should receive screening for TB before delivery. Infants and indeed every child should be isolated from individuals who have active pulmonary TB pending full recovery of such a person that is when the individual is no longer contagious (Madhi et al., 2011).

Infants exposed to individuals with active pulmonary TB should be tested using purified protein derivative (PPD) skin test as well as a chest radiograph. Irrespective of test result outcome, all infants exposed to TB should be treated with isoniazid for three months. A repeat PPD test should be done and depending on the outcome, treatment may be discontinued. With a positive PPD, isoniazid prophylaxis should continue with the full course of treatment (Faix, 2007). All HIV infected children should be tested for PPD every year, beginning from twelve months of age.

2.9.5 General Medical Care for All HIV Exposed Infants.

Studies have provided conflicting reports on the association between low birth weight and preterm delivery in HIV infected women. However, low birth weight and pre-term delivery may accentuate risk factors for post-neonatal morbidity and mortality plus other adverse events such as neurological challenges. Thus, HIV exposed new-borns should be monitored closely for features of low birth weight and preterm delivery as well as postnatal exposure to infectious agents that might compromise their health. They should be screened for syphilis, hepatitis 'B' and hepatitis 'C', in cases where the mothers' status is unknown. If the mother's hepatitis 'B' surface antigen test is positive (HBsAg = positive), the new-born should be

administered with both hepatitis 'B' immunoglobulin and hepatitis 'B' vaccine at birth. The booster doses of the vaccine should be given at one month and six months of age. Additionally, HIV exposed infants require standard immunization protocol. This includes tetanus toxoids, Haemophilus influenza b conjugate vaccine, inactivated poliovirus vaccine, pertussis vaccine and hepatitis 'B' vaccine (Zimlich, 2018). Careful consideration must be taken when inoculating live virus vaccine to HIV exposed infants to ensure the safety of both the infants and their family members. The combination measles-mumps-rubella vaccine should only be given if their immune system can sustain it. Varicella vaccine can also be given if their immune system can cope with it. In all cases, the benefits of the immunization should be explained to the parents and parental consent should be sought before the exercise. The child should also be inoculated with the influenza vaccine every year starting from six months of birth until HIV infection has been excluded.

In general, immunocompromised children do not respond well to immunization. Because of this problem, infants born to HIV-positive mothers who have received vaccine-preventable diseases such as varicella, tetanus, and measles should be evaluated for passive immune prophylaxis, irrespective of their immunization status unless serologic assay proves enough antibody concentration. At every contact, the parents and caregivers should be educated, particularly concerning symptoms of HIV and opportunistic infections. HIV infected children are at increased susceptibility to bacterial infection; hence any sign of fever requires prompt evaluation and presumptive treatment until the cause has been fully established. Parents and other family members should be counselled about prevention exposure to opportunistic infections. For children in malaria-endemic areas, the use of insecticide-treated bed nets may reduce exposure. Other appropriate measures include proper cooking of food (reduce salmonellosis), boiled water (protect against giardiasis and cryptosporidiosis). Finally, these

children should receive a continuous assessment for nutritional intake, ensuring that mixed feeding is completely avoided in the first six months of life.

2.10 Impact of Paediatric HIV Exposure or Acquisition on Children.

2.10.1 Morbidity and Mortality

HIV epidemic has a considerable impact on the child's survival; either directly because of mother to child transmission or indirectly through HIV related morbidity and mortality among parents and caregivers. The scale of the problem regarding the challenges they encounter in life is enormous and these problems are intrinsically and intricately inter-dependent, starting from increased morbidity and mortality to psychosocial development challenges.

Survival and well-being of perinatal HIV exposed children largely depends on two conditions: their own HIV status and the health condition of their parents. Parental death may affect a child's well-being in different ways. Data on the impact of the mother's death on child survival concerning HIV are conflicting. While some studies reported adverse effect or child's death following maternal mortality (Brahmbhatt et al., 2006; Kuhn et al., 2008; Ndirangu et al., 2012), others did not find any effect(Ryder et al., 1994; Taha et al., 2000). Moreover, the loss of one parent to AIDS may likely be followed by the death of the other parent after perhaps a protracted illness if both are infected.

The longevity and cause of mortality in HIV exposed children differ by location. In low and middle-income countries, HIV/AIDS accounted for 2.1% deaths, and in sub-Saharan Africa, an average of 3.6% mortality rate in under-5 (Stanecki et al., 2010). Data obtained from Africa suggest mortality rates of 13-24% among HIV exposed infants and 20 to 32% for age 2years.

Within regions, mortality rates varied. In Uganda 68% and Rwanda 57% mortality rate among under-5 HIV-infected children (Dabis et al., 1995).

The loss of a parent is likely to result in impoverishment: parents being the breadwinner of the family. Orphaned children often face a loss of income; economic burden associated with medical care and funerals as well as reduced household and agricultural income. Additionally, they face psychosocial challenges ranging from stigmatization and discrimination within the community.

2.10.2 The Economic Impact

In many settings, especially in sub-Saharan Africa, the death of a parent diminishes the income of the orphaned households by 20 to 30% compared with none orphaned households (Foster and Williamson, 2000). Data from urban households in Cote d'Ivoire suggest that when a family member develops AIDS, the average household earning plummets to about 60% due to loss of income (Foster and Williamson, 2000). Asides this, the expenditure on health care increases four-folds and family savings depleted while caring for the sick; leading the family into bankruptcy. Similar studies report that orphaned households face food insufficiency, resulting in poor dietary intake to about 41% (Miller et al., 2006). Often, orphaned households embark on asset selling to pay medical bills and cover funeral costs. All these factors deepen their economic miseries.

2.10.3 Impact on Child Education

The HIV epidemic continues to bear negatively on child education. Children who are living with HIV and those affected but uninfected (lost paternal vs maternal vs dual or infected parent/parents) face increased developmental and educational disadvantage relative to other children (Guo et al., 2012; Parchure et al., 2016). Among the dominant factors that

mediate the impact of HIV on the education of this group are gender, poverty and parental loss (Guo et al., 2012). The underlying cause of their increased disadvantage to education borders on their health condition, recurrent illnesses and malnutrition (H. K. Singh et al., 2008) as well as HIV associated neurocognitive impairment (Laughton et al., 2013). In a study that evaluated the impact of HIV on the education of HIV infected or affected children in India, the authors reported that 4.8% of them either dropped out or never enrolled in school while 9.23% performed poorly and lagged behind age-appropriate standard (Parchure et al., 2016). The odd of being out of school or lagging far behind in class performance were higher for HIV-infected and affected children, and this was commonly associated with illness.

2.10.4 Psychosocial Impact of HIV on HIV Infected or Affected Children

HIV in children exposes them to experience the same stressors of terminal diseases. Neurological and neuropsychological developmental challenges (Manji and Miller, 2004) are among the initial neurological manifestations of the disease in children (Leserman, 2000; Mellins et al., 2003). They express signs of depression, anxiety, and feelings of isolation. Other conditions are anxiety disorder, attention-deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder and mood disorder. Data from a prospective cohort study found 67% of psychiatric disorders in HIV-infected children compared with 17% (Mellins et al., 2009). Children who grow up without the tender care and positive emotional support from their parents tend to express less empathy to others. Additionally, these children are often stigmatized. Stigmatization stems from a societal perception about HIV and its association with immoral behaviours (sexual promiscuity and intravenous drug use). Children also suffer associative stigma when their parents are known to be infected with HIV.

2.11 Chapter Summary

2.11.1 **Conclusion**

The first cases of HIV were identified among homosexual men in the USA in about three decades ago. The virus has thus spread to every part of the world with sub-Saharan Africa having the highest burden of the infection. Currently, 36.7 million people are living with HIV, worldwide, of whom 25.6 million live in LMIC. Women and children are disproportionately affected. As of 2016, 17.8million women and 2.1 million under-14 children were living with HIV. Most children become infected through their undiagnosed HIV-positive mother through MTCT. Both infected and affected children face untoward hardship ranging from socio-economic, morbidity, and mortality. Nigeria currently has the highest child infection in the world at 270,000. The virus destroys the CD4 T-helper cells rendering the immune system helpless and resulting in AIDS, giving the opportunistic infections a chance to overwhelm the body system. Morbidity and mortality from HIV related illnesses are most common in LMICs, including Nigeria.

Chapter 3 : The Testing, Diagnosis and Essential Prenatal Care for PMTCT of HIV

3.1 Introduction.

This chapter will present a brief description of the HIV test with a focus on pregnant women. The chapter also includes an overall goal of HIV testing. The current guideline for HIV testing in Nigeria concerning prenatal care and advances in test offers are discussed. Equally discussed in this chapter are the essential prenatal care with emphasis on the role of antenatal services.

3.2 A Brief Overview of the Epidemic.

Prenatal HIV infection is a threat to global childhood survival, particularly in developing countries where a high burden of infection exists, such as Nigeria. Historically, the prompt identification of HIV infection in pregnancy was of little benefit to both the woman and her unborn child who had a poor prognosis in the absence of ART treatment. Of late, evidence of public health benefits of testing and treatment have emerged following the advent of HIV medication.

Generally, about 30% of individuals living with HIV worldwide are unaware of their serostatus (UNAIDS, 2017a). In terms of pregnancy, approximately 90% of the global 1.5 million HIV-positive women who become pregnant each year reside in Africa. Less than half of them know their HIV status and 20% receive poor antenatal services: another situation that increases the risk of MTCT of HIV (UNAIDS., 2017). HIV testing rate among pregnant women increased from 26% in 2009 to 45% in 2016, but only 15% of young women aged 15-25 learned their HIV Status (UNAIDS, 2014e). Likewise, the number of women aged 15-49 acquiring HIV only dropped by 3% from 2009 to 2015 due to the low uptake of HIV tests (Wang et al., 2016).

Undiagnosed HIV in women carries two major consequences. First, the women are at greater risk of transmitting the virus to their unborn and breastfeeding babies and their sexual partners, as they are unable to take HIV medications, which inhibit viral replications and significantly reduces the risk of onward transmission (Hawkins et al., 2005). They cannot also make an informed decision about their sexual behaviours since they do not know their serostatus. In addition, women who receive a late HIV diagnosis face the risk of serious clinical illnesses, which may affect both her quality of life and that of her baby (Hawkins et al., 2005).

Most children who become infected with HIV acquire the virus from their HIV-positive mother during pregnancy, childbirth or breastfeeding (UNAIDS., 2016b). This happens when effective treatment is not established during the periods when infection can take place. Most children living with HIV live in LMICs, where HIV/AIDS remains a major cause of death in children (UNAIDS., 2016a). WHO estimates under-5 mortality rates among children born to HIV infected mothers to be between 2-5 times more than those born to HIV uninfected mothers (Boerma et al., 1998). More so, almost all these children die before five years of age in countries with high prevalence and lacking treatment program (Boerma et al., 1998; Adetunji, 2000). The drivers of high MTCT in sub-Saharan Africa, including Nigeria, are high rates of heterosexual transmission, suboptimal infection prevention measures (poor test acceptance during pregnancy and delivery) and limited access to overall HIV prevention interventions. Transmission risks ranged between 15% at 6-weeks and 26% at 18-months and 11% at 6-weeks and 18% at 18-months in 2010 and 2016 respectively. Figure 3.1 shows the trend of susceptibility and actual acquisition of childhood HIV within 6-weeks of delivery between 2010 and 2016.
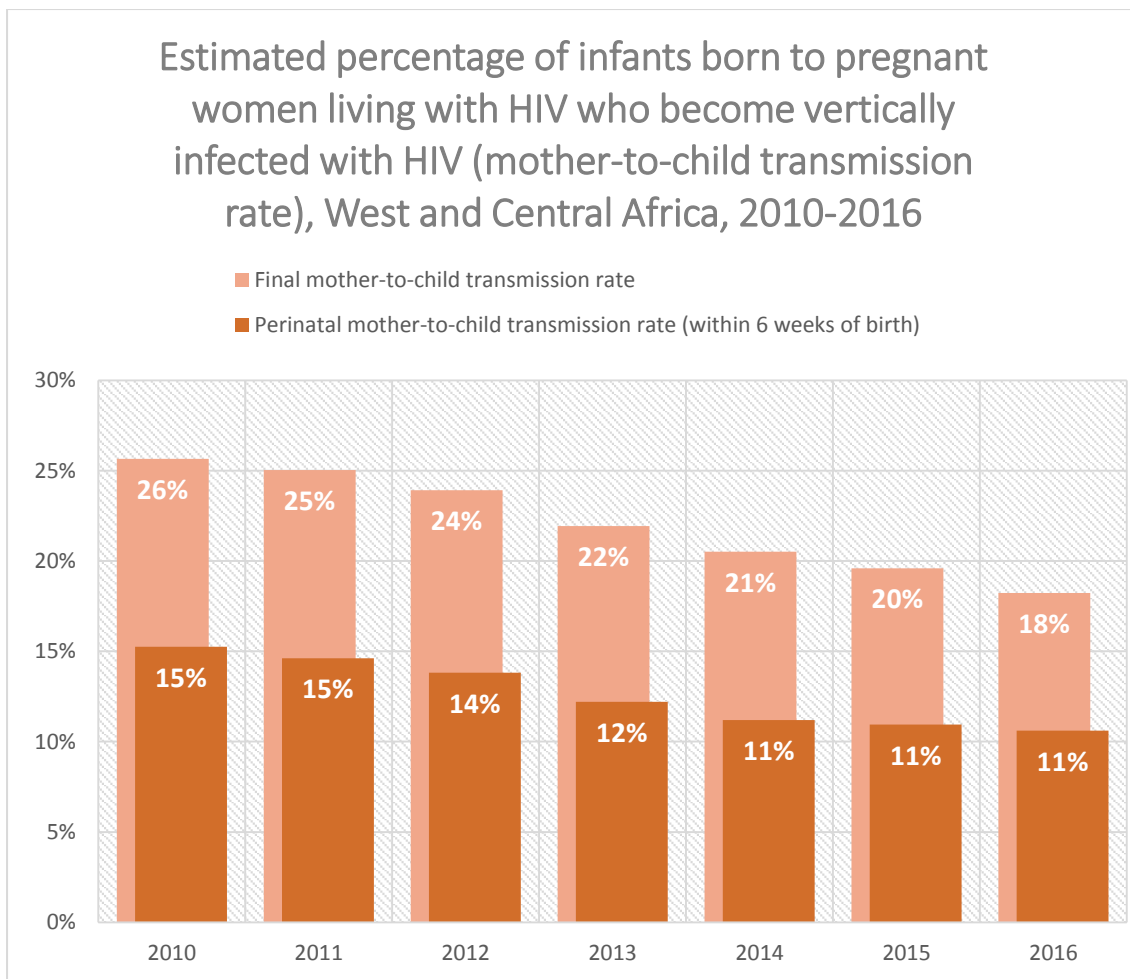
Figure 3-1 Infant exposure and final vertical transmission in West and Central Africa (UNAIDS, 2017b).

3.3 Screening – A Public Health Approach To Mitigating Spread Of Infectious Diseases .

3.3.1 Justification for Screening for Diseases Including HIV

Screening is an important tool for public health strategy in identifying the presence or absence of disease in people who are not manifesting symptoms of the disease so that treatment can be initiated early enough to mitigate the health impact of the disease, and for infectious diseases; steps can be taken to minimize the likelihood of transmission to others. HIV infection, like many other diseases, requires screening test because:

i. It is a serious and infectious disease that can be identified before symptoms manifest;

ii. Many infected pregnant mothers use health care but are not offered HIV screening until they become symptomatic;

iii. Early diagnoses before symptoms begin to manifest and treatment can prolong life and reduce transmission rates (Sheehy et al., 2009). Identifying women living with the virus and introducing potent ARV early in pregnancy can substantially reduce vertical transmission.

iv. There are non-invasive technologies to correctly diagnose the virus.

Screening can reduce morbidity and mortality from an HIV infected person. Undiagnosed individuals face a greater risk of morbidity and mortality from AIDS-related diseases, in addition to greater transmission rates of 3.5 folds than people who know their status (Gary Marks et al., 2006). Identifying individuals infected with HIV early helps to reduce these risks. For instance, in the United States, screening of blood before transfusion has nearly eliminated transfusion transmissible HIV (Dodd et al., 2002). In a like manner, knowledge of one's HIV-positive status can reduce one-third of onward transmissions to others. For instance, in a meta-analysis comprising nearly 20,000 participants, Weinhardt and colleagues (1999) reported that, following HIV counseling and testing, HIV-serodiscordant and seropositive couples reduced the rate of unprotected sex and increased the rate of condom use, hence reducing the couple risks of reinfection and transmission to others. More so, identifying and treating asymptomatic HIV infected pregnant women with potent ARV significantly reduces MTCT (Weinhardt et al., 1999). Overall HIV testing enables seropositive individuals to have medical care, improve their health outcomes and reduce both vertical and horizontal transmission.

Pregnant women need to be screened for HIV because:

First, there are potent antiretroviral drugs that concurrently improve the life of the infected mother and reduce transmission rates to the infant (Birkhead et al., 2010b; Nesheim et al., 2012). Second, ARV drugs are most effective when initiated as early as possible, certainly, before symptoms develop. Evidence shows that when ARV treatment is commenced during gestation, the transmission rate is reduced from 30% to less than 1% (Branson et al., 2006). Essentially, early diagnosis and prompt treatment with combination ARV drugs, results in better outcomes for the mother-infant pair (Chetty et al., 2012; Cherutich et al., 2012). Although, some studies reported an association between utero exposure to ARV drugs and risk of birth defect in HIV exposed children whose mother received treatment for PMTCT, the benefits of preventing transmission surpasses the side effects of the drugs (Tonwe-Gold et al., 2007; Pena et al., 2013; Sibiude et al., 2014).

3.4 Models of HIV Testing

3.4.1 Client-initiated VCT

Screening for HIV has evolved ever since the earliest report of the virus. For many years, the primary model of providing HIV test has been client-initiated VCT through static based centres, in which individuals actively seek HIV test from a health facility. This method is often bolstered with outreach testing activities through fairs in religious and public places and mobilization marketing to encourage individuals to test. Before the test is conducted, the individual receives pre-test counselling concerning the disease, test and treatment options, in the event the result turns out seropositive. Written informed consent is usually required before conducting the test. Although this medium has helped many people to learn their HIV status, it is a passive strategy for identifying infected individuals and may miss many people. Moreover, most testing use techniques and equipment that usually require two-weeks

waiting time between testing and availability of result, and facility-based testing are prone to lower rates of return for post-test counselling and receipt of result (Matovu and Makumbi, 2007). Largely, client-initiated VCT could not offer enough coverage and HIV testing remain low particularly in resource-constrained settings.

Often, individuals infected with HIV visit health care settings multiple times without receiving an HIV test. Empirical findings suggest that many opportunities to identify those infected with the virus exist (clinical settings, including ANC) but are often missed. For instance, Gunn et al., (2016) showed that only 60.7% of ANC attendees in sub-Saharan Africa received HIV test as part of prenatal care; and countries like Nigeria and Congo had 54.4% and 45.4% pregnant women respectively who received HIV test during ANC. In South Africa, the same problem of low-test acceptance persisted despite the wide availability of VCT and PMTCT services. Although the government mounted comprehensive treatment program, many South Africans remained unaware of their HIV status despite unacceptable prevalence rate of 30.2% among pregnant women (Tariq et al., 2018) and 10.6% for the adult population even though many of the people consulted their family physicians (Rehle et al., 2010; Zuma et al., 2016).

3.4.2 Provider Initiated Routine Opt-Out Testing

'Provider-initiated VCT' with the option of refusal is one of the alternative models for offering HIV screening as a continuum of care. With this method, HIV testing is normalized (Rice-Davies, 2016). The health care provider prescribes HIV testing to all patients as a standard of medical care after brief health education. Routine testing is a striking departure from long-standing "HIV exceptionalism" that has distinguished HIV testing from other communicable diseases in two discernible respects. First, the standard self-referral and second, the historical prerequisite for formal pre-test counselling and the requirement for the client's active

consent (signature) on forms (de Cock et al., 2003; WHO, 2007). Routine testing minimizes the task on clients to seek testing at VCT designated sites thus protecting clients from the potential stigma associated with accessing service at a known HIV testing centre. Moreover, for individuals who tested positive to HIV, and those requiring additional health-related services, routine testing has the additional benefit of being located within a health care facility where such service could easily be assessed.

3.4.3 Mandatory HIV Testing

Mandatory HIV testing is the screening of an individual for HIV without consent, confidentiality or privacy (Beggs and Jernigan, 2001). Mandatory testing is principally born out of the desire for the public interest. With this arrangement, the test result may be linked to the individual and unauthorized persons may have access to the information. Mandatory HIV testing is different from anonymous and unlinked HIV testing that is commonly in use in clinical practice. Ideally, mandatory screening for HIV is employed in investigating cases of sexual assault.

The Proponents of mandatory testing argue that it will protect patients and healthcare workers from occupational exposure. It will promote the early identification and treatment of infected individuals and halt the spread of the virus. They also argue that it will follow the same pattern with other mandatory medical screenings. Conversely, the opponents of this principle argue that coerced HIV testing is never acceptable, regardless of the source of the coercion from family member, health care provider or a partner. This group argued that mandatory testing violets the right of an individual to choose what is best for oneself. It is not to the public health interest, as this will undermine prevention efforts by driving a certain population to go underground into hiding. UNAIDS and WHO proscribe coerced testing except

in limited conditions such as screening for transfusion transmissible diseases (TTI) or any blood-borne diseases as well as the screening of donors for organ or bodily fluid transfer.

Traditionally, HIV exceptionalism has been the dominant approach for HIV testing in the early period of the epidemic when a lack of treatment and threat of stigma diminished the benefits of testing (WHO, 2007). However, with the advent of efficacious antiretroviral drugs (ARV), the United Kingdom (UK), the United States of America (USA) and many other developed countries have since implemented routine HIV testing, and routine testing is the standard of care both in clinical and ANC settings (Jamieson et al., 2007). Likewise, until recently, client-initiated VCT approach of HIV testing has largely remained the only strategy for HIV testing in many African countries and clearly outside the purview of standard medical care, leaving a large number of mothers untested and consequently many unborn babies vulnerable to HIV infection.

No country has ever reduced MTCT without first tackling the problem of HIV testing rates among pregnant women. The experience of Nigeria is not different from the rest of the world. HIV counselling and testing have been premised on client-initiated VCT technique, globally. In the 2007 NARHS Report, only 14.5% of Nigerians ever had HIV tests, leaving the majority of others unaware of their serostatus (FMOH/NACA, 2015). Though progress has been achieved, test acceptance remains suboptimal and constitutes a major barrier to effective PMTCT. The NARHS report of 2012 showed that 23.5% and 29.6% of men and women respectively have ever tested for HIV, of whom, 68% of men and 63% of women received post-test-counselling. Likewise, in 2014, the total number of individuals aged 15 years and above who underwent HIV test rose to 26%, an increase equivalent to 64.7% from the previous audit. Regardless of this improvement, over one-third of Nigerians was yet to receive an HIV test, an indication of

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the magnitude of the problem (NACA, 2015). Testing rates among pregnant women only doubled from 1,706,350 in 2013 to 3067514 in 2014, even though the failure of women to access test results due to the unavailability of rapid testing remained a significant challenge to PMTCT service delivery. Overall, nationwide, less than half (46%) of pregnant women have had testing and received their HIV test results. Access to other PMTCT services remained low at 30%. Of 222,129 pregnant HIV-positive women 63,350 received ARV prophylaxis to prevent MTCT in 2014, an increase of 9.5% from 57,871 in 2013 (NACA, 2015).

Available data show that often health care providers miss many opportunities to test women during pregnancy. From 2007 to 2009, the proportion of pregnant women who received HIV tests only increased from 3% to 13% notwithstanding 75% ANC attendance for at least once (Isezuo and Onayemi, 2004). Unpublished data from general hospitals suggest that more than 85% of pregnant women visit the health care facility to seek other medical care during pregnancy. A medical audit of ANC facilities in North Central Nigeria showed that 60% of women admitted in the postnatal ward had undiagnosed HIV during pregnancy, of whom 18% of their babies had perinatal HIV infection (Okechukwu et al., 2008).

3.5 WHO/CDC Recommendation for Testing Pregnant Women for HIV

3.5.1 The New Recommendation

To tackle the problem of testing, WHO and partner agencies such as UNAIDS and Centres for Disease Control (CDC) released new guidelines recommending 'Provider initiated opt-out' VCT, (routine testing) to all clinical and ANC settings. The goal of the new approach was to ensure equitable and universal access to HIV testing and counselling. In recent times, the standard approach for providing HIV testing and counselling has been client-initiated (self-referral) HIV testing and counselling. This approach is also known as voluntary counselling and

testing (VCT), in which individuals actively seek an HIV test at a health care or community outreach facility. Testing is only conducted after the individual has received comprehensive pre-test counselling and signed a consent form. However, uptake of client-initiated HIV testing and counselling is being diminished by low coverage of services, poor return rate, fear of stigma and discrimination, and the view by many people, including those in high HIV burdened communities that they are not at risk. According to the world health bodies, many opportunities to diagnose women in pregnancy are being lost, using client-initiated counselling and testing. Realizing the challenges inherent with a client-initiated testing approach, WHO/CDC reviewed the screening program and made new recommendations.

Tagged 'provider-initiated testing and counselling' with the right of refusal women are only tested for HIV after a brief health education during the antenatal clinic. Under this approach, HIV testing is regarded as a standard component of medical care.

Emerging evidence shows that this strategy has the potential to increase the uptake rate, improve access to care and support for women living with HIV. Also, based on WHO/UNAIDS findings, the new guidance will improve the mother's health and reduce paediatric transmissions. Accordingly, the protocol for testing under this model is as follows:

HIV screening forms part of the routine battery of prenatal medical screening during pregnancy.

HIV testing is conducted after the woman has been informed about the testing unless the woman declines (opt-out).

 Separate written consent is no longer required for testing; consent accrues from general consent from medical care.

In communities with a high prevalence rate among pregnant women, repeat testing is required in the third trimester.

3.5.2 Motivation for the New Guideline

The opt-out strategy of HIV testing and counselling has already been introduced in a variety of clinical settings in many low-income countries, such as Botswana, Malawi, Uganda and Zambia, Kenya. It is also in-use in pre-natal settings in developed countries parts of Canada, Thailand, the United Kingdom, and the United States. However, there are disparate success rates in and within different regions. Evidence to date indicates that the Client-initiated VCT approach could not attract enough people to test due to low coverage of services, fear of stigma and discrimination and feeling by many of the individuals, even among the high-risk population that they are not at risk. Although the United States and other developed countries experienced similar setbacks, these countries have successfully implemented routine ANC HIV testing and it is now the standard of care in those countries. The main justification for adopting routine testing was to improve HIV testing rates among ANC attendees; increase the number of pregnant women who learn their HIV status and for the infected mothers, gain access to PMTCT and support services.

Several studies have evaluated the effectiveness of provider-initiated routine opt-out HIV testing model in parts of the world. For instance, in 2004 in Botswana, following low antenatal HIV testing, routine screening was introduced as a strategy to improve testing rates among pregnant women in key ANC settings. After the intervention started, the testing uptake and the number of HIV-positive women who knew their serostatus increased to nearly double-folds (Creek et al., 2007). Between June-November 2005, Provider initiated VCT was implemented at four ANC facilities in Zimbabwe due to the low uptake of HIV tests. The findings showed that HIV testing among pregnant women increased from 65% during VCT

opt-in to 99.9% during opt-out with the corresponding higher number of identified HIV-positive women and case identification rates (Chandisarewa et al., 2007).

In some parts of the world such as Nigeria, South Africa, India, Mozambique and Kenya where routine testing is not rigorously implemented, MTCT continues to remain high due to the failure of the health care providers to offer HIV testing and other PMTCT services to all eligible clients. A study in New Zealand suggested that until the invention of a cure or vaccine for HIV, all health care providers have a role in reducing the burden of the infection (Rice-Davies, 2016). Given the different epidemiological and contextual situations, however, it is not possible to extrapolate results from the USA, UK or Zimbabwe to Nigeria.

The health care providers do indeed have opportunities to prescribe HIV testing to pregnant mothers. For instance, more than 60% of pregnant women in Nigeria attend at least one ANC visit and give birth in clinical settings thereby offering plenty of opportunities for the provision of HIV testing and other PMTCT services (WHO report: 'Opportunities for Africa's newborns., 2007). Besides, most women who do not utilize ANC services occasionally access healthcare services for other medical reasons. Therefore, this approach is a good medium to reach many mothers. This is especially important when currently at nationwide, approximately 17% of pregnant women in Nigeria receive HIV tests (Ekman et al., 2008). Hence, the adoption of innovative approaches that are feasible and acceptable is urgently required.

Concerns for the implication of adopting such a policy have been raised, specifically on how it affects women, as clearly more women than men would inevitably learn their HIV status, and this might result in violence against them. Some experts have also raised fears about the likelihood of poor application of routine testing principle of informed consent, and chances that women could be tested without their consent. Overall, broader or nationwide adoption

of such a policy requires more elaborate evidence-based findings from settings-specific context. Such considerations for attaining the finest or most 'efficient' level of HIV testing technique also requires evidence-based information on resource use associated with the different HIV testing techniques, and the level of benefits derived by the target population and the society in general. In Nigeria, there is growing consciousness that decision-makers should prudently allocate resources; individuals, groups and civil societies are beginning to hold the government accountable for equitable and prudent resource allocation. On their part, the government is beginning to respond by creating agencies charged with enforcing quality service at low costs. For instance, the 'SERVICOM' is a governmental agency born out of a commitment to ensure that customers receive value for money. The Nigeria ministry of health has a dedicated unit whose responsibility is to recommend health care interventions based on cost-effectiveness analysis.

As an essential part of the provision of quality clinical service based on value for money, this study examines the clinical and cost-effectiveness of two different approaches (Client-initiated VCT versus provider-initiated routine opt-out) for offering HIV-test to pregnant women.

3.6 HIV Counselling and Testing- A Tool for Demystify the Pandemic.

3.6.1 HIV Counselling and Testing: The Cornerstone to Prevention, Treatment and Support.

HIV testing and counselling is the linchpin to prevention treatment and support. To ensure that individuals can freely express their right to learn their HIV status and that persons with HIV can take advantage of improved access to antiretroviral (ARV) treatment provided in the 90-90-90 initiative, HIV testing and counselling must be substantially scaled-up. This must be done through ethical, innovative, and practical approaches to delivery. Testing and

counselling services must be easily accessible, especially in settings where those most likely to benefit from the knowledge of their HIV status can be accessed (ANC, tuberculosis, sexually transmitted infections, and acute medical care). Simultaneously, people who want to learn their HIV status should have good access to voluntary counselling and testing in a variety of venues.

HIV testing and awareness of one's HIV serostatus have both individual and public health benefits. Person-centred benefits arise mainly from the prospect to access care and treatment that can decrease HIV-related morbidity and mortality. HIV medical care, which happens after an individual has been tested and known his HIV status (either HIV-Positive or HIV negative status) may involve all or some of the following: prevention, primary medical care, and treatment of opportunistic infections, and treatment with antiretroviral medications. These have resulted in extensive reductions in adverse health outcomes, as well as a decrease in the incidence of opportunistic infections, and improved life expectancy (Marks et al., 2005; Branson., 2010; Cohen et al., 2011). The main public health advantage of testing is to reduce the spread of HIV due to decreased risk behaviours in individuals who know their infection status. In general, around three-quarters of HIV-infected persons are infected through sexual contact (Boily, 2009), and individuals who are aware of their HIV-positive status modify their transmission risk. In a meta-analysis, Marks and colleagues reported that high-risk sexual behaviour significantly reduced in individuals living with HIV who are aware of their infection to those who are undiagnosed of the infection. In another study, researchers found that HIV-infected individuals who are unaware of their serostatus account for approximately 70% of sexually transmitted HIV infections (Marks et al., 2006). They also have a transmission rate of more than three-folds more than individuals with known diagnoses.

Early identification of HIV is important because it creates an opportunity for timely access to care, which can reduce immunologic suppression and reduce the time people can transmit HIV. HIV testing at the onset of acute HIV infection (AHI) is mainly imperative because of the high level of risk of transmission during this phase (Cohen et al., 2011). AHI is the period of first 10–12 weeks following HIV acquisition when high levels of aggressive viral replication occur (Branson, 2010). During this period, the individual has a very infectious virus in plasma and genital secretions and persons with AHI frequently engage in sexual contact more often than those with later stages of infection (Rapatski et al., 2005). Individuals with AHI have more than ten-folds chances to transmit HIV per sex act and more than 25 times as likely to infect HIV as those with known HIV infection (Marks et al., 2005). Brenner and colleagues reported that individuals with new infections (i.e., people infected less than 6-months following seroconversion) accounted for almost half of onward HIV transmission.

Plasma HIV RNA levels are directly proportional to HIV transmission (Baeten et al., 2011), thus higher genital HIV RNA levels appear to be related to increased transmission rate as well. The administration of HAART has proven to be efficacious in the reduction of HIV RNA and has resulted in decreased transmission (de Martino et al., 2000; Sturt et al., 2010). This has led to a growing interest in using ART as an HIV prevention intervention due to its public health benefits. Experts have advocated the 'test and treat' model in resource-constraint settings to reduce HIV transmission and incidence rates. In a study using mathematical models, it was estimated that a policy of universal annual voluntary testing and followed with ART treatment could decrease HIV incidence to less than one case per 1000 individuals within 10 years and reduce HIV frequency to less than 1% in 50 years.

These points highlight HIV testing as a public health approach for preventing HIV that requires ardent attention. The scale-up is required to address equity of coverage, access to care and availability of quality interventions that can improve the over-all need for universal knowledge of HIV status. The approach must work within the confines of acceptable HCT conduct and should be tailored to the local epidemiology as well as other contextual issues. It must take full cognizance of the right-based approach to HIV testing: adhering to the human rights of individuals undergoing the test and maintaining the ethical principle of HIV testing and counselling (WHO Guidelines Approved by the Guidelines Review Committee, 2015).

3.6.2 The guiding principles for voluntary utilization of HCT services

Irrespective of the HCT model of service delivery, the fundamental principles regarding the five Cs, (Consent, confidentiality, correct test result and linkage to care) must be adhered to in all circumstances.

3.6.2.1 Consent

The general rule is that all individuals, including young adults, must make their own decision regarding having an HIV test, without being pressured or coerced. Dependent on the policy of the country, adolescents who have attained the legal age of consent or are deemed as mature minors can consent for an HIV test. The age of consent for HIV testing differs from place to place. In countries where the age of consent is not specified in national policies or guidelines on HIV/AIDS, countries may consider adopting the age of consent to medical procedures. Care providers need to understand the legal age of consent to test for HIV, as well as adolescents who are considered 'exceptions' to the standard age for consent policy, for example, 'mature minors' or pregnant adolescent girls, and be guided by the best interests of individual adolescents.

There are various policies guiding consent for HIV testing. In a certain type of HIV testing policy, specific consent for testing does not apply because general consent for medical care is considered to cover consent for HIV testing. Individuals receiving HCT must give their consent (verbal consent is sufficiently enough, and written consent may therefore not be required) to receive counselling and testing services before the test is conducted for them. The health care should explain to the client the process of HCT and their right to decline the offer. Regarding routine testing, the removal of the requirement for written informed consent may encourage individuals to participate in HIV testing.

3.6.2.2 Confidentiality

HCT services must be carried out in the spirit of confidentiality indicating that information exchanged during this period must not be disclosed to anybody else without the explicit permission of the client. Even though confidentiality must be maintained, this should not be used to reinforce stigma, secrecy or shame. The caregiver should ascertain who the client may wish to confide in (Family member or friend, shared confidentiality with a partner or even with an appointed health care provider- any of these is often highly beneficial) and the circumstance they would want this to be done.

3.6.2.3 Counselling

HCT services should be accompanied by a piece of well-articulated, high-quality pre-test information. This may be provided as a group pre-test health education with clear information about HIV and the benefits of testing. A couple or individualized testing can also be performed. Post-test counselling should follow receipt of the test result. It is highly recommended that facilities should incorporate quality assurance mechanism and mentoring system to ensure the provision of high-quality counselling. An effective HIV/AIDS counselling

should have a combination of respect, genuineness, and congruence, empowerment, and self-responsibility as well as confidentiality.

Here, respect means accepting the client by showing positive regards irrespective of the client's background (values or behaviour) and whether the counsellor approves of it. The client's rights to their personal feelings, beliefs, choices and opinions and refrain from being judgemental. Again, counselling should be honest and transparent. Being genuine and keeping the client's program in focus. Regarding empowerment and self-responsibility, clients are equipped to take charge of themselves, develop and use resources that will make them real agents of change in the counselling agenda including in their normal lives. Confidentiality is an important part of counselling. Under no conditions should a breach of confidentiality occur as it is vital to the preservation of trust between health care practitioners and their patients. Disclosure of the HIV status or any other data to anyone without the express consent of the client is illegal.

3.6.2.4 Correct Result

The Provision of correct results to the correct client is an essential component of HCT service delivery. Incorrect or poor-quality test result arises from multifaceted factor ranging from improper storage of test kits, poor product performance, and user error in conducting a test or in interpreting the test result, transcription or clerical errors misuse of the testing algorithm, lack of supportive supervision and training and lack of standard operating procedure (SOP). To address these challenges effective quality assurance mechanism must expand along HCT service to ensure the provision of a quality test result. This may involve both internal and external measures, and where necessary the support of the National

Reference Laboratory may be sought. This includes the provision of effective referrals to follow-up services as indicated, including long-term prevention and treatment support.

3.6.2.5 Linkages to appropriate care and treatment

HCT should link clients to appropriate care services to meet their individual health needs, as this is important in providing essential care. This involves referral to PMTCT services, support, and care as well as long-term treatment and prevention support. According to the WHO, timely "linkage to care" means an initial encounter with an HIV health care provider in no more than 90 days of diagnosis.

3.7 HIV Counselling and Testing Service Delivery Points.

3.7.1 Platforms for Delivering HIV Test.

Currently, there are various entry points for people to learn their HIV status within the HCT model. Most HCT strategies follow similar procedures. Typically, an HIV test is offered in one session, using a serial HIV testing algorithm. Pre-test and post-test counselling are provided involving basic HIV information, the testing procedure, risk reduction strategies and interpretation of positive and negative test results as well as partner notification and disclosure. Consent is inferred by implicit or explicit depending on the model. Referral for HIV care and treatment is provided for HIV-positive cases. Unless in rare circumstances, HIV testing is provided free, voluntarily and in private. Pregnant women are also encouraged to test with their partners (couples testing). An offer of HIV testing could be obtained in two broad ways: Client-initiated VCT (self-referral VCT) or provider-initiated VCT (Routine opt-out testing). Client-initiated VCT is the traditional HIV testing approach in which individuals voluntarily seek testing on personal motivation. With provider-initiated VCT, an HIV test is

given to individuals or a group of people with the option to refuse. Here consent is inferred implicitly.

3.7.2 Stand-alone HCT.

Stand-alone services are provided away from the health facilities, usually in freestanding centres. This is the conventional HCT strategy across the world. Stand-alone provides HCT to the general populace, including pregnant women who access it based on client-initiated VCT. In some circumstances, this approach provides additional HIV care and prevention services. Written or verbal consent is obtained from clients before an HIV test is performed. An incentive to this is that the counsellors are normally from the same community who understand the culture and values of the community. Clients receive comprehensive counselling with test results likely to be ready on the same day. The disadvantage is that service users are normally stigmatized thus discouraging individuals from seeking service. Individuals identified with HIV are referred to local health centres for treatment and follow-up, and for pregnant mothers, to PMTCT centres.

3.7.3 Integrated Health Facility Model.

HCT Integrated service is a method in which HCT is given alongside other subsidiary services such as maternal child health (MCH), STIs, tuberculosis and family planning. In most cases, HCT is given through provider-initiated opt-in, where the client is required to give written consent. Although this provides a convenient way of delivering HIV testing, individuals whose lifestyle suggests exposure to infection may intentionally avoid using such facilities to avoid being isolated and tested. Linkages to HIV treatment and care can be expedited with the on-site treatment centre, although prognosis may be poor if the patient is already in advanced stages of HIV infection.

3.7.4 Mobile Outreach or Door-To-Door HCT.

Mobile outreach HCT is generally a home-based provider-initiated HIV testing strategy. An HCT mobile team moves from door to door offering counselling and testing to clients at home. The community campaigners ensure that all family is well mobilized. Door-to-door HCT is delivered to all willing adults and under-15 children, especially those whose mother is living with HIV, unknown status or deceased. This method specifically targets certain populations, such as Hard to reach (nomads, fishermen, women in purdah, people living in remote areas) and most at-risk populations such as men who sleep with men (MSM), intravenous drug users (IDU) and those incarcerated (prisoners). Using this method, previously underserved populations and rural communities receive HCT. Moreover, family members provide support for one another, in case of a positive test result. However, a decline of the test by the family head may discourage the rest members form testing. Those who are HIV-positive are referred to the local health centre for care and treatment. Infected pregnant women receive PMTCT interventions.

3.7.5 Couple HIV Testing

Couple counselling and testing is the simultaneous offering of HIV counselling and testing to two or more individuals who are in or in the process of starting an intimate relationship. In couple testing, both partners (husband and wife or sex partners) receive pre-test counselling together, blood sample drawn for test and both parties receive test results and post-test counselling together. The benefits of partners learning their HIV test results together are numerous. First, it helps them to support each other, especially if one or both partners turn out HIV-positive. Second, it also enables them to support each other in accessing and adhering to ART regimen for their own health as well as for PMTCT. In the case of serodiscordant

partners, the HIV negative can take preventive measures, using the ART regimen for prophylaxis. Couple testing is equally helpful for a partner to make an informed decision regarding reproductive health and family planning.

3.8 Benefits of HIV Testing.

3.8.1 Role of HIV Testing.

Achieving the sustainable goal of prevention and treatment is anchored on knowing one's HIV serostatus, making HIV testing services a vital entry point to a continuum of care. A comprehensive HIV testing service includes counselling, linkage to appropriate care as well as laboratory quality assurance. The benefits of testing depend on the quality of services offered to the clients and close collaboration with other health services. Through linkages with other health services such as treatment and support programs, HIV testing is an important weapon that diminishes the impact of the HIV epidemic in any society (De Cock et al., 2006).

The benefits of HIV testing are numerous. Testing is a strong tool against stigma and discrimination. Through testing both the infected and the affected receive psychosocial support and the infected are connected to appropriate care and support services. Most importantly, the value of counselling and testing lies in linking individuals to services that are accessible, acceptable and effective. Undiagnosed or late HIV testing is associated with poor testing outcomes, including worsening health condition, death (de Souza-Thomas et al., 2005), and poor response to ART (Stöhr et al., 2007) and the expensive cost to health care services (Krentz et al., 2004).

Testing for HIV started in the latter part of the 1980s when there was virtually no effective treatment and fear and frustration abound. During this period, testing for HIV was synonymous with a 'death sentence' because of the stigma associated with a positive HIV-

result. A certain group of people who are regarded as high-risk individuals such as gay men discouraged members from testing due to the associated stigma and discrimination against homosexual men. Some opinion leaders joined in discouraging people from testing, as there was no treatment for the virus. Those who tested positive experienced intense psychological distress. Testing for HIV was, therefore, viewed as ineffective intervention, which carried risk, and with no obvious clinical benefits.

Following the advent of highly active antiretroviral therapy (HAART), the clinical response changed considerably with emphasis on the need for people to take an HIV test, and of course, take the test regularly at least once in a year. For the pregnant woman, an initial test in the first trimester and a repeat test in the third trimester for women who tested negative (Lockman and Creek, 2009). This is because early detection of the virus results in better health outcomes when antiretroviral treatment is commenced concomitantly with the diagnosis. Moreover, timely treatment reduces the risk of vertical transmission, which doubles in the new acquisition of HIV during pregnancy (Lockman and Creek, 2009). A report from a meta-analysis of clinical trials in African countries suggested that prior to the advent of ARV treatment, child mortality due to HIV- associated-illnesses was 35.2% in the first year of life and 52.5% in the second year of life (Newell et al., 2004). In this review, child mortality differed according to geographical location and was related to maternal death and low CD4 count (<200µl), including child HIV infection and timing. There is a strong correlation in the survival rate of children who acquired the infection from their HIV-infected mothers receiving HIV treatment compared to their counterparts whose mothers are not on treatment (Brahmbhatt et al., 2006). Children with late infection had a better prognosis compared with those with early infection thus demonstrating the need for effective PMTCT, early infant diagnosis and support for the infants and their families.

3.9 Devices for Testing HIV

There are now wide varieties of HIV screening tests available worldwide, including in Nigeria. A diagnosis of HIV is conventionally determined through a serological investigation. While most HIV testing devices rely on body fluid, usually blood to detect antibody or to detect P-24 antigen to HIV-1 or HIV-2 others utilize saliva, urine or other body fluids. Many of these devices can produce test results within a short time, making it possible for the same-day result. Serologic assays for testing HIV-1/2 antibodies and detection of HIV-1 P-24 antigen are broadly categorized into two: the first line assays or screening assays and the second- and third-line assays also known as the confirmatory and tiebreaker assays, respectively. The first line assay usually has high specificity and is used to make a presumptive diagnosis when a reactive test result occurs. The second- and third-line assays are used to double-check the outcome of a first-line assay. Simple assays, rapid diagnostic tests (RDTs) and enzyme linked-immune-assays (EIAs) may all serve as presumptive test assays (first line). These set-ups may also be used as second or confirmatory assays depending on the circumstance. The third line assay (tiebreaker) is normally invoked to resolve discordant test results.

3.9.1 Rapid Diagnostic Test Device

Rapid diagnostic tests use either immuno-chromatographic (lateral-flow) or immune-filtration technique to detect the presence of HIV-1/2 or p-24 antigen to HIV-1. Specimens for this test include finger-prick capillary blood, venous whole blood, whole blood, serum, plasma or oral fluid such as saliva. Generally, results from immuno-chromatographic and immuno-filtration-based assays can be ready within 30min and 5min respectively. However, these results are obtained from colour band formation, which is subjectively read, culminating in the possibility of individuals with colour blindness wrongly interpreting the test result. These

formats are ideal for use in both facility and community-based testing centres as well as stand-alone health centres.

RDTs are recommended for resource-limited settings due to its simplicity, quick turnaround time and low cost compared with laboratory-based diagnostics such as western blots and EIAs. Aside from the cost, the test procedure is straightforward and can be performed by a layperson with high accuracy after receiving minimal training. Additionally, it uses neither cold chain reagents nor expensive equipment requiring highly skilled maintenance.

3.9.2 Simple Assays

Another diagnostic tool is the simple instrument-free assay, which is like RDTs except that it requires a cold chain. Some of the examples of this kind of assay include latex agglutination and combo assays, which detect the presence of either or both HIV-1/2 antibodies and HIV-1p24 antigen. It also requires precision use of pipette, requiring a higher level of skills than RDTs. Simple assays are less rapid than RDTs and require between 30 minutes to two hours to be performed. As for RDTs, simple assays are read visually by the user/operator.

Essentially, simple assays require venous whole blood of which drawing the blood sample requires a phlebotomist to draws the appropriate specimen. Capillary blood or oral fluid cannot be used in this type of assay. Moreover, simple assays are not as quick as RDTs. As with RDTs, the simple assay requires visual reading of the result. This technique is most appropriate for laboratory or facility-based testing.

3.9.3 Enzyme immuno-assay technique

Enzyme immunoassay for detection of HIV is typically a laboratory-based technique for identifying antibodies to HIV-1/2 and or HIV-1p24 antigen. These are mainly used in health

centres with large specimen turnover. This format requires expensive equipment and highly skilled personnel to perform the test. Besides whole blood, it may also require processing the sample further to obtain serum or plasma. In other words, EIAs require experienced and proficient staff to process the test. Some EIAs are fully automated and results obtained from this technique very accurate due to the ability to successfully detect both antigen and antibodies to HIV. The WHO endorses a national algorithm that includes RTDs, simple assays or EIAs.

Yet, meeting the demand creation for HIV testing is still a challenge. Currently, many pregnant women with HIV in Nigeria do not know that they are infected, and the few who do, often learn their status late when they are seriously immunocompromised, leading to poor health outcomes and continuing transmission in both vertical and horizontal routes. Therefore, the WHO as a body continues to modify and recommend new guidelines for HIV testing in order to address the challenges inherent in the current approaches.

3.9.4 Guidelines on HIV testing in Nigeria.

The current National HIV/AIDS preventive policy recognizes that all Nigerians have an inalienable right to know their HIV status. This guideline stipulates the provision of testing centres at strategic points within the community and making services available and accessible to individuals in need. HCT is anchored on written or verbal consent that is aligned with the client-initiated VCT approach and follows a serial testing algorithm with appropriate referral to prevention, care, and treatment. While stand-alone HCT is currently the dominant approach, the service can be used to address the broader health needs of the community, such as unmet maternal child health, family planning and the likelihood of STIs and sexually reproductive related needs.

3.9.5 Impact of the Current Testing Policy on Test Acceptance

Historically, HCT has been premised on client-initiated VCT technique in Nigeria. HCT is the linchpin to PMTCT and various HIV prevention services such as treatment, care, and support. It provides opportunities for individuals to learn about HIV and AIDS, know their serostatus, behavioural changes and strategies to cope with a positive result. However, with the client-initiated VCT approach, HIV test acceptance continues to be suboptimal. In the 2007 NARHS Report, only 14.5% of Nigerians ever had HIV tests, leaving the majority of others unaware of their serostatus (NARHS., 2015). Likewise, the NARHS report of 2012, showed marginal improvement: 23.5% and 29.6%, HIV testing rates for men and women respectively, of whom, 68% of men and 63% of women received post-test-counselling (NACA., 2015b). Equally, in 2014, the total number of individuals aged 15 years and above who underwent HIV test rose to 26% an equivalence 64.7% rise from the previous audit report. Despite this improvement, over one-third of Nigerians have never had an HIV test, an indication of the magnitude of the problem (NACA., 2015). Testing rates among pregnant women doubled from 1,706,350 in 2013 to 3067514 in 2014, but many of the tested women could not receive test results due to the need for a return visit (NACA., 2015b). Overall, nationwide less than half(46%) of pregnant women have had and received HIV test results (NACA., 2015). Low uptake of HIV testing among pregnant women constitutes a major challenge to access PMTCT services including ARV drugs and support services. Because of these challenges, access to other PMTCT services has remained low at 30%. In 2014, of 222,129 pregnant HIV-positive women, only 63,350 received ARV prophylaxis for PMTCT, an increase of 9.5% compared to 57,871 compared with the previous year in 2013 (NACA., 2015).

Screening for HIV has evolved since the earliest report of the virus. For many years, HIV "exceptionalism" has dominated the centre stage of HIV testing giving rise to poor public health approaches. According to Bayer and colleagues, HIV exceptionalism is the idea of treating HIV/AIDS differently from other STIs or lethal infectious diseases. One such way is through testing involving client-initiated VCT, in which individuals actively seek HIV tests on their own volition from either stand-alone centres or health care facilities. Before the test is conducted, the individual receives pre-test counselling concerning the disease, test and treatment options, in the event the result turns out seropositive. Written informed consent is usually required before conducting the test. This medium, though, has helped many people to learn their HIV status but it is limited in coverage. VCT could not offer enough coverage because the method is premised on the strict requirement of various items different from conventional medical consultation and patients are often stigmatized.

Second, health care providers are presumably more knowledgeable in their disciplines than the patient does. Yet, HIV testing is left in the hands of inexpert client to initiate whether to or not to have the test without formal health education by health professionals. The likely implication is that many people who would have been diagnosed on time are left to report only when their health condition has deteriorated from AIDS-related illnesses.

Third, naturally, doctors and other health professionals, depending on their specialties anyway, are empowered to discuss serious medical issues and identify an important course of action, including tests for the patients without undue bureaucratic bottlenecks. In most cases particularly in developing countries, the HIV test still requires signing a consent form, a requirement that does not apply to other medical tests. In so doing, the HIV test is isolated from other medical investigations, thereby creating fear and disincentive in the minds of

potential patients. That is not all; patients are often subjected to long waiting hours at the VCT centres before they receive HIV counselling and subsequently asked to return later for receipt of results and post counselling. The need for a repeat visit at a later period for post-test counselling is another disincentive for clients who live some long distances away from the VCT sites, considering the cost in both financial and workforce time. Because of these difficulties, many people especially pregnant women who have serious medical needs to undergo an HIV test failed to do so. Often, individuals infected with HIV visit health care settings multiple times without receiving an HIV test. Empirical findings suggest that many opportunities to identify those infected with the virus do exist in clinical and ANC settings, but are often missed. For instance, Gunn et al., (2016) showed that only 60.7% of ANC attendees in sub-Saharan Africa received HIV test as part of prenatal care; and countries like Nigeria and Congo had 54.4% and 45.4% pregnant women respectively who received HIV test during ANC despite an average of 70% ANC attendance. In South Africa, a similar problem of low-test acceptance persisted even when HCT and PMTCT services were available. The report showed that despite government commitment in the provision of comprehensive HIV treatment program, due to high prevalence of HIV: 30.2% among pregnant women (Barron et al., 2013) and 10.6% for the general adult population, up to half of the individuals who consulted their family physicians never sought for testing (Rehle et al., 2010; Shisana et al., 2016). Figure 3.2 below, shows a graphical illustration of testing rates among pregnant women in the twenty-two priority countries.
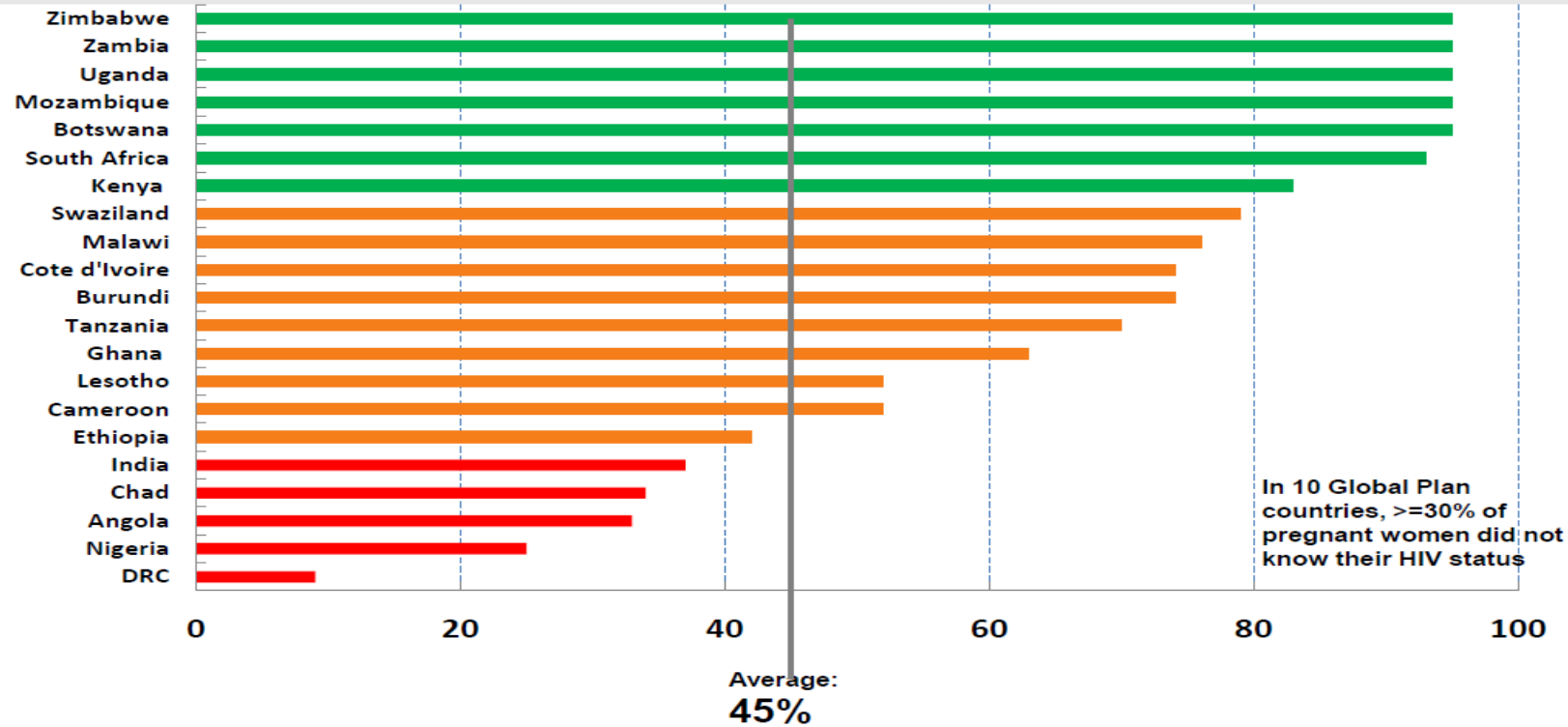
Figure 3-2 A comparison of HIV testing rate in the twenty-two priority countries.

In Nigeria, from 2007 to 2009, the proportion of pregnant women who received HIV tests only increased from 3% to 13% notwithstanding 61% ANC attendance for at least once (Isezuo and Onayemi, 2004; National Population Commission, 2014). Unpublished data from general hospitals showed that more than 85% of pregnant women visit health care facilities to establish their pregnancy during the first trimester. A medical audit of ANC facilities in North Central Nigeria showed that 60% of women admitted in the postnatal ward had undiagnosed HIV during pregnancy, of whom 18% of their babies had perinatal HIV infection (unpublished data, n.d).

HIV is now regarded as a chronic disease, of which a considerable number of infected individuals remain healthy on treatment. Potent combination antiretroviral drugs can concurrently improve the life of the infected mother and reduce paediatric HIV transmission, even in breastfeeding populations (Birkhead et al., 2010b; Nesheim et al., 2012). ARV drugs are most effective when initiated as early as possible, certainly, before symptoms develop. Evidence shows that when ARV is commenced during gestation, the transmission rate is reduced from 30% to less than 1%. Essentially, early diagnosis and prompt treatment with combination ARV drugs result in better outcomes for the mother-infant pair (Coovadia et al., 2012). Although, some studies reported an association between utero exposure to ARV drugs and risk of birth defect in HIV exposed children whose mother received treatment for PMTCT, the benefits of preventing transmission surpasses the side effects of the drugs (Tonwe-Gold et al., 2007; Sibiude et al., 2014).

The public health approach is now paradoxical: while most industrialized countries, where HIV prevalence is low are achieving universal HIV testing, the reverse is the case in parts of Africa, where prevalence is high. Many women in Nigeria are undiagnosed of their HIV

infection and this remains a threat to the risk of passing the virus unknowingly to the unborn child. With a substantial number of HIV-infected mothers going untested or untreated, the repercussion is daring, and the current testing approach has a minimal effect at the population level. Provision of ART treatment to all mothers has been suggested and might be plausible if HIV screening has not been possible, but it stands a less than ideal solution if used to avoid HIV testing due to health risks associated with the regimen.

Evidence to date indicates that the Client-initiated opt-in approach could not attract enough people to test due to low coverage of services, fear of stigma and discrimination and feeling by many of the individuals, even among the high-risk ones that they are not at risk. No country has ever reduced MTCT without first tackling the problem of HIV test acceptance, particularly among pregnant women. In Nigeria, the burden of HIV among women attending antenatal clinics (ANC) was 4.6% in 2008 and approximately 190,000 (15%) HIV-positive mothers (15%) out of 6 million women give birth annually. The greatest risk of HIV infection for a Nigerian child is MTCT. The experience of Nigeria is not different from the rest of the world. In sub-Saharan Africa, without any prevention, around 16.5-26.4% of children who are born to HIV infected mothers will contract the virus during the peripartum period. Table 3.1 below, presents the factors that drive MTCT in the hardest-hit countries. From the table, it is obvious that there is a strong association between the uptake of ART regimen for PMTCT and reduction in transmission rate. For instance, South Africa recorded 90% ARV coverage and transmission rate has been reduced to 6%. On the other hand, in Cameroon, ART coverage is only 61% while the transmission rate is as high as 25%. But, the result of the effectiveness of HAART was derived from data from the trial and carefully supervised population studies, which report findings based on investigations different from the realities of whole healthcare systems. Nigeria had only 27% ART for PMTCT coverage in 2013.

Table 3-1 Uptake of interventions for PMTCT in the first eight priority countries

What does the data tell us in 8 countries contributing to up to 68% of new infections in 2013:

Countryb	No. HIV+ pregnant women delivering (% of total Global Plan pop), 2013	Mother to child transmission (MTCT) rate overall , 2013	MTCT rate at 6 weeks, 2013	Number of new infections (% Global Plan burden), 2013	ARVs for PMTCT coverage , 2013	PMTCT regimen policy as of July
South Africa	260,000 (20%)	6%	3%	16,000 (8%)	90%	B+ (early)
Nigeria	190,000 (15%)	26%	14%	51,000 (26%)	27%	B
Kenya	79,000 (6%)	16%	7%	13,000 (6%)	63%	B+ (early)
Mozambique	100,000 (8%)	12%	5%	12,000 (6%)	84%	B+ (scale up)
Uganda	120,000 (9%)	13%	6%	16,000 (8%)	75%	B+ (national)
Tanzania	100,000 (8%)	16%	7%	16,000 (8%)	73%	B+ (scale up)
Zambia	78,000 (6%)	15%	4%	12,000 (6%)	76%	B+ (early)
Cameroon	38,000 (3%)	25%	10%	9,500 (4%)	61%	B+ (early)

Source: UNICEF analysis of UNAIDS, 2013 HIV and AIDS estimates, August 2014.

3.10 ANC service

3.10.1 Outline of ANC Service Delivery in Nigeria

In recent years, ANC service coverage has gained momentum in Africa region, with over two-thirds of pregnant women accessing at least one ANC visit during the entire period of pregnancy (Ornella et al., 2012). However, the full benefits of the life-saving potential of ANC for both the mother and the baby can only be achieved when the woman attends a minimum of four visits, which enables her access to the full package of essential ANC interventions (Ornella et al., 2012; Tunçalp et al., 2017).

Worldwide, approximately 529,000 women die every year from complications resulting from pregnancy and childbirth. In Nigeria, almost 59,000 pregnant women die from preventable pregnancy-related complications. In fact, a Nigerian woman plus her unborn baby is 500 times more likely to die during childbirth compared to her European counterpart (Alkema et al., 2016). Within Nigeria, mortality ratio is about 800-1500/100,000 live births with stark variation across geo-political zones (165 in southwest compared with 1549 in the Northeast) as well as urban and rural settings. According to the Ministry of Health, a significant proportion of these deaths are preventable with judicious utilization of ANC services. As an indispensable link to the continuum of care, ANC presents opportunities to deliver effective maternal-child health interventions to reach many pregnant women. According to national statistical data, ANC utilization in Nigeria is 61% on average although women in North-west Nigeria access the lowest ANC attendance at 41%, and only 12% deliver with the support of skilled birth attendants (National Population Commission (NPC) and ICF International, 2014). In the South-Eastern part, more than 91% of the pregnant women utilize ANC and 82% of them assisted by skilled birth attendants (SBA) during delivery. Similarly, a high level of

utilization is documented in the South-West with 90% and 83% ANC visits and SBA assisted delivery respectively. These stark differences in service utilization may be related to differences in cultural practices, varying levels of education, religion and socio-economic structures. Notably, delivery at herbal settings and outside the health facility without a skilled birth attendant is practically a norm in the northern region (NACA, 2015b).

ANC is a vehicle for the delivery of multiple intervention programs aimed at minimizing prenatal health risks and improving the woman's health during pregnancy and childbirth. ANC provides a vital opportunity for regular check-ups, which allows midwives or doctors to identify health treat and prevent potential health challenges during pregnancy. It is an opportunity to encourage healthy lifestyles that benefit both the mother and her unborn child (Ornella et al., 2012). The full utilization of antennal health care services contributes to optimal health outcomes for the mother-infant pair. Essential ANC service involves the identification and management of obstetric complications such as preeclampsia, and management of communicable diseases such as HIV, syphilis and other sexually Transmitted Diseases (STI's). This framework also presents an opportunity to encourage healthy behaviours such as safe sex practices, appropriate breastfeeding options for HIV positive mothers, the use of skilled attendants at birth as well as planning for optimal birth spacing (Schild et al., 2008).

The WHO recommends that PMTCT services should be fully integrated into the ANC program. In line with this guideline, many countries have adopted and adapted the WHO approach, and HIV screening is offered to all pregnant women on opt-out strategy during the ANC visit. In addition, there are strong political commitments and increased resource allocation to PMTCT interventions. This is because the HIV pandemic is eroding the hard-earned gains of child

survival that was recorded in the past decades. Success stories have already been recorded where countries are at the level of the elimination stage. Cuba took the lead when in 2015; it received validation for the elimination of vertical transmission of HIV. Thailand and Belarus are countries that have followed the trend of eliminating MTCT following the implementation of the WHO recommendations concerning integrating PMTCT interventions into ANC.

Nigeria is yet to develop a policy framework based on these WHO guidelines. Currently, the PMTCT program is still fragmented and mostly offered as a 'stand-alone' program. The first PMTCT program was initiated in 2002, in six tertiary institutions across the six geopolitical zones of the country. This was later scaled up to eleven centres at the end of 2003. In 2010, the program recorded an accelerated expansion and strengthening of service through decentralization and integration into primary health services. Two years later, a strategic plan for widespread scale-up was developed, and twelve states plus FCT, which combined bear 70% of the nation's MTCT epidemic, was selected for the piloting.

A review of the performance of PMTCT services in the country suggested a remarkable improvement in the number of pregnant women who received counselling and testing from 1,706,502 in 2013 to 3,067,514 in 2014, indicating 79.8% increase (National Population Commission (NPC) and ICF International, 2014). Similarly, the proportion of pregnant women who are living with HIV and receiving ARV treatment for PMTCT increased from 57871 to 63350, an increase of about 9.5%. In addition, in 2014, the figure for HIV positive pregnant women who received counselling for family planning doubled. Notwithstanding, the coverage and utilization of PMTCT services remain unacceptably low at 30.3% due to poor testing rates (National Population Commission (NPC) and ICF International, 2014). This shortfall demands

an aggressive and pragmatic approach to accelerate PMTCT services in the country, perhaps the type that follows WHO recommendation (Dans et al., 2007).

3.10.2 The Role of Antenatal Care (ANC) in the Delivery of PMTCT Services

Pregnancy is an important period in a woman's life and presents an important opportunity to promote healthy behaviours and good parenting (Ornella et al., 2012)). Antenatal care (ANC) is one such unique public health interventions through which women receive essential medical care during pregnancy. The provision of good care to the pregnant woman is essential for the health of the mother and the proper development of the infant. Good ANC service is a gateway for the pregnant mother and her family to access healthcare services including the services of trained skilled attendants which contribute to the quality of care in pregnancy (Ornella et al., 2012; Tunçalp et al., 2017). Antenatal care allows the woman to receive focused care; screening for health risk, prevention, and management of pregnancy-related or concurrent diseases, health education and health promotion (Tunçalp et al., 2017). Moreover, ANC plays a critical role in reducing maternal and child mortality and morbidity through prompt detection and treatment of pregnancy-related complications and prompt isolation of pregnant women who have high chances of developing complications during labour and delivery and linking them to an appropriate level of care (Carroli et al., 2001). Again, because communicable diseases such as HIV and malaria are important causes of maternal morbidity and mortality resulting in approximately 25% of maternal deaths, ANC provides an essential platform to manage concurrent diseases through an organized service delivery (Souza et al., 2013).

Essentially, in low-middle-income countries (LMICs), ANC utilization has nearly doubled after the introduction of the WHO model of ANC (Tunçalp et al., 2017). This model is a high impact

goal-oriented approach, which is rooted in evidence-based research performed at four important periods during pregnancy. However, worldwide, during the periods of 2007 to 2014, approximately 64% of pregnant women utilized at least four standard visits recommended by WHO (Villar et al., 2001). Simkhada and colleagues (2008) in a review identified six main barriers to access of ANC, although context and country-specific, which include availability, accessibility, affordability, cultural norms and patriarchal (where male partner decide for the woman) (Simkhada et al., 2008). However, the authors suggest that formative education is a panacea to women's full participation in ANC. This implies that much still needs to be done regarding mediating factors that impede access to these essential services.

3.11 Factors That Influence HIV Testing

3.11.1 Factors That Impact on Test Acceptance

Barriers to HIV testing uptake are factors that limit individuals from seeking HIV tests. Conversely, the enablers of test acceptance are the strategies that encourage HIV test acceptance in society. Understanding these factors and addressing the issues that deter individuals from seeking HIV testing is vital in scaling up HIV testing services.

Musheke and colleagues (2013) in a systematic review synthesized over forty articles on factors that influence HIV test acceptance in sub-Saharan Africa. The studies, which were conducted in thirteen African countries, reported eight key elements that affect testing uptake in this region. The reasons are:

i. First, the enablers of testing uptake are worsening state of health or death of intimate partner/child, improved testing strategy (such as mobile testing approach) and reducing or eliminating stigma and discrimination as well as outright removal of direct and indirect

financial costs associated with HIV testing. Other reasons are the availability of treatment, social networks, and care services.

ii. Second, the primary barriers to testing acceptance are comprised of lack of confidentiality by the health care provider, perceived low risk of infection and perceived psychology-social burden associated with testing (Musheke et al., 2013).

3.11.2 Low perception of risk of infection

A lack of physical manifestation of HIV symptoms or not feeling unwell are often cited as reasons for not wanting an HIV test. In a modelling study examining determinants of HIV testing among couples in Nigeria (Lepine et al., 2015), participants alluded to their state of good health as the reason for not seeking test. In a survey of ANC attendees in rural Nigeria, respondents reported that testing is only necessary when engaged with multiple or casual partners and when HIV symptoms manifest (Omolase et al., 2010). HIV testing uptake has consistently been low in Nigeria; limiting access to prevention and treatment strategies because of these barriers. Many women, particularly the sex workers in Nigeria anchor their belief on fatalism and therefore do not view themselves as being susceptible to contracting HIV (Ankomah et al., 2011). Thus, encouraging the unabated spread of HIV infection in society.

3.11.3 Fear of Possible Outcome

 In the (Musheke et al., 2013) review, the commonly cited barrier for HIV testing is fear of the negative consequences of learning one's HIV status. In one study in Nigeria, which explored perceived barriers to HIV testing among pregnant women in an urban health facility, the participants reported fear of being divorced, discriminated against and possible receipt of positive HIV test results as reasons for not accepting testing. Most of the respondents (82.7%) identified fear of the possible outcome as a barrier to test acceptance. This study established

a strong association between fear of the consequences of testing and HIV test uptake. The study did not report the proportion of HIV-positive women. However, it found that fear of the consequences of testing: HIV-positive test result, stigma, and discrimination meant that most respondents choose not to know their HIV status. The most significant fears were that of dying and divorce.

3.11.4 Stigma and Discrimination

Stigma and discrimination associated with HIV testing often exist in the community as well as in the health care settings. Any form of discrimination related to HIV often leads to poor quality of care for individuals living with HIV and deters potential clients from accessing care. These factors undermine HIV prevention efforts by limiting access to life-saving services. Recognizing the realities of HIV/AIDS and understanding the root causes of HIV related stigma and discrimination are important in mitigating their impact and in dispelling the myths and misunderstanding that often follow HIV activities.

A survey of 201 health personnel in a tertiary health centre, in northern Nigeria, on their attitude towards people living with HIV showed considerable stigma and discrimination (Pauline Justin et al., 2017). The respondents were comprised of medical doctors, laboratory scientists, and other health professionals. The study found that over one-third of the respondents accepted causing shame through their attitude towards people living with HIV while 15% reported rejecting and denying them treatment.

 In another study, Ijadunola and colleagues (2011) conducted a school-based survey among university undergraduates in Nigeria to evaluate the HIV prevention needs of 252 students. In the study, 90.5% (228) of the participants reported that they had never taken an HIV test in the past. This is because receiving an HIV test or being seen at a VCT centre would mean a

loss of moral standing due to its strong association with promiscuity, prostitution and drug addiction (Ijadunola et al., 2011). Other common reasons cited by the participants for not testing are lack of knowledge of HIV testing centres (25%), fear of possible positive results (24%) and perception of low exposure to HIV infection (18%).

One study conducted in North-Central Nigeria reported that inadequate VCT centres, stigma, discrimination, and lack of family support were the main reasons limiting pregnant women from taking an HIV test. Of the 384 pregnant women attending ANC, about 55% could not test for HIV citing inadequate VCT facility, the impact of an HIV diagnosis and lack of support from the family members, particularly their husband to a diagnosis (Hembah-Hilekaan et al., 2012). Similarly, in a cross-sectional survey conducted in 67 HIV counselling and testing facilities in parts of South Africa (Mohlabane et al., 2016), the authors reported various limiting factors why people do not test. Among the reasons are lack of knowledge of where to access testing service, fear of receiving HIV-positive results and death plus an unwillingness to divulge personal information to the health care provider.

3.12 Cost Effectiveness of HIV Testing.

3.12.1 The Economic Impact of HIV Testing.

Among the 21 priority countries, Nigeria has the slowest decline in new paediatric infections. From 2001 to 2009, new infections in children declined by only 2% whereas eight other priority countries from the same region reduced incidence among children by 30-60% (UNAIDS, 2013a). Moreover, despite the burden of vertical transmission, PMTCT of HIV services reach only 30% of the women in need (UNAIDS, 2014e). This is in contrast with PMTCT coverage in Botswana and South Africa, which have achieved 100%, and 80% coverage, respectively (UNAIDS, 2014e).

Following the Joint United Nations Program on HIV/AIDS goal for global elimination of new HIV infections in children, Nigeria intends to scale-up access to PMTCT services. To achieve this, the government has declared its intention to embark on the new PMTCT guidelines released by UNAIDS, an agency of WHO. The guideline recommends that all pregnant women receive HIV testing on the framework of provider-initiated routine HIV testing; this is a slight departure from the client-initiated approach. HIV counselling and testing have been an important component of HIV prevention, care, and treatment. Screening, among other reasons, enables the health care providers to initiate early medical interventions to people living with the virus and provide counselling to reduce the risk of acquisition and transmission. Understanding the costs and the extent to which existing and potential interventions improve population health helps, the decision-makers choose interventions that maximize health for available resources. The cost of HIV testing may occur from direct or indirect costs and could affect an individual's access to service. Direct cost are costs associated with purchasing the service while indirect costs may arise from financial costs associated with transportation and time.

A study in the United States of America examined the impact of reducing the time spent on HIV testing and counselling through same-day results and post counselling. In the study, Kassler and colleagues (1997) reported that same-day receipt of results led to increases in the number of people learning their serostatus: 4% and 16% increases for infected and uninfected clients, respectively. Moreover, 88% of the respondents reported that same-day result was preferred to return visit result collection (Kassler et al., 1997).

3.13 HIV Testing and Access to Antiretroviral Therapy for PMTCT

3.13.1 Role of ART in the Perinatal Reduction of HIV Acquisition

Anti-retroviral therapy (ART) is the cornerstone of PMTCT the package. Many trials have demonstrated the efficacy of ART in reducing mother to child transmission of HIV (Fowler et al., 2016). Presently, there is no cure for HIV, but there are treatments to improve the health of people living with the virus and to reduce the risk of infection to others. Anti-retroviral (ARV) medications alone can reduce MTCT risk from 15 to 45% to less than 5% in settings that practice breastfeeding such as Nigeria (Zolfo et al., 2010). ART drugs inhibit viral replication of HIV in the body and support the immune system to recover and repair itself from further damages from the virus.

For PMTCT, ART medications suppress the viral load in an infected mother and reduce the risk of onward transmission to the infant during pregnancy, delivery, and breastfeeding (Gourlay et al., 2013).

At the onset, the use of ARV in pregnancy was complicated and considered too expensive for economically constraint countries, and possibly too toxic due to the haemolytic effect of the drug, especially in a population with poor nutritional status. However, guidelines for the provision of PMTCT have evolved, particularly within the African context, following the initial introduction of ARV drugs for PMTCT in 2000. The first recommendation was short course prophylaxis usually started late in pregnancy in which mothers and the children were administered with single dose Nevirapine (NVP), and the subsequent amendment in 2004 and 2006 introducing the use of combination antiretroviral therapies for the pregnant women for their health. The later recommendations in 2010 include an option (B), which streamlined prophylaxis for PMTCT of HIV and actual treatment of an HIV-positive woman for their health

(W. H. O. WHO, 2012). Currently, option B+ is the standard of treatment and includes initiating ARV therapy for all mothers living with HIV, irrespective of serological and immunological status and continuing for life (Zolfo et al., 2010). In addition, option B+ is a simplified treatment version, which provides protection against MTCT of HIV in future pregnancies as well as protection against transmission in discordant partners.

Emerging evidence shows that option B+ is very effective in the prevention of vertical transmission in low-middle income settings. Earnshaw and Chaudor (2008) observed that the impact of the stigma associated with HIV has a long-standing negative impact on the overall prevention effort. For those who are already living with the virus, the mechanism is enacted stigma (real experience of discrimination), anticipated stigma (the belief that one will experience discrimination from people around) and internalized stigma (the agreement with oneself of negative beliefs and feelings) (Earnshaw and Lewis, 2008). These result in unusual psychological and behavioural traits, including poor health outcomes. For the undiagnosed individuals, the stigma mechanism of prejudice, discrimination, and stereotypes drive them underground, resulting in social exclusion and distancing of oneself from seeking service. The consequence is further spread of the virus in the society with concomitant AIDS-related illnesses.

3.13.2 Situational Analysis of PMTCT Activities in Nigeria.

The federal republic of Nigeria with support from development partners established the PMTCT program in 2001. The PMTCT sites were originally located one in each of the six geographical zones of Nigeria, including the Federal Capital Territory, Abuja. This, later scaled-up to include more centres to facilitate coverage and improve the accessibility of PMTCT services. From 2000 to 2015, the PMTCT sites have grown from seven to more than a

thousand-folds of over 7265 PMTCT centres across Nigeria. However, this rapid proliferation

of PMTCT centres has not transformed into significant improvements for tangible outcomes

of PMTCT service delivery. In 2015, Nigeria continued to bear the highest burden of MTCT of

HIV infection accounting for 15% of the regional burden (UNAIDS, 2016). Table 3.2 below is a

summary of the present PMTCT related activities in Nigeria.

Table 3-2 Cascade of selected PMTCT activities in Nigeria between 2000 and 2015 (NACA., 2015a)

Activity	Situation
Number of facilities offering PMTCT	Grew from 7 in 2000 to 7,265 centres.
Number of first ANC visits by expectant mothers.	2,849,864 (an increase of 46% from previous years)
Number of women who tested and know their HIV status.	2,780,867 (Representing 45% of the total number of women who became pregnant in 2015).
Proportion of pregnant women living with HIV who been diagnosed with the virus.	42.6% (75,855) of the total HIV-positive mothers.
Proportion of HIV positive pregnant women on ARV for PMTCT.	70.8% of 75,855 women and representing about 30% of the estimated HIV positive women in the country.
Number of babies born to HIV-positive mothers tested for HIV (PCR) within 2months of birth	Only 30% of 53,677 of mothers living with HIV and receiving ARV drugs.

Chapter 4 : Literature Review: Clinical Outcomes of Routine opt-out Antenatal human Immunodeficiency virus screening: a systematic review.

4.1 Introduction.

The aim of this chapter is to summarise and present the results of previous research work (published articles) on the clinical impact of provider-initiated routine HIV testing. The findings from this review will form the framework for understanding the field that characterizes the focus of the research described in this thesis. This part brought about the prospects for articulating a critical view of the real "meaning" of the data collected when the data analysis phases of the study were reached. This review work has already been published (Appendix A)

Given the high prevalence of HIV infection among pregnant women in Nigeria and the high number of undiagnosed cases, HIV/AIDS represents a considerable public health challenge for the country. As very sensitive and specific rapid tests emerge, and early treatment profoundly alters the disease course, testing for HIV represents a vital program for the treatment and prevention of the virus, particularly PMTCT. Besides, the innovative use of rapid test kits, with the promising feature of timely test results, usually within 30 minutes, the need for a return visit for post-test counselling may be abolished, with extremely high-quality results (sensitivity 98% and specificity 99%). This signifies an additional resource for HIV-prevention. Indeed, this may contribute to decreasing loss to follow-up, a major challenge of the traditional VCT.

To effectively inform decision-makers and since accurate data about the burden of HIV are often lacking, screening intervention should monitor costs and effectiveness aimed at evading screening implementation that might result in additional health expenditures. Lately, many studies have examined the cost-effectiveness of routine HIV screening from diverse backgrounds; regarding settings, prevalence rate, and target population and screening frequencies. However, data for these studies have been heterogeneous in respect of screening methods and methodology. To fully understand and appreciate the impact of this heterogeneity the present study also, embarked on a systematic review of existing literature in this subject area. The outcome of the review was subsequently published and this formed part of the conceptual framework for making a case to conduct this study. The full version of this published systematic review is contained in the appendices of this thesis.

4.2.1 Aims and Objectives:

To evaluate the clinical outcome of routine screening of human immune-deficiency virus (HIV) in antenatal clinic (ANC) settings.

4.2.2 **Background**

Despite the growing advances in HIV management, nearly 30 percent of the estimated 1.5 million seropositive pregnant women are undiagnosed. Routine opt-out testing is a strategy endorsed by the World Health Organization (WHO) in 2007 to increase testing rates in clinical settings. However, it is unclear how this has contributed to testing uptake.

4.2.3 Design

A systematic review of relevant published literature.

4.2.4 Methods

A comprehensive electronic search for relevant studies in Science Direct, MEDLINE, SCOPUS, CINAHL, and PubMed was conducted with search terms, Box 1. Hand searches were also conducted for additional resources. There were no geographic restrictions. Searches were restricted to English languages and studies conducted between1998 to 2015; totalling 1091 were retrieved and carefully appraised for review. Eighteen studies were eligible for review: eight from Africa, five from the USA, three from Europe, and one from Australia and one from Asia. The outcomes of interest for routine HIV testing were compared to other modalities of HIV testing for ANC. Data were extracted from relevant articles; critically appraised, synthesized and the report presented.

4.2.5 Results

Fourteen studies reported increases in HIV testing rate. Following the introduction of routine HIV testing rates increased from values ranging from 68 to 99.9 percent and the median value of 88 percent. The comparison studies reported testing uptake of 22 to 93.5 percent with a median value of 59 percent. Maternal HIV case detection rates nearly doubled following the adoption of routine testing at values of 99 and 45 percent during opt-in. Linkage for treatment and care for Prevention of vertical transmission was reported on six studies and results ranged between 12.9 to 77.2 percent.

4.2.6 Conclusion

The findings show that irrespective of HIV epidemiological scenarios routine testing gave more women the opportunity to learn their HIV status and take measures for prevention of mother-to-child transmission of HIV (PMTCT). Future studies should focus on identifying

strategies for improving linkages for treatment and care for the prevention of vertical transmission.

4.2.7 Relevance to Clinical Practice

Understanding the contributions of RT in ANC would help practitioners adopt the novel testing model for more mothers to learn their HIV status for PMTCT.

4.2.8 Key words

Routine testing, Antenatal, HIV infection, Prevention of vertical transmission, Counselling and Testing.

4.2.9 Introduction

Following the discovery of human immune-deficiency virus (HIV) in 1981, major scientific advances in the prevention and care for people living with the virus have emerged (Mnyani and McIntyre 2009, Padian *et al.* 2011). Mother to child transmission of HIV (MTCT) is the common route that children become infected with HIV(WHO/UNAIDS., 2016). The use of highly active antiretroviral therapy (HAART) is reported to be effective for prevention of mother to child transmission (PMTCT) of HIV (Ngemu et al., 2014). The new WHO guidelines recommend the administration of lifelong HAART to all HIV-positive pregnant and breastfeeding women, irrespective of clinical or immunological status, to reduce vertical transmission to nearly 1% (Fowler et al., 2016)

However, despite the rigorous effort towards the eradication of the virus, a high number of infections continue to take place, especially in sub-Saharan Africa. In 2014 alone, of 220,000 children globally, who were newly infected with the virus, 190,000 were from sub-Saharan

Africa(UNAIDS, 2016c). Moreover, in 2014, nearly 85% of 1.5 million pregnant women living with the virus reside in Sub-Saharan Africa(UNAIDS, 2016a).

The critical gateway to access HIV treatment, care and support services including the HAART regimen is knowledge of HIV status. For the pregnant woman, a positive test result is necessary to access care, support, and treatment not only for herself but also for her unborn baby and serodiscordant partners. However, an empirical finding shows that 30% of pregnant women are undiagnosed during pregnancy and nearly 20% do not receive formal antenatal clinics (Nygaard et al., 2008). The proportion is even higher in middle-low income countries where 54% of the mothers do not receive an HIV test during pregnancy(UNAIDS, 2014e). Similarly, in 2014, the incidence of vertical transmission in the African region where 1.3million HIV-positive pregnant women reside was reported as 26%(UNAIDS, 2015a). Undiagnosed individuals pose challenges to prevention effort as they carry a nearly 3.5-fold risk of transmitting it to uninfected persons than those who have knowledge of their serostatus (Gary Marks et al., 2006; Cherutich et al., 2012). Moreover, although people infected with the virus might not be adversely affected at the onset of the infection, late diagnosis leads to greater morbidity and mortality with 76% of the cases resulting in AIDS-related deaths (Antinori et al., 2011). Early identification and management of the virus during pregnancy decrease transmission rate and improves the health outcome of the mother-infant pair (Davis et al., 2013; Meyers et al., 2015). However, despite the key role of HIV testing in the continuum of prevention and treatment, the testing rate has remained relatively inadequate for a variety of reasons for different settings ranging from lack of prenatal care, the inability of the health care provider to recommend an HIV test to all patients and legal barriers (Droste, 1998; Coenen et al., 2008). The multiple benefits of treatment with antiretroviral combination

therapy in pregnancy demand an effective, acceptable and proper approach to case detection rate(Cohen et al., 2010).

In the past, HIV testing and counselling (HTC) was offered in health care facilities and 'stand-alone' voluntary counselling and testing (VCT) centres. HTC began with health care personnel recommending HIV test for individuals who present with symptoms or lifestyle indicative of exposure to HIV. This methodology is characterized by too little and too late detection rates; since the identifiable symptoms usually emerge after repeated visits with the healthcare provider (Barbacci et al., 1991; Burke et al., 2007). The VCT was later adopted as a pragmatic approach usually 'stand-alone' centres available for individuals to have an HIV test on their own volition (Du et al., 2012; Odimegwu et al., 2013). With VCT, an HIV test is offered to the woman after a detailed pre-test counselling; active consent and the woman are often asked to return 1-2 weeks later, for post-test counselling. Studies in ANC-linked VCT reported willingness to test, but poor post-test return rate (Knut Fylkesnes and Seter Siziya, 2004; Baiden et al., 2005).

In response to this problem, in 2007, WHO reviewed the guidelines and recommended the adoption of 'routine offer' of HIV in clinical settings including antenatal clinics (ANCs). Unlike the VCT, routine offer is 'provider-initiated' testing and counselling (PITC). Under this model, an HIV test is recommended for all pregnant women, irrespective of the level of risk exposure (Costello et al., 2013) and test performed as a standard group of tests unless explicitly refused by the woman. The lengthy pre-test counselling witnessed with VCT is replaced with concise pre-test information that meets the minimum standard for informed consent (Hensen et al., 2012b).

The emergence of routine testing was also complemented using the rapid HIV test kit. The rapid HIV test kit is relatively easy to use, at low cost and produces results quickly (Chang et al., 2006) usually in less than 30 minutes and women are able to receive post-test counselling on the same day without a prolonged waiting period lasting up to 1-2 weeks as obtained with enzyme-linked immunosorbent antigen (ELIZA). This means that those who are living with the virus can begin to receive all the necessary support they need in one day. The test result obtained from the rapid HIV test kit is quick, dependable and cost-effective (Wilkinson et al., 1997; Wolf and Walensky, 2007). This technique has been integrated into many ANC settings and it is considered a standard technique for HIV testing for various countries (Pilcher et al., 2010).

The millennium development goal6 (MDG6) sets a target of 2015 to halt and reverse the spread of HIV. Except in a few instances, there still exist significant gaps in access to PMTCT interventions and world policy commitment. However, to boost their efforts to meet this target, countries have appropriately adopted the routine model of PITC in clinical settings, particularly in ANC. However, it is unclear how much the adoption of such a policy has contributed to halting and reversing the spread of HIV in ANC settings or the clinical impact on implementing such a policy.

A systematic review of available research evidence was undertaken to gain a deeper understanding of the clinical impact of routine antenatal HIV testing. The systematic review is a powerful framework to summarize evidence-based and clinically relevant information for the health care providers (Sauerland and Seiler, 2005). As a powerful tool for summarizing relevant studies, it analyzes study findings with objectivity, especially when resolving issues

where study conclusions are divergent. We intend to find and recommend the most efficient strategy for increasing HIV testing uptake in pregnancy.

The findings in this review will be of great relevance to the adoption of best clinical practices for increasing HIV testing, especially for the countries that are still struggling with antenatal testing uptake.

4.3.1 Study design: A systematic review of available relevant published literature.

4.3.2 Methods: We adopted a five-step standard PRISMA approach to conducting a systematic review (Moher *et al.* 2015). Box 2 briefly itemizes the steps we followed to ensure high standard quality articles.

4.3.3 Research question for the review

The question motivating this review, and for which search strategy was formulated, was; 'what are the clinical outcomes of routine antenatal screening of HIV of the following measures: (i) HIV testing uptake, (ii) Linkage to treatment (iii) rate of vertical transmission?'.

4.3.4 Study Design Process

An evaluation of studies involving a pre-post or multi-arm designs comparing women or cohort of women who received the routine offer of HIV testing in the antenatal setting to either another group who did not receive any form of screening or those who received another model of HIV screening. The intervention group is made of those who received routine HIV testing while the comparison group (control) are those who did not receive any model of screening or those who received another model of HIV screening (such as mandatory or VCT).

4.3.5 Search Strategy

We used a multi-stage search strategy to identify relevant studies for an appraisal. Firstly, using the search terms as described in Box 1. Searches were carried out using the following electronic databases, with a date range from the 1st of January 1998 to the 30th of December 2015: MEDLINE, SCOPUS, CINAHL, Science Direct, and PubMed.

We restricted our search to publications in English, but no geographical restrictions. Hand searching for further relevant studies was conducted on the selected studies. We retrieved 1091 articles from online sources only as represented in Table 1.

4.3.6 Study selection criteria

Studies were considered eligible for inclusion if they met the following criteria:

The literature published in a peer-reviewed journal.

Evaluated a routine model of HIV intervention conducted in the ANC setting.

Used a pre/post or multi-arm study design comparing pregnant women who received the intervention (routine HIV testing) in an antenatal setting to those who did not or those who received another comparison, HIV testing model, to any of these primary outcomes: (i) HIV testing uptake, (iii) rate of vertical transmission (ii) Linkage to treatment.

The sum of retrieved articles from all electronic searches is 1091plus additional six articles retrieved from hand searches totalling 1097. After 409 duplicate copies were removed, 688 articles were left. A reviewer independently screened the titles and excluded another 595 articles that are non-relevant to the review. The remaining 93 records were shared via Endnote to two reviewers, who independently appraised and categorized their choices based on the following ratings: 'very relevant' and 'not relevant'. Thereafter, they compared results

and discrepancies were resolved by consensus. Forty-two articles were classified 'very relevant' and were considered further for the review while 51others were excluded as they were adjudged 'not relevant'. Finally, full texts of the remaining 42 articles were obtained and once again, two reviewers independently appraised all full-text articles using the inclusion criteria. Out of which, 12 were excluded based on study design, nine did not satisfy the target population and three could not be located. An independent reviewer resolved differences and discrepancies on the rating at this stage. Figure1 depicts the flowchart for the selection of eligible articles.

4.3.7 Definition of Routine Opt-Out

The definition of routine opt-out testing is according to the Centres for Diseases Control (CDC) and 2007 World Health Organization guidelines. Specifically, a health care provider must prescribe an HIV test to individuals, couples or groups of pregnant women with abridged pre-test information and post-test counselling. These individuals, couples or groups must have the opportunity to learn their HIV status in the process or refuse to be tested if they feel it is not in their own best interest. Though the WHO/CDC 2007 definition of routine opt-out HIV testing was adopted for this study, we did not confine our study to articles published before this period. Instead, we broadly included all articles that met the definition above and stringently assessed all the evidence on the approach to HIV testing irrespective of the terminology used to describe it.

4.3.8 Data extraction

A member of the study group extracted the data and exported the information into the two standardized extraction forms. One of the two extraction forms was for study design while the other was for data relating to HIV testing uptake, tables 2 and 3 respectively. We equally

extracted data on linkage to ARV and characteristics of programs (setting, location, and country); years (period of study); comparator intervention; length of follow-up; outcome measures and study design. The quality of articles was appraised using the PRISMA protocol (Moher et al., 2015).

4.3.9 Heterogeneity of studies

Various terms have been used to describe 'routine opt-out' antenatal HIV screening under the studies in review ranging from 'universal testing' but all have retained the basic principle that HIV testing is offered to groups of pregnant women with the option to decline. Studies were also performed under different approaches whereas some (The Netherlands, Uganda, Malawi Canada, and England) were evaluations of intervention using secondary data generated from interventions implemented in facilities others (Botswana, Burkina Faso, USA, and Zimbabwe) assessed the impact of policy change on activities of interest. Some studies also undertook extensive staff training prior to the commencement of the intervention (Simpson et al., 1999; Stringer et al., 2001; Chandisarewa et al., 2007; Creek et al., 2007a; Kasenga et al., 2009a; Byamugisha et al., 2010a) whereas others did not report undertaking such an exercise (Barbacci et al., 1991; Patrick et al., 1998; Jayaraman et al., 2003). There was no staff training (Shanks et al., 2013; Flynn et al., 2017). Also, in the dissemination of information at the community level concerning the introduction of routine testing, some studies reported using leaflet (Simpson et al., 1999), while widespread community mobilization was reported in another study (Chandisarewa et al., 2007).

4.3.10 Characteristics of Studies

The details and characteristics of the eighteen articles that met the inclusion criteria are presented in table 4. Most of them were non-randomized studies (16) that assessed the

impact of the introduction of routine testing in ANC settings and compared results to the control group prior to the intervention. Two randomized trials were also included in this study (Barbacci et al., 1991; Simpson et al., 1999). There are variations in sample sizes and the number of clinics from 695 to 135,481pregnant women and 1 to 13 respectively.

Eight in total were conducted in Africa (Cartoux et al., 1999; Creek et al., 2007a; Chandisarewa et al., 2007; Moses et al., 2008; Hahn, 2009; Kasenga et al., 2009a; Mirkuzie et al., 2010; Byamugisha et al., 2010b), four in the USA (Barbacci et al., 1991; Patrick et al., 1998; Stringer et al., 2001; Jayaraman et al., 2003), three in Europe (Simpson et al., 1999; Sherr et al., 2006) and (Boer et al., 2011). Others are one from Asia (Tay and Emmanuel, 2003) and one in Australia (Jayaraman et al., 2003).

Some studies also undertook extensive staff training prior to the commencement of the intervention (Simpson et al., 1999; Stringer et al., 2001; Chandisarewa et al., 2007; Creek et al., 2007a; Kasenga et al., 2009a; Byamugisha et al., 2010b). Also, in the dissemination of information at the community level, some studies reported using leaflets (Simpson et al., 1999) while widespread community mobilization was reported in another study (Chandisarewa et al., 2007). Four studies reported on staff training prior to the introduction of routine HIV testing. Two studies conducted community mobilization (Simpson et al., 1999, Chandisarewa *et al.*2007) and another two studies conducted counselling both in English and in local languages. In addition, three other studies reported staff training prior to the study (Chandisarewa et al., 2007*,* Creek et al., 2007, Byamugisha et al. 2010)

4.4 Results

The primary and proximal outcomes of interest in this study are HIV testing and case detection rates among pregnant women. The distal outcome is linkage to treatment. Fourteen studies

presented results for testing rates (Simpson et al., 1999, HIV Testing Among Pregnant Women—United States and Canada, 1998-2001, 2002, Cartoux et al., 2001, Stringer et al., 2001, Tay and Emmanuel., 2003, Jayaraman et al., 2003, Centre for Diseases Control 2004 (CDC), Van't Hoog et al. 2005, Sherr et al. 2006, Chandisarewa et al. 2007, Creek et.al. 2007, Moses et al. 2007, Kasenger et al. 2009, Byamugisha et al. 2010).

The introduction of routine HIV testing triggered significant changes in testing rates and receipt of test results, ranging from 68% in a study in Kenya (Van't Hoog et al. 2005) to 99.9% in Zimbabwe (Chandisarewa et al., 2007). Likewise, a study reported dramatic increases in the annual testing rate with the implementation of routine testing at 28% against 9.2% with opt-in (Jayaraman, Preiksaitis & Larke 2003). Before the introduction of routine testing, the testing rate trend was much lower in the ranges of 22% in Uganda (Byamugisha et al., 2010) and highest at 93.3% in Burkina Faso the only study which recorded impressive uptake with VCT (Cartoux et al., 2001). Following the adoption of routine testing, receipt of the test result was almost concurrent and congruent with the testing rate as the report showed 99.8% and 82% in Zimbabwe (Chandisarewa *et al.*2007) and Botswana (Creek et.al., 2007) respectively.

Five studies reported results for maternal HIV case detection rates (Barbacci et al. 1991, Jayaraman, Preiksaitis & Larke 2003, Chandisariwa et al. 2007, Kasenger et al. 2009, Boer *et al.* 2011). The findings show 3.3 and 2.4 per/10000 detection rates with opt-out and opt-in respectively (Jayaraman, Preiksaitis & Larke 2003). Other studies reported in absolute numbers strongly suggest that the opt-out model significantly increased with almost two-fold increases in HIV case detection rates against the opt-in strategy (Barbacci et al. 1991, Chandisariwa et al. 2007, Kasenger *et al.* 2009, Boer *et al.* 2011). This implies that more women living with the virus were identified during the routine testing (Barbacci et al. 1991,

Jayaraman, Preiksaitis & Larke 2003, Chandisariwa et al. 2007, Kasenger et al. 2009, Boer et al. 2011). Six studies recorded results for linkage to treatment and care (Van't Hoog et al. 2005, Creek et.al. 2007, Chandisariwa et al. 2007, Kasenger et al. 2009, Mirkuzie et al. 2010, Byamugisha et al. 2010).

Out of the six studies, four indicates significant linkages to treatment and care of identified seropositive patients as expressed in absolute numbers (Van't Hoog et al. 2005, Chandisariwa et al. 2007, Mirkuzie et al. 2010, Byamugisha et al. 2010). However, although there were improvements in linkages for treatment and care, studies indicate that up to 25% of the positive women were never linked (Van't Hoog *et al.* 2005, Chandisariwa et al., 2007, Creek et.al. 2007, Kasenger et al. 2009, Mirkuzie et al. 2010, Byamugisha et al. 2010).

4.5 Discussion

The finding shows that routine antenatal HIV testing gave more women the opportunity to learn their HIV status. Although testing uptake was relatively low in the African region at an average rate of 79.6% compared to developed countries such as Europe and America with rates of 89.5% and 88.4% respectively, significant improvement was recorded across all regions. This finding is consistent with the findings in other systematic reviews of routine testing (Hensen (Baggaley et al., 2012; Kennedy et al., 2013). This is promising, as high testing uptake will certainly reduce the incidence of mother to child transmission of the virus. Implementing routine testing in ANC increases the chances of achieving universal HIV testing and presents an opportunity for women to avail themselves of appropriate treatment and care. However, the studies recorded poor linkage of the identified women to treatment and care. Approximately, 25% lost opportunity to linkage for treatment and care was reported in spite of the significant improvement in maternal case detection rates, which almost doubled

following the introduction of routine testing. Further studies should be undertaken to identify reasons for this lost opportunity. This finding is crucial to the public health reduction of both vertical and horizontal transmission of the virus since knowledge of HIV serostatus is a critical step to accessing treatment and care. For instance, in the USA, lack of knowledge of serostatus constitutes a major prevention barrier since 20% of the undiagnosed individuals are responsible for 70% of new HIV infections that occur every year (Hall et al., 2012).

The findings of this review should be viewed in light of some limitations. Although it has in an attempt to pool all relevant studies included evaluations that conceptualized and demonstrated the basic principles of routine opt-out HIV testing, we identified dissimilarities among them. Since a few studies were conducted prior to WHO revised recommendation in 2007, countries with the penchant to eliminate or at least halt the scourge have ostensibly introduced routine opt-out testing. The idiosyncratic approach implies that the quality of services was, however, not the same across countries. For instance, in a study in the USA, there was evidence of a study participant's bias. The intervention and control groups had significant differences in geographical location (different clinical settings), social and demographic characteristics. Consequently, the study findings cannot conclusively be attributed to the introduction of this intervention.

Although two of the studies reported that counselling sessions were conducted in local languages and the women comprehended the basic information (Cartoux et al., 1999; Stringer et al., 2001), one study reported lack of counsellor's skill to present basic pre-test counselling information leading to poor conception and feeling of coercion to undergo an HIV test (Byamugisha et al., 2010b). Counselling is a panacea to successful HIV prevention and treatment services (Avinash, 2015). For a successful intervention, competent and well-trained

personnel should be involved, and counselling sessions presented in the language the women understand very well. Moreover, although, this intervention specifically targets pregnant women, at present, only those who report to clinical settings benefit from the service. A significant proportion of the women, especially in developing countries are unduly disadvantaged since they patronize traditional birth attendants (TBA) or deliver at home where the intervention is not offered. This cohort of women also faces a greater risk of HIV infection from the unethical practice of re-use of unsterile instruments. A study in India demonstrates that only 12% of TBA reported ever hearing about HIV/AIDS (Madhivanan et al., 2010).

Furthermore, in the case of testing technique, before the advent and universal availability of rapid HIV test kits, HIV tests were conducted using enzyme-linked immunosorbent assay (ELISA) and women returned for their test result in approximately 1-2 weeks later. However, with the availability of rapid HIV test kits, the difficulty, especially with result collection was ameliorated and women were able to collect their result and post-test counselling almost at the spot without an additional visit to the clinic. The newer studies were mostly conducted using a rapid HIV kit and the study in Malawi succinctly pointed out the resultant higher testing rates (Moses et al., 2008).

We are also conscious of the ambiguity in the use of and meaning of the terms 'routine testing', opt-out, PITCT and 'universal' and understand the confusion they might pose to the readers in relating them to the exact context which they have been applied. Though there might be slight differences in the terms, they have been constantly used interchangeably throughout this review.

The findings further show that the adoption of routine HIV testing in ANC is clinically effective and dramatically increased testing rates in all the regions of the world, irrespective of the HIV prevalence rate (generalized or localized epidemic) in the society. Routine testing allowed more women to learn their HIV status. Knowledge of the HIV status of the pregnant mother is fundamental to HIV prevention not only to her unborn baby but also to her sex partner and the society in general. Routine HIV testing led to increased testing rates among antenatal mothers and with the introduction of rapid test kits, very expedient. However, this is only efficient when followed by prompt linkage of the mother-infant pair to appropriate medical care and onward initiation of antiretroviral therapy (ART) for PMTCT. The findings show that significant lost opportunities to linkage for treatment, care still exists, and no reason was adduced to it. It further recorded poor counselling skills on the part of the health care provider. These pertinent issues require urgent evidence-based resolutions considering the critical roles they play in HIV prevention efforts.

4.6 Matters Ensuing from the Literature Review

4.6.1 Heterogeneity in the Implementation and Testing outcomes

The review presented in chapter 4 of this thesis indicates a wide gap in testing outcomes using the provider-initiated approach, both within and between settings. There is also a considerable lack of homogeneity in the adoption of the program. Indeed, when painstakingly put together, it becomes clear that results from previous studies on the impact of routine HIV testing are inconclusive because they cannot be viewed as being complete or robust as they failed to follow the WHO guidelines and are often inconsistent in the implementation of the intervention. Added to this, until now, no empirical study has considered the cultural dimensions of provider-initiated routine offer of HIV test. Culture has a significant impact on

beliefs and causes of disease, how and where patients seek help and the kinds of treatment communities prefer.

4.6.2 Rationale for the Evaluation of Provider-Initiated HIV Testing Approach in Nigeria.

Recent reports show that in the low-middle-income countries (LMICs), around 600 million adults (≥15 years) received HIV testing services between 2010 and 2014 (WHO., 2015b; Rachel., 2015) and specifically in 2010, around 95 million; an increase from 67 million tests in 2009. Likewise, in 2014, approximately 150 million people, including children, adults men, and women across 129 LMIC received HIV testing and their test results. Such a magnitude of scale-up has been possible largely through the adoption of the routine offer (Opt-out approach) of HIV testing. This model has been very important for expanding testing, especially in LMICs where test acceptance has been historically low despite the high prevalence of HIV infection. Because many women living with HIV in Nigeria are unaware of their status (UNAIDS, 2017a), the country may benefit from the introduction of this model of testing (routine opt-out) in ANC since many attendees would have the opportunity to know their status. Besides, contextualizing the study will help the decision-maker understand both the economic and clinical impact of the programme before wide-scale implementation.

Despite the large-scale testing of HIV in LMIICs, however, the review found disparate test acceptance rates. Although the majority of the studies recorded test acceptance of ≥85% in various ANC settings, the testing rate varied from 35% to 99.9% (Ibekwe et al., 2017). This wide-range raises a question about its universality and is a source of concern as it suggests that the program has not been successful in some settings and therefore the routine offer of testing cannot be conclusively viewed as being successful. Furthermore, recent reports suggest that poor quality HIV testing services (HTS) are occurring in these settings, particularly

in resource-limited countries (Klarkowski et al., 2009). Data from the review above (Chapter 4), Shanks and colleagues (2013) and Flynn and colleagues (2017) reported these challenges. In their respective reports, adoption of the provider-initiated routine offer was marred by wide variations in style and quality of implementation, indicating that this model of HTS has not kept pace with the expected standard relative to the original benchmark. This implies that many settings have not implemented routine HTS within the WHO recommended guidelines. For instance, an audit in three African countries reported significant rates of false-positive results (2.6%-4.8%), using routine testing (Shanks et al., 2013). The authors ascribed this error to challenges arising from task shifting from Physicians, laboratory technologists or nurses to other non-medical providers without adequate training. Similarly, a recent policy analysis of 48 countries suggests that only 20% of national HIV testing strategies based on opt-out strategy conformed with WHO recommendations (WHO, 2015b; Flynn et al., 2017), thus raising some critical questions regarding the standard. None of the conforming studies was conducted in sub-Saharan Africa. Likewise, in other reviews, wide variations in the contents of pre-test information (Ujiji et al., 2011; Hensen et al., 2012a; Rujumba et al., 2013), evidence of coercion, lack of autonomy and lack of informed consent (Ujiji et al., 2011; Bain et al., 2015), were all identified as limiting factors associated with the implementation of routine testing. Furthermore, when Botswana introduced the routine testing policy in their antenatal clinic, the intervention outcome was mitigated with unfavourable post-test attitude. Although the testing rate increased from 75.3% during the 4-months opt-in to 90.5% during the 3-months opt-out, this impressive uptake was diminished by poor return rate for test result (Seipone et al., 2004; Rennie and Behets, 2006). These challenges added to recent policy commitment aimed at reaching UNAIDS target of 90% of undiagnosed people knowing their status have heightened the need to contextualize routine offer of HIV testing in Nigeria.

Routine offer (Opt-out approach) of HIV testing that follows the World Health Organization (WHO) guidelines has the potential to meet the prerequisites necessary for HIV testing, including legal and ethical ideals (Kosack et al., 2017). Studies suggest that the introduction of such a strategy within a validated national testing algorithm has been shown to yield highly promising outcomes where pregnant women regard testing as helpful and empowering, thus giving them the opportunity to make an informed decision (Hensen et al., 2012b; Logan and Laurel, 2017). In the present study, strict adherence to the WHO guidelines was followed, including adequate training of the health care providers to ensure strict adherence to best practices.

4.6.3 How setting in Nigeria differs from other settings.

Nigeria bears the second largest HIV burden of infection in the world: accounting for over 3.2million people and one-third of new infections that occurred in 2016 in sub-Saharan Africa (UNAIDS, 2017a). Notwithstanding its high burden of infection, PMTCT programmes reach only 30 percent of eligible mothers (NACA, 2017), whereas, in other African countries with a high burden of infection such as South Africa and Botswana, PMTCT coverage is around 80 and 100 percent, respectively (Taylor et al., 2017). In addition, from 2009 to 2011, eight countries in the region reduced paediatric HIV infection by 30 to 60 percent while Nigeria achieved only a 2 percent decline (UNAIDS, 2013a) following low levels of HIV test acceptance and access to antiretroviral treatment.

The global expansion of access to combination antiretroviral treatment (cART), propelled by the aspiration to reach the 90-90-90 target (know the status, receive cART, achieve viral suppression respectively) has been the benchmark for measuring country's progress. While each element of the 90-90-90 goal is essential, the first target, 90% of all people living with

HIV knowing their HIV status, is perhaps the most significant because it is the cornerstone for achieving the rest objectives. In the high burden HIV infection among pregnant women in a densely populated Nigeria, reports show slow progress to effective prevention efforts. In Nigeria, in 2017, approximately 35% of mothers were tested for HIV, fewer than in 2015 when nearly 45% received an HIV test (UNAIDS, 2018). Of the women identified HIV-positive in 2017, approximately one-third were initiated with ARV for PMTCT. In the same year, 36,000 children became infected with HIV, a figure that has been rising since 2014 (UNAIDS, 2018). Early infant diagnosis (EID) has also been reported to be abysmally low at 12%. In contrast, in Cote d'Ivoire, 92% of pregnant mothers tested for HIV at the end of 2017. Of whom, 70% of the infected women received ART and 70% of their infants received EID (UNAIDS, 2018). People living with HIV who are unaware of their HIV status cannot benefit from treatment as prevention; therefore, they constitute the unknown epidemic that is responsible for new infections, including MTCT (Supervie et al., 2014). Such people are also inclined to late HIV diagnosis and late initiation of cART, resulting in deteriorating health outcomes: treatment failure, poor CD4 cell recovery, and comorbidities.

These circumstances added to the complexity of Nigerian society in-terms of multi-ethnic and multi-religious dimensions, as well as multi-cultural ideology demand for setting's specific understanding of the program. Regarding ethnicity and religion, these are distinctive qualities of the community that affect the group within it, their association with one another and to the whole (Hirschman, 1979; Fylkesnes and Siziya, 2004). Thus, country-level contextualization studies: as conducted in Zimbabwe, Botswana, and Kenya, for instance, are a worthwhile trajectory to incorporate local priorities, health systems characteristics and data into the evaluative process (Hutubessy et al., 2003). For instance, regarding cultural and religious perspectives, Nigeria is deeply enshrined in gender inequality within the context of

patriarchies (Makama, 2013). The majority of Nigerian societies are patriarchal where the husband is the main decision-maker, particularly on matters bordering on family issues and health-seeking behaviour (Feyisetan, 2000; Oyediran and Odusola, 2006). Here, the commonality of the collective belief system is that the only office for women is the 'kitchen'. Hence, women lack the power to make certain decisions without consulting their husbands. Also, the Nigeria tribal societies (family codes of behaviour, resource distribution and power allocation) ascribe diminutive positions to women, to the extent that women, particularly the married ones hardly partake in decision- making even on issues concerning themselves. Husbands are responsible for making critical decisions for their spouses, including in health matters (Oyediran and Odusola, 2006). The three dominant religions in Nigeria (Christianity, Islam and traditional worship) reinforce this subordinate position for women (Para-Mallam, 2006). In fact, religion is a critical weapon to enforce patriarchies, given the high connectivity and spirituality that Nigerians, mostly the women attach to religion. The subservient role of women and their inferiority disposition to men is further deepened with restrictive legislation that reduced women as the property of the husband (Golden, 2006). Simply put, power is in the hands of men, while women are historically subjugated: literally to be of no values. Certainly, patriarchy in Nigeria is the core basis for lack of access to and control over resources, thus giving rise to systematic discrimination and exclusion of women from decision-making.

Equally social cohesion is a feature of Nigerian society. Here, social cohesion as a concept denotes the idea of forming shared values and a community of understanding, enabling members to have a sense that they belong to a common enterprise, facing shared problems, and that they are members of the in-group community (Cadena-Roa et al., 2012). This structure bonds people together-encourages trust, solidarity and shared goals among

members. Perhaps, the most glaring example is the Ibos, which has an ethos norm of inclusiveness, whereby a whole community gets together to build a house for a new couple. This, to a large extent, highlights the level of oneness and connectedness within this particular tribe.

To put these whole concepts to a proper perspective, and in comparison with regional countries, Nigerian societal and healthcare structure is largely a clear departure from other African countries such as Zimbabwe, Botswana, and Kenya where routine HIV testing has been evaluated. In these countries, there exist relatively gender equality, which empowers women to exercise their fundamental human rights (Singh et al., 2013). In Zimbabwe, for instance, gender equality is a principle enacted in their constitution and legal system, which seeks to guarantee gender equity as well as equal treatment for everyone, irrespective of religion, class or tribe (Jacobs, 2000). Zimbabwe has also ratified Convention on the Elimination of All Forms of Discrimination against women, including domestic violence, land ownership and access to quality health care services (Pasura, 2010). Likewise, in Botswana, the country's 1971 act empowers women to own property (Casimiro, 2009). The married Persons Property act gives equal rights to couples; thus, women can make decisions and take control of their sexuality. Besides, Botswana and Kenya are both signatories to the 1997 Blantyre Declaration on gender and development that proscribed laws and practices that discriminate against women (Banda, 2002). Although, with recent gender-based equality improvements (Para-Mallam, 2010), it is possible that the 21st century Nigeria society could be witnessing some modifications to patriarchy: the system that decapitates women's values and limits their potential to rise beyond societal norms and practices. The present study examined how all these factors affected health-seeking behaviours in the context of HIV testing/ test acceptance among pregnant women attending ANC in Nigerian.

4.7 Clinical Literature Review Summary

4.7.1 Conclusion

The findings from this review indicate a wide gap in testing outcomes both within and between settings. Testing activities also varied in many aspects. First, test acceptance ranged from 29% to 99.8%. Second, some literature recorded extensive staff training before the implementation of the program while others did not report on this feature. Third, some trials were an evaluation of a program implemented in ANC while others evaluated the impact of policy change on activities at the facility level. Counselling and testing information, given to women during pre-test session also varied: a study reported wide-spread community mobilization, and another recorded the use of leaflets while others did not report any form of mobilization. Added to this, until now, no reasonable work has considered the cultural dimensions of provider-initiated routine offer of HIV.

Given the dire need to improve ANC test acceptance rate and the potential benefits of adopting provider-initiated routine HIV testing, it was therefore recognized that a study is required to evaluate not only the clinical-effectiveness but also the cost-effectiveness. Information from the economic trial can be used to appraise decisions of health care coverage, resource allocation and understand current costs and forecast future expenses, each of which can result in improvements in quality of care.

In light of the above information, a review of current literature on the economic impact of the program-routine offer of HIV in ANC was undertaken and this is presented in the next chapter 5.

Chapter 5 : A review of the economic impact of routine HIV testing in ANC

5.1.1 Introduction

The previous chapter 4 demonstrated the clinical impact of provider-initiated routine ANC HIV testing. This chapter presents yet another review results of the program from the economic perspective. Decision-makers are constantly confronted with countless essential questions related to the allocation of funds based on the quest to optimally allocate resources and minimize waste. Important decisions in the use of public funds can affect the economy of the whole country. However, understanding the economic impact of different policy options is essential in resolving these challenges.

In light of these circumstances, books, scholarly articles and other sources relevant to identifying information on the economic impact of routine testing were summarized and critically evaluated in relation to research problems pertinent to this thesis. Therefore, this chapter will present literature that investigated the economic impact relating to the provider-initiated offer of HIV testing. Also, the chapter will identify and highlight the existing gaps in the literature. A full version of the publication is appended as appendix B.

5.1.2 Objectives

 To evaluate the economic impact of routine testing of Human Immune deficiency Virus (HIV) in antenatal clinic (ANC) settings.

5.1.3 Background

Many children are being infected with HIV through mother to child transmission (MTCT) of the virus. Most of these infections are preventable if the mother's HIV status is identified in a

timely manner and appropriate interventions put in place. Routine HIV testing is widely acclaimed as a strategy for universal access to HIV testing and is being adopted by developed and developing poor income countries without recourse to the economic impact.

5.1.4 Study Design

A systematic review of published articles.

5.1.5 Methods

Extensive electronic searches for relevant journal articles published from 1998 to 2015 when countries began to implement routine ANC HI testing on their own were conducted in the following databases: Science Direct, MEDLINE, SCOPUS, JSTOR, CINAHL and PubMed with search terms as listed in box 1. Manual searches were also performed to complement the electronic identification of high-quality materials. There were no geographical restrictions and language was limited to English.

5.1.6 Results

Fifty-five articles were retrieved; ten were eligible and included in the review. The findings showed that many programmes involving routine HIV testing for pregnant women compared to the alternatives were cost-effective and cost-saving. Data from the reviewed studies showed cost savings between $5,761.20 and $3.69 million per case of previously undiagnosed maternal HIV-positive infection prevented. Overall, cost-effectiveness was strongly associated with the prevalence rate of HIV in various settings.

5.1.6 Conclusions

Routine HIV testing is both cost-effective and cost-saving compared to the alternatives. However, there are wide variations in the methodological approaches to the studies. Adopting a standard reporting format would facilitate a comparison between studies and the generalizability of economic evaluations.

5.1.7   Relevance to clinical practise

i.   Healthcare decision-makers should understand that routine ANC screening for HIV is both cost-effective and cost-saving.

ii.   Addressing late identification of prenatal HIV is crucial to reducing MTCT at minimal health care spending.

5.1.8 Keywords

Routine testing, Antenatal, HIV infection, Prevention of mother to child transmission, Counselling and Testing, Cost-effectiveness.

5.2.1 Introduction

The Human immune deficiency virus (HIV) pandemic has claimed many lives all over the world, including children. Approximately 3.2 million children are already living with the virus and 170,000 others became newly infected in 2015 compared to 220,000 in 2014(WHO and UNAIDS., 2016). Globally, in 2015, it was estimated that 1.5 million pregnant women were living with the virus and nearly 30% of them were unaware of their serostatus, of whom 15-20% never attended formal ANC services(UNAIDS, 2016a). Pregnant mothers who are unaware of their seropositive status unknowingly transmit the virus to others including their unborn children, resulting in high medical and economic costs to the health care system

(Rahangdale and Cohan, 2008). Most children become infected through perinatal transmission(UNAIDS., 2016c). More than 90% of them live in sub-Saharan Africa, where there is limited access to basic prevention interventions(WHO/UNAIDS/UNICEF., 2011). Increasing the frequency and uptake of HIV testing is pivotal to early identification of mothers living with the virus for prompt initiation of HIV treatment and a better prognosis for the duo of mother and child. This is because the early commencement of effective anti-retroviral (ARV) drugs improves the health outcomes of both mother and child in addition to reducing the spread of the virus to the woman's sex partners (Becquet et al., 2009).

As a major health problem, the WHO is intensifying efforts to reduce the scourge and has recommended new intervention approaches for prevention of mother to child transmission (PMTCT) of HIV. The pragmatic approaches include firstly, the adoption of routine HIV testing policy in all ANCs, which is aimed at increasing testing rates and secondly, adopting the use of option B+ for treatment of mothers for PMTCT (Dzangare et al., 2016; WHO/UNAIDS/UNICEF., 2011). Routine testing is provider-initiated HIV testing and counselling with the option to decline (opt-out). Option B+ requires administration of life-long combination ARV drugs to the identified seropositive pregnant woman for her health and that of the baby (Fowler et al., 2010; Kim et al., 2015). Identifying mothers living with the virus are a critical care and prevention tool (Baggaley et al., 2012; Sullivan et al., 2017) especially in the era of option B+ for rapid access to ART for pregnant women in hard to reach communities (Zarocostas, 2009; Chi et al., 2013).

Although routine HIV testing has successfully improved access to screening in some parts of developed countries (Dyalchand and Sinha, 2010; Dzangare et al., 2016), the relative economic impact of this strategy has not been fully established. Many health care

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interventions are expensive, and the decision-makers require appropriate information to make informed decisions before allocating scarce resources efficiently. Generally, economic efficiency is a crucial centrepiece for policy-making and evidence-based medicine. As an important tool for overall health care financing, the costs and values of alternative interventions are compared to create greater care and longer life values for the society (Robinson, 1993; Rothberg, 2004). Explicit resource allocation should be premised on comparing the incremental costs and consequences of alternative health care interventions considering the limited available resources accessible for the provision of health care, particularly in resource-poor settings (Cunningham, 2000; Teerawattananon et al., 2007). To employ such an approach, it is essential to appraise and establish what constitutes evidence concerning health-enhancing interventions. An intervention is considered cost-effective if the additional resources required in implementing it result in health gains that are sufficiently justifiable in terms of outcome.

Technically, there are four main types of economic evaluations, namely:

i. Cost-effectiveness analysis (CEA) which reports outcome measure in natural units such as cost per case averted.

ii. Cost-benefit analysis (CBA) which reports the outcome measure on monetary units.

iii. Cost-minimization analysis, in which case, only costs are considered, as it is assumed that the alternative interventions have similar outcomes.

iv. Cost-utility analysis (CUA) which measures the quality-adjusted life-year (QALY). QALY means one year of life lived in perfect health and is a gold standard for economic evaluation because of its comparability across disease areas (McPake and Mills, 2000).

Normally, an economic evaluation is measured for a particular purpose and this determines which cost should be included in the analysis. For instance, if it is for the health provider viewpoint, only costs associated with health care provider will be considered in the study, while if it is from a societal perspective a more elaborate societal costing including the ones incurred by the patient such as loss of income will be included (Robinson, 1993; Tacconelli, 2010a).

Health economists proclaim that economic evaluation is one aspect of an overall health care evaluation process; the common vehicles for the conduct of the study are trial-based and decision analytical modelling (Buxton et al., 1997; Berger et al., 2009). The trial-based economic evaluation involves the collection of primary economic data for resource utilization (human and material inputs), application of appropriate sample size and use of statistical economic end-point under real-world condition (Sculpher. et al., 2006). As a favoured method for the conduct of economic evaluation, it has low marginal costs (Tacconelli, 2010b)); the intervention of interest is compared with the existing practice under natural conditions (Sculpher. et al., 2006). Although this method has the advantage of high internal validity and timeliness, it does not measure long-term economic impacts (Berger et al., 2009). Decision analytical modelling studies involve the collection of secondary data from a variety of sources (existing clinical trials, observational studies and so on) and applying statistical tools (decision tree analysis, multivariate analysis) to determine the best cost and consequences of alternative interventions. This method can evaluate any relevant economic decisions, account for uncertainty, provide evidence on key contributions and forecast long-term economic impacts (Sculpher and Drummond, 2006). Generally, the hierarchy of evidence supports trial-based over decision analytical modelling study design owing to reliable cost valuations, which influence robust outcomes (Buxton et al., 1997; Rothberg, 2004; Tacconelli,

2010a). In reality, the two methods are complementary to each other rather than alternatives (Buxton et al., 1997; Claxton et al., 2006). Nevertheless, for the purpose of this study, we synthesized a wide range of high-quality studies comprising of trial-based studies and decision modelling studies. A high-quality systematic review of interventions is a panacea to identifying suitable evidence-based alternatives that replace the existing ones (Cunningham., 2000; Sackett., 2000; Akobeng., 2005). Ideally, economic decisions should rely on data obtained from systematic review provided the studies are sufficiently homogenous to be comparable and the results generalizable to a population with different baseline risks, instead of a specific population group identified for an individual trial (Tacconelli., 2010b). Undertaking a systematic review is essential because it employs rigorous, orderly and transparent methods to reduce bias in results (CRD's., 2009; Nagappan., 2013).

The essence of this paper was to address the need to assess the usefulness of value for money in selecting a given intervention, in this case, a novel HIV testing model. As applicable in most other preventive healthcare services, both direct and indirect costs of delivering screening can be expensive. Sound policy-making on how best to achieve high sustainable and equitable HIV testing coverage in any given setting is predicated on the ability of those in authority to access and implement evidence-based best practices that provide enough benefits to justify the cost. To guide the clinical administrators to achieve this purpose, we embarked on a systematic review of the available literature on economic evaluation of different techniques of offering HIV tests to pregnant women in ANC. As such, synthesis and summary of quality evidence-based articles were undertaken, appraised and results presented, and then conclusions and recommendations made.

5.2.3 Methods

The review followed a standardized approach of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) (Moher et al., 2015).

5.2.4 Reason for the Review

To establish if it is cost-effective to adopt routine HIV testing in ANC settings.

5.2.5 Research Question

Is the introduction of routine HIV screening in ANC cost effective?

5.2.5 Search Strategy

Extensive database searches employing rigorous search methods for retrieving relevant materials were undertaken. The process involved a multi-stage strategy used to retrieve potentially relevant articles and carefully appraising them for eligibility. We included studies published from 1998 to 2015, when countries began to implement routine HIV testing on their own, before 2007 WHO recommendation. The following were the electronic databases that were searched, with search terms combination box 1, and dating from 1998 to 2015 to enable retrieval of up to date articles: Science Direct, MEDLINE, SCOPUS, JSTOR, CINAHL, and PubMed. Hand searches were also conducted, and reference lists of key studies checked for relevant articles. There were no geographical restrictions and only articles published in English were included.

5.2.6 Selection Criteria

The inclusion of studies for review was based on the following criteria:

Studies conducted on the economic evaluation of routine HIV screening for pregnant women

The studies were published in a peer-reviewed journal.

The studies reported relevant outcomes (such as quality-adjusted life-years QALYs, averted cases of infection, etc.) of the economic evaluation of routine testing in ANC settings.

The studies were conducted between 1998 and 2015 when some countries began to adopt routine HIV testing.

5.2.7 Exclusion of Studies Was Based on the Following Criteria

Multiple publications of the same study.

The studies considered the economic effectiveness of routine HIV testing other than for pregnant women.

The studies evaluated the economic impact of a different HIV testing model for pregnant women in an antenatal clinic setting.

The studies did not involve an ANC care intervention.

The studies were conducted in an ANC setting without a comparator group.

From the electronic database searches, fifty-one published articles were retrieved. An additional four potentially suitable articles were selected from the hand searches.

5.2.8 Appraisal of Studies for Quality and Relevance

Quality assessment of the studies was measured using a standardized tool (Moher et al., 2015). This tool relied on checking the quality of the studies based on appropriateness of methodology, the reliability of data collection and analysis, internal and external validity, the clarity of the findings and conclusion, and the reporting of ethics. Based on these criteria each study was graded and assigned an overall score of 'Low', Medium or 'High'.

This assessment aimed to provide a balanced estimate of the validity of the research findings. Two reviewers performed the data extraction and quality assessment independently and a third reviewer ensured inter-rater reliability.

5.2.9 Data extraction

One of the reviewers removed duplicate copies amounting to thirty; the remaining twenty-five copies were shared through Endnote to two reviewers who independently examined the study abstracts based on the following predetermined standards:

(i) The study conducted an original economic analysis that is, not a review study (ii) the study answered the identified review question (iii) the study investigated relevant outcome measures (quality-adjusted life years QALYs, averted cases of infection, etc.).

Two reviewers appraised the abstracts of the twenty-five articles and the third reviewer resolved any discrepancies. Fourteen potentially relevant articles were retained and considered for further review, while eleven of the studies were excluded because they did not examine the cost-effectiveness of HIV testing. Assessment of the methodological quality was evaluated using standard economic evaluation inclusion criteria described in the PRISMA guideline (Moher et al., 2015). Full texts of ten out of the fourteen selected articles were identified while full texts of the remaining four articles could not be located.

At this stage, two reviewers independently extracted the data into a standard extraction form and a third reviewer double-checked the data for accuracy. Data extracted included the type of economic evaluation conducted, main outcome measures, discount rates, sensitivity analysis, and study results. The Author, country of study and year of study are displayed.

5.2.10 Heterogeneity of the Studies

Due to methodological variations among the studies, it was impossible to compare the original study outcomes, arrive at a concise cost per outcome metric for the interventions or perform a meta-analysis. Because of the significant differences in the methodological approaches, we resorted to a narrative synthesis of the outcomes instead of the formal meta-analysis (Tacconelli, 2010b). The narrative synthesis constructively and concisely describes the statistical significance in the nature of storytelling, using words to summarize and explain the findings of multiple studies (Rodgers et al., 2009). Adopting a narrative approach enabled us to (i) Formulate a theoretical framework on the impact of the intervention; (ii) synthesize the findings (iii) Consider likely causes of differences between data and (iv) Assess the robustness of the findings and then present conclusions. A carefully conducted narrative synthesis makes findings in meta-analysis more meaningful. To maintain accurate reporting and synthesis, this paper has relied on expert recommendations of credible research panels (Buxton et al., 1997; Moher et al., 2015).

5.3.1 Results

Overall, we identified ten eligible articles, 90% of which were rated of medium or high quality. Articles were considered of 'Low' quality if it met four or less of the seven criteria, 'Medium' if only five and 'High' if it met all the criteria. The ten studies measured the cost-effectiveness of routine HIV testing in antenatal settings using either RTC or modelling approaches. The geographical representations of the studies were as follows: three from Asia, two from Australia, four from Europe, and one from the USA. We could not identify any article conducted in Sub-Saharan Africa, the economically constrained region with a high burden of the disease. Overall, the largest number of studies was conducted in the United Kingdom. All

the studies conducted in the various countries showed similarities in their findings and indicated that the introduction of large-scale routine testing in ANC would be cost-effective.

Postma and colleagues (2000) reported that a testing cost below $57.72 is likely to result in favourable incremental cost effectiveness for routine HIV testing in ANC settings. The findings showed that a testing rate below $14.43 would translate to cost-effectiveness for universal testing for two MTCT averted cases. However, with routine testing, the cost for an HIV infected child is $42,544.64 less when compared to no screening situation and the net cost per life-year gained is $4,824.65. At a lower prevalence of 1/10,000, the cost per life-year gained increases to $166,669 (Postma et al., 2000).

Another important study observed that the cost-saving of routine maternal diagnosis for HIV infected babies and the life years gained compared to the selective screening of the mothers was cost-effective for the society (Ades et al., 1999a). The findings showed that routine testing of pregnant women for HIV would save $13,966.40 and this sum of money would have been spent in caring for an infected child. There was also an additional gain of 5.9 child life-years. The study further recorded net post-test cost amounting to $21,708.61 would produce a gain of 6.4 life years and a net benefit of $71,791.67. The study by Ades et al (1999) reported that compared to selective testing; routine screening of HIV in pregnant women would result in 6.392 life years and an additional expenditure amounting to $21,692. The study further indicated that commitment of $1,462,450 for additional life year will yield a benefit of $71,791.67 and could be available to detect the additional seropositive mother in the ANC.

According to Chowers & Shavit (2013), the application of universal testing was both cost-saving and cost-effective only if universal screening is restricted to high HIV prevalent cities. The study report that the incremental cost of routine screening compared to selective testing

was $1million indicating a cost of $500,000 for each case of an HIV positive child averted (Chowers and Shavit., 2013). Another study, which conducted the incremental cost evaluation, observed that the incremental benefit of universal screening far outweighed the incremental cost of targeted screening, irrespective of the epidemiological situation. Postma and colleagues (1999) demonstrated that the lifetime medical and social cost of caring for an HIV child is $256,805. Based on this finding, the study concluded that routine testing is cost-effective when a net cost of less than $5,761.20 and $28806 per each life year gained in high and low prevalence areas respectively. The study by Bramley (2003), which compared the economic impact of universal screening to targeted testing, observed a significant economic cost of nearly two-fold per HIV averted cases. The findings showed that routine testing of pregnant mothers resulted in 1.15 avoided cases of infection in babies and a net gain of 41.97 discounted life years for mother-infant pair whereas selective testing yielded less than 0.5 avoided cases of infection in babies (Bramley et al., 2003). This result is in line with a similar study, which investigated the economic impact of routine screening in ANC in a high prevalence setting (Ades et al., 1999b). According to Graves (2004), routine HIV testing compared to voluntary counselling and testing (VCT), resulted in 6.95 new diagnoses during pregnancy and 1.73 averted infections of the infants with 46.97-discounted life years gained (Bramley et al., 2003). Moreover, in the absence of any screening intervention, 104.6 children would be infected while with the adoption of (VCT) the rate of infection would drop to 44.8 children (Immergluck et al., 2000). In addition, if routine HIV testing were solely implemented, the HIV infection rate in the children would decrease to 40 cases. The result of this study further showed that routine screening of 100000 pregnant women would result in a cost saving of $3.69 million and $269.445 when compared to no screening and VCT respectively.

A study by Kumar et al. (2006) reported that routine HIV testing would cost $3.82million and prevent 9880 new cases of vertical transmission, which translates into savings of 131,700 life years. The result showed that the average cost of averted HIV infection is $386.84 and annual reductions in potential years of life lost (PYLLs) is $29.03 (Kumar et al., 2006). Moreover, implementing this intervention in high HIV prevalence states would result in 45% of this reduction in terms of HIV cases prevented and life years lost at 20% of the cost, implying that approximately $181.38 per averted HIV case or $13.61 per annum reduction in PYLLs. Another study observed that in the first three years of implementing routine HIV testing in the ANC setting amounted to $1,576,167.72 and six out of seven averted vertical transmissions(Lee and Wong, 2007). This study compared an economic evaluation of routine testing to 'no screening' during pregnancy. The findings showed that approximately $262,694.62 was the cost per HIV infection averted, while the cost of discounted life years gained was $10,195.73(Lee and Wong, 2007). Rozenbaum et al. (2008) evaluated the cost-effectiveness of routine testing against 'no screening' and documented a significant economic gain in the study at various epidemiological levels. The study recorded that routine HIV testing of pregnant women could prevent 2.4 vertical transmissions with saving of up to $202,677.72 health care cost for each averted HIV infection per child (Rozenbaum et al., 2008). At a prevalence rate of 9.3/10,000 pregnancies, routine HIV testing reduced $110,289.50 and saved 74-life years saved (LYs) against no screening. However, at the prevalence rate below 6.9 cost-saving diminished and remained at a threshold of $22,809 per LY gained above the rate of 1.4. Therefore, considering a worst-case scenario at a prevalence rate of 5.0 HIV testing remained cost-effective at $7,407.22 per LY gained.

5.3.2 Discussion

This study has looked at a wide variety of economic evaluations of routine HIV testing. Considering all the necessary factors, it was a unanimous conclusion of all the reviewed studies that routine HIV testing in pregnancy was both cost-saving and cost-effective. The findings further showed that despite any epidemiological levels the incremental benefit far outweighs the incremental cost. These findings are consistent with other systematic reviews of the economic impact of routine HIV testing conducted in other clinical settings (Dibosa-Osadolor and Roberts, 2010). A study conducted in a similar health care program, which reviewed drug abuse treatment and HIV prevention in pregnant women, reported that it was cost-effective to embark on such interventions (Ruger and Lazar, 2011).

It is pertinent to note that although this review, as presented in this paper, provides some useful information; it is, however, fraught with significant methodological limitations. Therefore, caution must be exercised when discussing this result. Firstly, some studies compared routine testing to 'no screening' instead of selective or targeted testing. 'No screening' approach amounts to depriving women known to be at high risk the opportunity to know their HIV status. Doing so has both ethical and legal implications. Moreover, selective testing is economically superior, and no expert group has ever recommended the adoption of 'no screening' as an effective strategy to fight the scourge. Secondly, as pointed out earlier, the centrepiece for a cost-effectiveness study is trial-based randomized controlled trials. With the trial-based method, data for different components of resource utilization is extracted directly from the clinical trial rather than from secondary data or arbitrary speculations, which may measure inferior health care outcomes. This technique reduces confounding factors, minimizes selection bias and improves the overall validity and reliability problems often

witnessed in modelling studies. However, most of the reviewed articles utilized modelling approaches. Modelling studies have limitations relating to selection biases and confounding factors. Data are gathered based on assumptions and the outcomes are usually speculative. These inherent limitations may mislead policy-makers since findings from such studies portray false expectations of program strengths and capabilities. Thirdly, there exists a dearth in the use of standard methodological guidelines for economic-evaluations among research experts. Most of the reviewed studies did not adhere to standard guidelines for economic evaluation research, resulting in poor validity and reliability of the outcome measures. This has also affected the likelihood of comparing cost impacts across the studies. Moreover, the majority of the studies never evaluated cost-utility analysis or incremental cost analysis, thereby restraining the opportunity of inferring the incremental or marginal differences in costs and outcomes of alternative interventions. The USA expert panel on cost-effectiveness in Health and Medicine released a standardized guideline for conducting cost-effectiveness (Gold., 1998; Berger et al., 2009). The guideline streamlined methods for conducting cost-effectiveness to improve its comparability. This guideline recommends that studies should factor in the following elements when conducting cost-effectiveness analysis:

i)   Cost estimates should be taken from a societal perspective and converted to a common year

ii)   A discounted rate of 3% for future outcomes and costs to account for uncertainty in values

iii)   Use of quality-adjusted life years as a standard outcome metric and,

iv)   IV) Performance of sensitivity analysis to account for possible error.

These elements are important in improving the quality and uniformity of economic evaluation studies including making the findings more meaningful to the decision-maker (Berger et al., 2009). However, despite the availability of these guidelines, evidence shows that methods of conducting these studies have not significantly improved. Most of these guidelines are rarely integrated into economic researches resulting in discrepancies in measurement outcomes (such as multi-variate regression, different cost measures, decision analysis measure, etc.). The limitless variations in these critical elements including different model assumptions, discount rates, and data estimations pose great challenges to the methodological strength and the ability to make rational comparisons of the research findings. Ruger and Lazar (2011) were explicit in their report about the impact of discrepancies in the application of methodological procedures. They noted that methodological heterogeneity limits interpretation and subsequent application of the findings for logical health care financing (Ruger and Lazar., 2011). Sonnad et al. (2005) noted that although improvements have been recorded in some aspects of the methodological procedures, significant gaps still exist. Rigorous methodological improvements relating to cost components and outcome measures of economic evaluation are important if the findings are to be relied upon for efficient resource allocation (Sonnad et al., 2005). For most studies in this review, the metric of measurements significantly differed from one another.

Last but in no way less important, despite the significant role of HIV testing in prevention and control of the infection this review discovered paucity in the economic evaluation of different ways of offering HIV tests, not only in the African region but also in other parts of the world. For instance, only one article was conducted in the whole of America and none in Sub-Saharan Africa. This discovery is worrisome considering the apparent benefits of this framework in health care financing. Most of the reviewed literature was conducted in Europe

and in other developed countries where HIV prevalence is already low. Although the findings provided robust evidence of the economic impact of different approaches of offering HIV tests, there is a need to replicate these studies in other regions of the world. Historically, countries differ in important aspects such as epidemiology and demographic characteristics, but certainly, the most significant differences lie with economic factors, which essentially determines the capacity to implement an intervention, for example, a nationwide universal HIV screening program. These factors cast doubt on the plausible transferability of these findings to other regions of the world since most of the studies were conducted in economically stable regions. In this circumstance, there is good reason to replicate these studies in other parts of the world, principally in low-income countries, which is struggling to contain the devastating impact of the virus in the face of the poor economic situation coupled with dilapidating health care system, which is necessary to combat the infection. For instance, the WHO (or any credible organization) should consider conducting researches depicting the African context in terms of the economic impact of the various HIV intervention programs including testing approaches in ANC. The findings can then be adapted to the country-level by the application of national data.

Over time, information about the impact of routine HIV testing is being made available. As a body of knowledge, they form part of the critical tool for not only academics but also policy decision-making. Although in evaluating the economic impact of these testing techniques, studies recognised different circumstances such as epidemiological characteristics, population targeted, economic situation (unit price) of the setting and technical efficiency for implementation, it is necessary for each setting to make a comprehensive analysis of their situations to understand how the intervention is most appropriate to them. By so doing, the efficient health care resource allocation will be maximized.

5.3.3 Conclusion

Following the well-proven efficacy of antiretroviral therapy in combating HIV, particularly for the prevention of mother to child transmission, lack of HIV testing among pregnant women remains a great challenge to utilizing this intervention. Routine testing of pregnant women for HIV has bridged this gap and many women can now learn their serostatus early in pregnancy with timely initiation of treatment if seropositive. Identifying as many pregnant women living with the virus as quickly as possible and commencing prevention treatment on time has tangible benefits of reducing the huge health spending in the treatment of the infected children, including discordant partners. In addition, there is a cost-saving arising from the improved health of the woman because of reductions in multiple hospitalizations from AIDS-related diseases. Although we found high-quality literature on the cost-effectiveness of routine HIV testing, none of these studies was conducted in Sub-Saharan Africa, the region hardest hit by the scourge. This underscores the urgent need to prioritize the much-needed health care research on economic evaluation of different intervention programs with the view to identifying the best alternatives with value for money. Upon this tool, those entrusted with the authority of allocating resources could choose wisely from a range of alternatives, for example, adopting routine large-scale HIV testing with the aim of maximizing health benefits for the society. Clearly, economic evaluation should be conducted according to the recommended expert guidelines using the standard methodological metrics for cost-effectiveness evaluation. Trial-based studies are recognized as the preferred and more reliable approach for conducting economic evaluation studies. This method inherently minimizes the risk of undue influences arising from confounding factors and reduces the impact of data biases on research outcomes, thereby giving rise to robust research findings useful for efficient clinical practice and prudent resource allocation. Overall, almost three

decades into the AIDS epidemic and billions of dollars of spending later, a significant proportion of vertical transmission continues to take place due to undiagnosed HIV in prospective mothers. A cost-effective Infrastructure to test women routinely during pregnancy is urgently needed to ensure effective PMTC program.

5.4 Dearth of Economic Evaluation

5.4.1 Justification for Cost-Effectiveness Evaluation in Nigeria.

In response to Joint United Nations Programme on HIV and AIDS (UNAIDS) vision 90-90-90 in relation to HIV testing, treatment, and viral suppression respectively by 2020 (UNAIDS, 2017b), Nigeria aims to scale-up access to PMTCT program. Implementation, however, requires an understanding of the economic impact of scaling-up the program. However, up to the point of compiling this data, there were no economic evaluations that have been conducted in any part of Africa or Nigeria, (section 5.3.1) hence the need for this study. Moreover, even among the existing literature, none was conducted using a cost-effectiveness approach. Cost-effectiveness analysis is a decision tool that describes interventions vis-à-vis cost per unit gain hence highlighting intervention that is comparatively inexpensive yet has the prospect to reduce the disease burden substantially.

Indeed, there is a dearth of economic evaluation on routine opt-out HIV testing in the African context as a whole, and particularly in Nigeria. For instance, of the ten reviewed studies on economic evaluation of routine HIV testing (chapter 5, section 5.4), none was conducted in Nigeria or any part of Africa. The review showed that all the studies were conducted in other regions (Three from Asia, two from Australia, four from Europe and one from USA.), and most studies based their analysis on narrow efficacy and effectiveness data or presumptive expert opinion (Adam et al., 2005; Chisholm and Saxena, 2012). Extrapolation of best available

international evidence from higher to lower income resource settings may often be misleading and problematic due to stack variations in both health systems and epidemiology. This condition can only provide an ambiguous indication of effectiveness in health and negate the variety or specificity of individual country backgrounds (Chisholm and Saxena, 2012). Lack of economic evaluation for key health programs such as routine opt-out strategy in LMICs including Africa is a serious challenge that hinders explicit priority setting at the country level. Moreover, this limits the understanding of the economic burden of the intervention and hinders the adoption of the program. Overall, priority-setting approaches evaluated in this review were inclined to overlook uncertainty, varying economic background and some other important considerations such as sensitivity- thus utilizing single-point estimates for effectiveness. Programmes that are viewed cost-effective in one setting may, therefore, not be in another due to differences in economic power (relative prices and costs) and disease incidence and the structure of the health system. The present study will be useful in providing data on economic-effectiveness from an African perspective, particularly in the Nigerian context. This would be the needed yardstick for countries in this region to consider the adoption of the intervention.

Therefore, the economic impact of this intervention was conducted using cost-effectiveness analysis, chapter 7.

5.4.2 Reasons for Focusing on Cos-Effectiveness Aspect of Economic Evaluation

Review studies presented in this thesis (chapter 5 section 5.3.1) were performed under valuations such as cost-benefit analysis and cost minimization as well as cost-utility analysis. Cost-benefit analysis is a technique for valuing both incremental costs and outcomes of intervention in monetary terms and so allows a direct understanding of the net monetary cost

of achieving a health outcome. But, the methods used to convert health outcomes in monetary terms remain rather controversial and this has limited wide adoption of this analysis. Cost-minimization analysis is a technique of determining intervention costs to understand the least expensive intervention while cost-utility analysis measures quantity and quality of life-quality adjusted life years (QALYs) (Palmer et al., 1999). Cost-minimization is ideal for comparing two programs or drugs that have been established to be identical in the dose and therapeutic effect but is not ideal for programs that differ in medical effect. Similarly, cost-utility analysis is contentious because of the problematic nature of assigning a value on health status or on changes in health status as perceived by different societies. None of the reviewed studies was performed under cost-effectiveness analysis, the type of economic evaluation that measures health benefits in natural units, typically as life-years saved or improvements in functional status (cost per infection averted, cost per DALY averted) (Palmer et al., 1999). Therefore, since in the case of this study, the problem to be addressed was: what is the best method of averting infection? Then the most suitable ratio with which to match programmes would be 'cost per cases averted. This is the standard approach for decision-making on medical interventions such as ANC screening for diseases. For instance, measuring cost-effectiveness in this study provided the opportunity to determine and compare cases of child HIV infections averted, cost per infection averted and incremental cost-effectiveness between the two interventions (routine testing and client-initiated VCT). Typically, cost-effectiveness analysis examines the incremental cost vis-à-vis incremental effectiveness of a new device(s), strategies or program(s) in comparison to the standard program (Phelps and Mushlin, 1991; Cohen and Reynolds, 2008). The main reason for adopting this method is because of its potential in identifying the best way of accomplishing a single objective by comparing effects and costs.

The 'rule of thumb' on the adoption of the new interventions under this approach is straightforward and follows a robust pattern as follows (Cohen and Reynolds, 2008):

i. Adopt the new intervention without further investigation only if benefits increase and costs decrease. With this result, the new intervention dominates the standard intervention. Similarly, a higher cost and lower benefits with the new intervention, it is dominated by the standard intervention and should not be adopted.

ii. Further information should be sought when cost and benefit both rises or when both falls. In a situation when both benefits and costs rise; determine that the new intervention that cost-effectiveness ratio matches come preselected cut-off point. Likewise, a fall in both costs and benefits for the new intervention should trigger an incremental cost-effectiveness analysis of the standard intervention (relative to the new) to check if it matches desired standards of cost-effectiveness. The same decision rule then follows in both cases: adopt the strategy as long as the incremental cost-effectiveness ratio does not exceed the desired standard of evaluation.

Additionally, the studies included in the review (Chapter 5) followed a less naturalistic design thus utilizing the modelling approach. The problem with economic modelling is that it is often biased in assumptions and poor sensitivity analysis, resulting in under or over-reporting (Petitti, 2009). In fact, there may be very little information to provide accurate transition probabilities. Besides, there are wide assumptions, and the challenges for making approximations or ranges are frequently ignored. So, the major problem with decision models is the assumptions made in constructing the models. However, the plausible way to tackle these challenges is to ensure that future initiatives are based on pragmatic responses to the imperfect data-clinical test.

The present study followed a clinical research approach. A consistent set of data was collected within the trial- that is patient-level data on costs and outcomes was obtained alongside the trial. Economic evaluations conducted alongside controlled trials provide an early opportunity to produce reliable estimates of cost-effectiveness at low marginal cost. Access to individual patient data also permits a wide range of statistical and econometric techniques. For example, this method enabled the researcher to examine the relation between events of interest and health-related quality of life or to explore subgroup differences.

Moreover, clinical studies offer analysts the prospect to evaluate the cost-effectiveness of an intervention under real-world conditions, while ensuring that: (i) the enrolled patients are true representatives of typical clinical caseloads (ii) a comparison of the intervention of interest with current practice (iii) and follow-up under routine conditions (Sculpher. et al., 2006). Participants in this study were typical pregnant women who attended ANC in the study facility from whom responses to the interventions were measured under natural conditions. Relevant data relating to costs were also obtained alongside the clinical study.

With this background understanding of evidence-based clinical and economic impact of routine HIV testing in different parts of the world, the present trial has adequately garnered relevant data that would support this research.

5.5 Research Questions

5.5.1 Highlight of the review

Whilst several studies have examined the clinical outcomes of provider-initiated intervention in Botswana, Zimbabwe, and Uganda (Seipone et al., 2004; Chandisarewa et al., 2007; Creek et al., 2007a; Wanyenze et al., 2008) to my knowledge there has not been any study focusing

on a systematic comparison of the different approaches in Nigeria. Besides, looking at the

magnitude of success rates achieved in countries that adopted routine testing and bearing in

mind the discrepancies in the adoption of the program (Hensen et al., 2012b) it is, therefore,

worthwhile to assess such a policy before adoption in Nigeria, where test acceptance in ANC

has historically been suboptimal. The current study is designed to determine whether the two

different methods for offering HIV testing in terms of different levels of information giving

and group/individual counselling, would result in significantly different testing rates.

5.5.2 Main Research Questions (Clinical-effectiveness)

1. Can a switch from client-initiated to provider-initiated routine HIV testing change the
following testing outcomes?

 i. HIV test acceptance rate.

ii. The proportion of HIV-positive women detected by the program.

III. The proportion of the identified women receiving cART for PMTCT?

2. Do age and socio-economic variables play a role in testing uptake?

i. Impact of religion on test acceptance.

ii. Impact of the tribe on test acceptance.

iii. Impact of age on test acceptance

3. Do the midwife's characteristics affect test acceptance?

5.5.3 Research questions (Economic-effectiveness)

Similarly, the review of the economic impact (chapter 5 of this thesis) has provided critical

information on the economic impact of this intervention in some regions of the world,

however, the reviewed studies employed alternative valuation methods such as cost-benefit, cost-utility, and cost minimization methods. In contrast, this study conducted cost-effectiveness analysis (Please, see chapter 7 section 7.5 of this thesis for the distinctions). Additionally, the economic situations and disease epidemiology of the study settings are different from Nigeria in both health care situations and disease burden. For instance, regarding staffing levels, training, funding, and infrastructure, Nigeria scored lower in these critical metrics when compared to the United States. Whereas the United States spent $9892 per capita on health, in 2017, Nigeria spent only $97 (World Bank, 2017). This parameter underscores the magnitude of variation in the healthcare system. Therefore, considering the important role of this intervention and the usefulness of economic evaluation in healthcare priority settings, economic evaluation using cost-effectiveness analysis depicting Nigeria's economic circumstances as well as disease burden and healthcare situation is warranted. The aim of the study was to measure the cost-effectiveness of routine HIV testing: additional costs to the healthcare system and the potential health benefits of implementing a voluntary opt-out care HIV screening program for pregnant women in Nigeria.

5.5.4 Main Research Questions

1. Would the adoption of provider-initiated routine testing be cost-effective?

i. Cost per HIV test

ii. Cost per new HIV diagnosis detected

ii. Cost per infection averted

The next chapter 6 focuses on the methodology for conducting this study.

Chapter 6 : Methodology

6.1 Introduction

The purpose of this chapter is to present the research methodology used in this study and to discuss how it has guided data collection, analysis, and interpretation of results. Specifically, the discussion is structured around research design, population sampling, data collection, and data analysis. First, the conceptual research framework and fundamental guidelines for conducting research were presented. The subsequent sections discussed the justification for the selected research approach and data collection phases for this study, which consisted of the preparatory phase, the pre-intervention and intervention phases. The ethical dimensions of the research were also discussed. Finally, the last section of this chapter concludes by explaining the methods for data analysis and a summary of the highlights of the chapter.

6.1.1 Research process and sampling method

Generally, empirical studies involve reviewing the theoretical and empirical findings on a subject area, which results in the fundamental understanding of the topic including identifying gaps and making case for further research (Trochim and Donnelly, 2007). As discussed in chapters 4 and 5 extensive reviews of published and unpublished articles were conducted to gain full knowledge of the existing method for offering HIV tests to pregnant women and to identify the problems associated with the current technique. Through the literature review, it was established that the use of client-initiated VCT results in suboptimal HIV testing rates among pregnant women and consequently results in high Mother to child transmission (MTCT) of HIV in Nigeria. These findings paved the way for the conduction of this research. The result of this study has the potential to provide valuable findings that would aid the policy-maker to adopt a new intervention policy to fill this gap in Nigeria.

6.1.2. Research approach and study design.

To gather the relevant data for this study, the researcher followed a quantitative research approach involving pretest, posttest (before, after) quasi-experimental design. Polit and Beck (2014) reported that the strongest method for validating evidence for a nursing practice involving the effectiveness of an intervention is to test it in an experimental study. Choosing an appropriate design and using a logical plan builds a strong foundation for accomplishing an effective and informative study outcome (Wolf, 2016; Melle, 2016).

Many methodological considerations that influence the overall quality of a study are normally deliberated on before the final selection of suitable study design for conducting scientific research, including the appropriateness, cost, and accuracy in performing, collecting and analysis of data (Muijs, 2011; Babbie et al., 2015). Normally, research designs are formulated to meet the unique requirements of a particular study. The quality and usefulness of the research outcome is typically a direct consequence of the amount of careful planning, requiring valuable time to be invested during the planning process (Bordens and Abbott, 2008) For instance, quantitative research is exceptionally suitable for undertaking studies seeking to establish a statistical relationship between variables and causation (Muijs, 2011).

Traditionally, quantitative research is considered the vehicle for conducting an objective and systematic study, to test theories, evaluate variables, establish relationships between them and determine the cause and effect interactions among the variables (Grove et al., 2015). It uses a statistical test specifically designed to compute the significance of the outcome and the probability that the findings are not a coincidence. Usually, in a quantitative study, data in the form of numbers are gathered to substantiate a hypothesis mathematically, using statistical analysis (Salkind, 2010). Studies start with theory, hypothesis, to numeric data and

statistical analysis to establish facts and reach new conclusions (Melle, 2016) and the findings are mostly confirmatory because the differences between the data and hypothesis testing are usually investigated systematically (Polit and Beck, 2014).

The choice of quasi-experimental design is because it is most suitable to answer the research questions and aims of the research. Quasi-experimental design often referred to as causal-comparative trial, seeks to establish a cause-effect association between two or more variables (White and Sabarwal, 2014). A quasi-experimental design (trial without randomization) like the experimental study is an approach that enables the researcher to administer the experimental treatment to the intervention groups (Polit and Beck, 2011). With this design, the intervention under investigation is tested to understand the degree to which it can achieve its goals, as measured by a predetermined set of indicators. The researcher does not randomize groups nor manipulate the independent variables. However, assignment to conditions is achieved through self-selection of participants to groups (White and Sabarwal, 2014). Quasi-experimental designs establish a comparison group, which has a close resemblance with the treatment group regarding baseline pre-intervention characteristics. The comparator group represents what would have been the impact had the policy not been implemented (White and Sabarwal, 2014; Creswell, 2014). Essentially, the intervention can be viewed to have caused the observable changes in outcomes between the treatment and the comparison group.

The preferred study design in situations involving comparison group where randomization is not feasible is the quasi-experimental design (White and Sabarwal, 2014). This condition occurs mostly in ex-post impact evaluation. In the current study, evaluation of the impact of the intervention would require ex-post evaluation; making quasi-experimental design the

preferred option. Moreover, according to white and colleagues, the timing of intervention and data collection for impact assessment should follow pre-intervention format t-1 for baseline and post-intervention t+2 for the end line, where 't' is the period (White and Sabarwal, 2014). Following this approach in the current study, the comparator group received the standard treatment (t-1) while the experimental group received the experimental treatment or intervention (t+2). The results of the two groups are compared with each other. Hence, the pretest-posttest design is a method whereby observation of the dependent variables was made at two points (before- with the comparator group after receiving the standard treatment and after-with the experimental group after the introduction of the new program) with the view to establishing a causal relationship (Polit and Beck, 2011). The results are often in numerical form, typically presented in tables with statistical analysis from which generalizable conclusions are drawn for the given population. Overall, the quasi-experimental design is employed to evaluate the effect of an intervention and if rigorous in design, provides strong evidence to guide the clinical practice. Quasi-experiment resembles true experimental research in many ways except the non-randomization of participants (Harris et al., 2006).

6.2 Reliability and Validity.

6.2.1 Overview of Reliability and Validity

In a quantitative study, the reliability and validity of the findings are essential components of the entire research (Heale and Twycross, 2015). These two terms are somewhat related but have a subtle difference. Whereas reliability refers to the ability to reproduce the study findings irrespective of how close it is to the true value, validity refers to the extent to which the findings are correct (Compton, 2005; Heale and Twycross, 2015). In other words, reliability refers to the ability to obtain the same value repeatedly while validity describes the degree

of accuracy of the findings. Validity is more likened with the credibility of a study. For instance, a result may be reliable but lacking in validity. Accordingly, validity is the degree to which an instrument measures an attribute for which it is designed to quantify (Compton, 2005). Various variables such as internal, external, and statistical factors may affect the results and therefore introduce threats to the consistency of the overall findings and conclusions. However, if either of these items is lacking in quantitative research, the researcher is not likely to arrive at a conclusion that could be used to make an informed decision. Thus, reliability and validity are very important concepts in empirical studies.

6.2.2 Reliability

This is a measure of the consistency or repeatability of the test result. In the case of this study, reliability was maintained through adherent to standard protocols, using accurate measuring instruments. For instance, blood samples were stored at the appropriate temperature, using the correct anticoagulant for the test, and product instructions were followed to the later. Potent and reliable test kits were procured from credible sources and the national protocol for HIV testing was adhered to. Reliability can also be improved by minimizing sources of measurement error such as data collector bias. Data collector bias was minimized by ensuring that the physical and psychological environment where data was obtained was comfortable in relation to privacy, confidentiality and general physical comfort. The clients were offered a suitable and comfortable chair in the sampling room. Windows were opened for cross ventilation. The door was closed during the sampling and a "do not disturb" placed on the door to ensure privacy and prevent interruption.

6.2.3 Validity

As mentioned earlier, validity refers to the extent to which an intended outcome is correctly measured. Broadly, validity is defined as the level to which a concept is accurately measured in quantitative research (Heale and Twycross, 2015). Therefore, validity is described as the degree to which a given construct is correctly measured in a scientific study. It includes the whole experimental idea and establishes whether the results obtained from the study meet all the requirements of the scientific research process. For example, a study designed to measure temperature, but which instead measures pressure would be lacking validity. Just to make a clear distinction between validity and reliability, using a simple analogy of a table-clock that rings at 8:00 every morning but is set to ring at 5:00. This alarm clock is reliable because it consistently rings at the same time, but it lacks validity because it does nothing at the right time.

There are two main types of validity: Internal and external validity. Internal and external validity are ideas that reflect the extent to which the outcomes of research are trustworthy.

6.2.3.1 Internal Validity

Internal validity describes the extent of trustworthiness to which research is conducted in terms of its structure). It focuses mainly on how scientific design is structured to establish a cause-and-effect relationship between treatment and outcome. Thus, internal validity refers to the degree to which the measured results reflect the true study results (free from errors) and can be attributed to the variables measured. Therefore, the reproducibility and accuracy of the test result are the utmost concern. It reflects the degree to which the study results are true and can be attributable to the variables measured. It measures if the independent variables are responsible for the cause-effect findings observed in the study. When the

observed cause-effect findings are biased by a confounding or extraneous variable, then it is not possible to draw valid conclusions regarding the association between variables.

In this study, internal validity was followed by defining and refining a research question, blinding and randomization of participants, establishing relevant experimental design and obtaining data and analyzing them with appropriate statistical methods.

Conversely, external validity reflects how applicable the findings are to the real world. The vital difference between external and internal validity is that external validity relates to how universal the results are while internal validity denotes the process of the scientific research method.

6.2.3.2 External validity

This is the application of the inferences of scientific learning outside of the context of that study. Put differently, it is the degree to which the results of empirical findings can be generalized to other circumstances. External validity is concerned with the ability to use study findings with certainty to other situations. The goal of external validity is to recognize the correctness of the research results, by checking whether it can be applied in other settings different from where the research was conducted. Specifically, external validity is concerned with whether the observed cause-effect connection of the dependent and independent variables in the research is generalizable or not.

In this study, the sampled population was a true representation of the population regarding relevant valuables such as gender and age. There were no sociodemographic restrictions on the study participants who met the basic inclusion criteria. Seeking for study participants is normally a challenging task, especially if the study involves invasive procedures or requires an extensive amount of time or other commitment from the participant. Enough study

participants were recruited for this study. In the event where the number of participants is not adequate, the generalizability of the study findings would be compromised. Holistically, steps were taken to improve the validity and reliability of this quantitative study through strict adherence to both the manufacturer's protocols as well as general laboratory rules. For instance, staff training was conducted, and qualified personnel performed the laboratory tests following the national algorithm. Both positive and negative test controls were conducted alongside patient samples.

6.3. Materials and Methods.

6.3.1 Testing Framework

In this study, 'routine HIV testing' would be defined according to the Centre for Diseases Control (CDC) 2007 revised guidelines, which prescribes offer of HIV testing to all individuals in clinical and ANC settings on non-risk assessment and with the options to decline (Branson et al., 2008). This model does not require an active or written consent and unless the individual actively declines to be tested (opt-out approach), an HIV test is conducted after brief health education. In contrast, voluntary counselling and testing (VCT) requires that the test be conducted after the client willingly and actively consents to be tested after the initial extensive pre-test counselling ('an opt-in approach').

This study is facility-based research conducted in an ANC hospital, which covers the majority of the population in the Federal Capital Territory, Abuja Nigeria. The target population was all newly pregnant women undergoing an ANC booking at the designated hospital. The design is a non-randomized control trial (NRCT) pre-test post-test (before-after) quasi-experimental design in which two cohorts of new ANC clients assessing ANC services received different techniques for offering HIV test. At the health facility, depending on the group, five trained

midwives offered the test to the women with either comprehensive pre-test counselling or streamlined health discussion printed on an ANC pamphlet. The first cohort of newly booked ANC clients was offered the existing model (opt-in VCT) of HIV testing from July- September 2016 (The comparator group). At the end of the first phase, the second phase was introduced from October to December 2016 involving the 'routine opt-out model' in which a new cohort of pregnant women newly booked for ANC in the same facility received the experimental opt-out offer strategy. Since this study involves a lifesaving intervention to HIV/AIDS, all pregnant women who accessed services during the study period (July – December 2016) were allowed to participate, to enable them to draw the benefits of being screened for HIV, figure 6.1. Acting otherwise would amount to unethical practice and invalidate the finding.
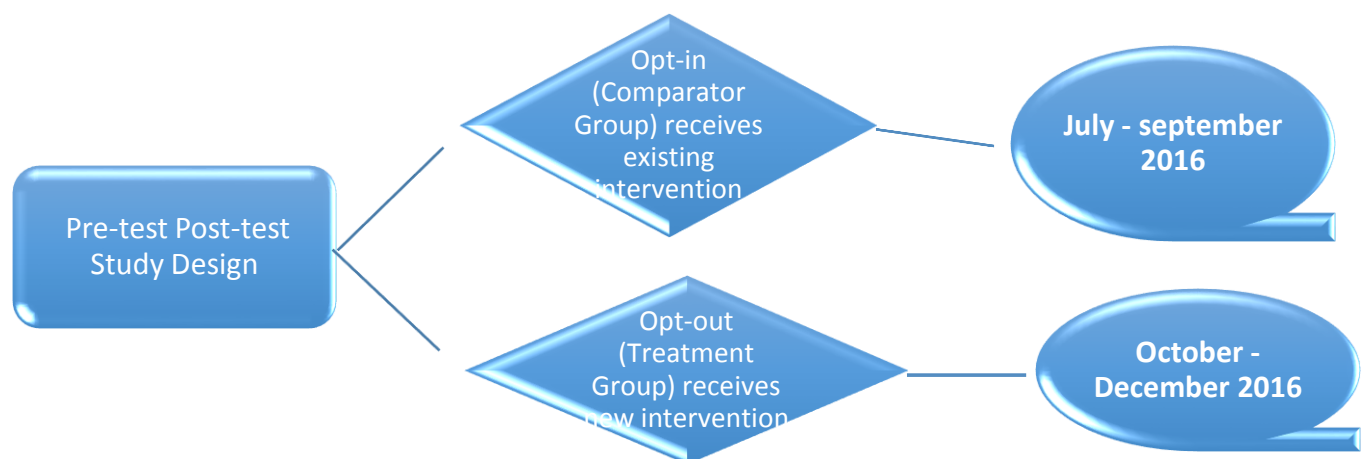
Figure 6-1 diagrammatic representation of the study design.

6.3.2 The study setting

The research was conducted in a hospital located in the Federal capital city (FCT), Abuja Nigeria. The facility has a bed space of 300. The hospital is one of the busiest health facilities and referral centres in Nigeria. With her rich state of the art equipment and highly trained and motivated staff, the hospital provides both normal deliveries and emergency obstetric care. Although a section of the facility provides niche medical services to the government functionaries, the hospital is the main referral facility for patients within and outside the Federal Capital City, particularly the neighbouring states. As one of the first six centres in the country to provide free medical services to HIV/AIDS victims since 2005, it has a dedicated HIV/AIDS clinic with specialist services and a well-trained workforce. Abuja was chosen for this study because its population has a relatively equal representation of all tribes in Nigeria. Abuja is also one of the cities in Nigeria with a high prevalence of HIV/AIDS at 6.5% compared with the national rate of 3.4% in 2014 (FMOH/NACA., 2015).

6.3.4 Study Population

The study participants were all pregnant women (Both Multi-para and Nulli- para) who were making a new ANC booking at the designated hospital during the six-month trial period, which started, from early July – December 2016. They must be between the ages of 15-49 years. The exclusion criteria were HIV-positive, under 15 years, as this group is unable to provide consent by themselves and language difficulty in cases where there was no interpreter. For instance, a woman who speaks and understands only French. Other exclusion criteria were un-booked ANC clients arriving for emergency delivery including those who failed to return a signed consent form.

6.3.5 Sample size determination

Determination of sample size requires a careful understanding of the main concepts of a study (Krejcie and Morgan, 1970; Chow, 2011). In fact, the sample size is but an aspect of the study design. The aim, nature, and scope of the study as well as the expected result of the study, are all the determining factors in enumerating sample size. As a key aspect of planning a clinical study, the determination of sample size requires a methodological skill. During this initial stage, the researcher is expected to establish the scope of the sample size fit for the study. Doing so depends on a variety of considerations, which have been highlighted above and each item is carefully deliberated at the beginning of the study (WHO, 1991; Lewis et al., 2001; Julious, 2005; Billingham et al., 2013). The number of study participants will have to be sufficiently large enough to permit comparison since it is practically impossible to study the whole population. Hence, a fraction of the population (participants) would be selected, which should be less in number (size) but adequately represent the population from which they were drawn. This would ensure that true inferences about the population could be drawn from the study findings. This group of individuals is referred to as the "sample". Hence, a sample is a segment, which is representative of a whole (Kadam and Bhalerao, 2010). Ideally, every individual in the given population should have an equal chance to be included in the sample. 'Power' is also a measure of the number of participants needed in a study. Power, in combination with sample size estimation, is used to quantify study participant load in order to answer a research question. Strictly speaking, the term 'power' denotes how many study participants needed to circumvent a type I or a type II error. These errors affect the way a null hypothesis is interpreted. For clarity, the null hypothesis is a general assumption or default position made at the onset of research. Usually, the null hypothesis states that there is no change between the treatment and control in terms of effects when a given intervention is

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introduced. The alternative hypothesis is that there is a change in terms of effect. Establishing whether the two groups are the same (accepting the null hypothesis) or there is a change (accepting the alternative hypothesis) could potentially result in either type I or type II error. A type I error occurs when we erroneously reject the null hypothesis that is, we claim otherwise (that is, conclude that there was a change) when indeed there was no change. Conversely, type II error is said to take place when we erroneously accept the null hypothesis that is, there is a change in the two groups and report there is none.

One daunting task in conducting research is sample size calculation and several studies point to this fact (Naduvilath et al., 2000; Noordzij et al., 2010; Shah., 2011). Although many published articles show methods for calculation of sample size, yet a lot of misinterpretations exist. It is crucial to note that the technique of sample size calculation varies for different study designs and one general formula does not suffice for all study designs. The specific formula applies for quantitative and qualitative studies depending on several considerations.

Normally, sample size quantification for quantitative study is determined using the following method (Charan and Biswas, 2013) :

Sample size = $2SD^2 (Z_{\alpha/2} + Z_{\beta)} / d^2$

Where,

SD = the standard deviation.

$Z_{\alpha/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ **(Read from Z table) at type I error of 5%**

$Z_{\beta} = Z_{0.2} = 0.842$ **(Read from Z table) at 80% power.**

d = effect size = difference between mean values.

From the above information, it is evident that sample size determination is an important aspect of a study protocol; however, it need not be performed in certain studies (Lewis et al., 2001; Julious, 2005). So, while not negating the value of sample size in clinical trials, formal sample size calculations for pilot and feasibility studies are unwarranted (Billingham et al., 2013). "For example, in a study of curative effect of the drug on a fatal disease such as AIDS, where a single positive result could be important, sample size calculation might be considered irrelevant" (WHO, 1991). Furthermore, if the goal of a study was simply for feasibility or piloting purposes, sample size determination will be needless (WHO, 1991; Lewis et al., 2001; Julious, 2005; Billingham et al., 2013). Unequivocally, the purpose of the current study was a feasibility study of provider-initiated offer of HIV test in ANC and therefore sample size calculation was not undertaken

6.3.6 Effect Size

Effect size is a method of quantifying the magnitude or level of change between two or more variables (Ferguson, 2009). It is most valuable for calculating the effectiveness of a specific program, relative to some comparison. Hence, the effect size can be described as the raw difference between the two-group averages, which is computed to translate the impact of an intervention to an easily comprehensible scale. This type of measure is a critical finding of quantitative research. Effect size helps researchers understand the magnitude of impact difference between groups and it is calculated using an easily understood and simple computational method. It answers the question, 'is it effective?' (Usually in a range of contexts). The formula for measuring the effect size is as follows:

(Mean of experimental group) – (Mean of the control group)

Standard deviation

This study attempted to calculate the effect size of the study program only to be limited by the nature of the outcome measure of the study, the measures were categorical (tested or not tested), which is not suitable for determining effect size. For instance, the group mean score and standard deviation are required to calculate the effect size, but these are not possible from the available data. The only plausible way to mimic the 'effect size' would be to undertake a 'systematic literature review with meta-analysis'. Meta-analysis is most valuable when an experiment has been replicated over time: the results of various reports are pulled together to create a single, exact estimate of an effect. This kind of synthesizing study results into one single effect size. Presently, meta-analysis is beyond the scope of this study. However, because meta-analysis may offer a precise and robust approximation after a rigorous combination of the available evidence, the researcher considers this aspect of the study a valuable recommendation for further study.

The different effect size estimates from various studies can easily be summed to give an overall best approximation of the level of the effect (Ferguson, 2009; Maher et al., 2013). This study could not compute the effect size because the outcome measure was a categorical variable, which means that it is not quantifiable in grades. The only plausible way to mimic the effect size would be to conduct a meta-analysis through merging data from other studies, and this is beyond the scope of the present study.

6.4. Enrolment process

6.4.1 Recruitment of participants

All new ANC clients applying for registration visit the booking desk to obtain general requirements for attending the facility, and specific conditions for ANC. At this period, they receive a booking date, ANC handbook and leaflets containing information about pregnancy,

sexually transmitted diseases (STDs), HIV infection and its consequences for mother and the infant, PMTCT and the recommended laboratory tests (refer to appendixes C-D). These have always been the routine of the facility. In addition, the ANC receptionist who is in charge of providing the initial registration information to intending clients seized the opportunity to share information about the research, and to invite them to volunteer as research participants. The receptionist hand-delivered copies of the participants' information sheet as well as the consent form to all new clients applying for ANC booking (refer to appendixes E and F). Equally, he verbally explained the aims of the study in both English and local dialects. The patient information letter contained information on the nature of the research and purpose. The principal researcher was also available to provide further information if the prospective participant sought one. This session allowed the women to discuss their concerns and receive the feedback she would need to enable her to make an informed decision. The women were asked to study and submit the signed consent form on their booking date if they wished to be enrolled in the study. They were specifically told to consent only after they had read and understood the research objectives and the level of their involvement. Equally, they were encouraged to seek clarifications elsewhere if they so desired. It was clearly stated that they could opt-out of participation at any point they wished, without giving any reason.

6.4.2 Registration Process

On the first full appointment (booking day) the midwife at the registration desk received the women. During which, the midwife obtained the woman's details including demographic information and entered them (Religion, tribe, age and education.) into the appropriate ANC login book. A full review of the woman's health and social needs as well as risk assessment, taking cognizance of the previous obstetrics, medical and surgical history was undertaken.

Also, the midwife checked and recorded the vital signs that included blood pressure and pulse rate as well as weight and height to calculate body mass index (BMI).

A brief discussion was held with the woman concerning the research before the midwife requests her to submit a copy of the signed consent form for enrolment into the study. For the exclusion criteria, (see section 6.3.4 of this chapter) concerning information about known HIV-positive results and language barrier (e.g. if the woman had language difficulty and there was no interpreter). At this point, these criteria were invoked. Each of the booked women was assigned to a team of clinicians, which included a midwife who supervised their ANC services. The midwife undertaking the booking inserted a colour code sticker into the woman's file to denote enrolment into the study, and for which intervention she belonged. Typically, women who enrolled from July to September 2016 were enrolled into the comparator (control) group. A yellow colour code indicated pre-intervention (control group) or the standard self-referral VCT; in which case, the woman would not be prompted for testing. She was, however; monitored for the uptake of HIV testing, and her response and the outcomes of testing were duly entered into the appropriate ANC HIV testing record book, appendix G. Before this study, women sought HIV testing through walk-in VCT approach based on self-motivation (FMoH Nigeria., 2011), Figure 6.2. This pattern remains applicable in other parts of Nigeria such as South-West, South-south and Southeast. However, in the light of current international consensus for universal attainment of HIV testing and leading evidence that good practice should involve easy availability of testing, all newly registered ANC clients had the opportunity to be tested. Posters were displayed in and around the facility to emphasize this message.

Figure 6-2 Depiction of Self-motivated walk-in HIV testing.

Conversely, a red colour sticker depicted routine provider-initiated opt-out HIV screening. In this case, the prescribing nurse grouped the women into 4-6 members to hold a group health discussion with the offer of HIV test. The main research outcomes as mentioned in the list of research questions (refer to chapter 5), were measured by a midwife checklist.

As practiced nationwide before the study, newly booked pregnant women received pamphlets containing recommended blood tests for pregnant women; this information was re-emphasized by advertorials, posters, and other health education magazines (see appendices C-D) placed in strategic positions in the hospital. To reduce bias in information dissemination, this practice continued at all times throughout the study period with the two study groups having the same chance of exposure to these materials.

6.5 Making of Discussion Protocol

Two different kinds of discussion protocols were formulated for comparison for the study: the minimal discussion (see Box 6.1) and the existing-comprehensive discussion (Box 6.2). The intention was to evaluate the optimal level of pre-intervention discussion (information) to reach informed decision-making and engender women's autonomous choice.

6.5.1 Development of Comprehensive or Standard Protocol

With the client-initiated testing approach, the woman on self-referral consulted the medical doctor to request for testing. The medical doctor enters the request into her folder and issues a note referring her to the counselling unit where the midwife dispensed counselling and testing services.

Following the standard practice in the study facility, a version of WHO guidelines for HIV counselling in ANC was adapted to develop the comprehensive protocol for HIV testing (WHO, 2002). This was done with the feedback and assistance from two veteran HIV counsellors who worked at the study centre but recently retired from service, (see below for the details). This protocol is like the current facility's protocol except that it is in a flipchart, to ensure uniformity.

The comprehensive discussion protocol is comprised of a range of information points, which the midwife counselled every woman in this group as follows:

i. The reason for offering HIV testing in pregnancy

ii. Routes of HIV infection and transmission

iii. The meaning of HIV test and what the test results are interpreted.

iv. The benefits and disadvantages of HIV testing in pregnancy.

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If after this initial dialogue, the woman still wants to undergo the test the midwife will proceed with the second list of points to discuss as detailed below:

v. Individual risk factor assessment (if the woman is willing to talk about it)

vi. Planning for a possible HIV-positive test result

vii. The available resources and support programs for HIV-positive pregnant women.

viii. What HIV antibody test involves and how the result is given.

6.5.2 Midwives Counselling Protocol Using Comprehensive Information

Introduction: In a private office, the midwife welcomes and identifies the client, then introduces herself. Primarily, I would want you to understand why you are receiving HIV testing and counselling. (She then proceeds with providing the following information, Box 6.1 below)

Box 6-1 Guide for Comprehensive Counselling Information

This is because a woman living with HIV can pass the virus to her baby during
i. Pregnancy,
ii. Labour
iii. In addition, to breastfeeding.
3. For women who took HIV tests and found HIV+, measures would be taken to reduce the probability of mother-to-child transmission.
4. **HIV**- what does this mean and how does it spread

I. HIV is the virus that causes AIDS. It destroys the immune system, rendering it ineffective to fight diseases and infections.

People become infected through:

i. Unprotected sex

ii. Sharing sharp objects such as needles when injecting drugs

iii. A mother to her baby during pregnancy and delivery

Currently in Nigeria, the rate of transmission in pregnant women is about 1 in 30.

The HIV tests

This is a blood test, which detects antibodies to HIV in an infected individual.

A positive test result would mean that the individual is infected with HIV.

The test does not show if the individual:

i. Has AIDS or not

ii. How long it will take to manifest AIDS

iii. When infection took place

iv. How infectious the individual may be.

v. The chances that the unborn baby will be infected or not

A negative test result means that:

i. The individual does not have antibodies to HIV

This is most likely to mean that the person is not infected with HIV

However, if one has been exposed to infection within the last 3months there are chances to be in the **'window stage'** and has not developed sufficient antibodies to HIV. If so, there is a need for a repeat test in 3months time.

Benefits of testing

i. Relief to know your status- especially if negative

If result chows HIV+:

i. There are medications for both the mother and the baby to reduce mother to child transmission rates and improve the woman's health.

ii. The woman can plan her labour to reduce the risk of passing the virus to the baby.

iii. Some specialists can help in the future.

iv. It can allow you to make choices about carrying on with your pregnancy.

v. This is an opportunity to receive relevant health education.

The disadvantages of testing:

i. There is no known cure for HIV

ii. There is still a lot of fear and misconception.

Even if negative, it can be during the waiting time for the test result

At the end of the session, the midwife asked the woman, if she had any questions /whether she would still want to have an HIV test.

For the women who answered 'no', the midwife halted further discussion about testing for HIV and she was reassured of adequate confidentiality. While encouraging her to reconsider her decision about testing in the future, she still received other ANC services.

For the women who answered 'yes', the midwife continued with the concluding part of the counselling. She probed further to find out if the woman has any concerns, which has prompted her to come for an HIV test. Both parties agreed on a plan for the likelihood of a positive HIV test result.

The woman nominated an individual who would support her when receiving her test result, if possible. She was encouraged to consider how to deal with intimate partner violence in the event of a positive test result.

The midwife provided her with information about the various community support programs that are available for people living with HIV (PLW), starting from i) People living with HIV Association (PLWA), ii) Women HIV and AIDS Network – information, iii) service and pressure group for women's issues and iv) consultant Obstetrician.

The woman was told that although no extra blood will be drawn, the battery of ANC tests includes syphilis, hepatitis B and C, haemoglobin (HB) and blood group. Equally, she was informed that the test result would be available same day.

Recap

At the end of the counselling session, the midwife highlighted the key points, which included the significance of testing in pregnancy, benefits and disadvantages of testing, how the results would be given, the importance of remembering that test result may be in window stage, and choice for HIV testing being autonomous.

Do you still wish to be tested for HIV?

The woman was given enough time to reflect on the issues discussed and the HIV testing consent form (Appendix E), issued to her. The woman filled, and signed or thumbprints the form, indicating consent to be tested. Once she signed and returned the form, it was filed in her personal folder. The midwife filled routine blood test request form including HIV test. The laboratory technologist drew a Blood sample for the tests into a blood container and labelled it with the patient's coded identifier. The test is taken, and individualized post-test counselling was offered.

6.5.3 Development of the Minimal Counselling Protocol

The minimal protocol followed 2007 WHO guidance on provider-initiated HIV testing and counselling protocol (WHO., 2007), and contained simple information about the benefits of testing. The researcher developed the protocol based on WHO recommendation and an experienced midwife counsellor refined the contents. The information on the minimal discussion protocol is as follows:

I. All pregnant women were encouraged to learn their HIV status.

ii. An HIV infected mother can transmit the virus to her baby during pregnancy, childbirth, and breastfeeding.

An undiagnosed infected mother who did not receive treatment for PMTCT has a 25% chance that the virus will be passed to her baby.

iv. If a woman has the virus and takes medication, the possibility of passing the virus to her baby is reduced to approximately 1%.

The two draft protocols were given to the midwives to read. In the training exercise, they gave feedback on challenges they could anticipate regarding the terminology and style. The feedback formed the basis for modification and the comments were addressed. The second draft was produced in flipchart format, which was made available to the midwives to test-run during the first week prior to the trial. Several issues still arose, especially regarding the wording and order of the protocols. At this point, the researcher involved an HIV counsellor veteran who applied her wealth of experience in rewording and resolved the issues. Considering these inputs, the final protocol was devised, as represented in box 6.2 below).

6.5.4 Streamlined HIV Counselling Information for Provider-Initiated Testing Approach

The information contained in the routine offer for HIV testing is as seen in box 6.2 below.

Box 6-2 Handbook for Streamlined Counselling Information

- HIV- this is a virus, which can be spread through blood, semen or vaginal fluid.

- The virus is the causative agent of AIDS as it gradually destroys the immune system making it incapable of fighting diseases.

- Usually, the latent period of developing AIDS is about ten years.

- HIV can be transmitted to the baby during the periods of pregnancy and delivery.

- If an infected pregnant woman is identified, special care is given to her and her baby to reduce the chances of mother-to-child transmission.

- If a woman tests HIV+, this means that she has the virus. This does not mean that she has AIDS.

- A negative test result means that the woman is free from the virus. However, it takes three months for antibodies to HIV to show; therefore, people who have been exposed are advised to have a repeat test.

- **Decision to test**

- ✓ The women were given the option to test immediately after the discussion or to defer testing to a later date.

- ✓ They were also at liberty to discuss testing with their partners and take the decision later.

- ✓ Women were given the opportunity to seek test elsewhere, especially in the neighbouring health facilities such as Garki and Wuse general hospitals. The midwife ended the discussion forum by requesting for questions from the group and asked them to inform her of decision taken regarding testing during individual medical check in her office.

6.5 Build-up to the Interventions

6.5.1 Meetings with the Relevant Stakeholders

Before the study, a meeting was held between the Chief Medical Director (CMD) and other relevant stakeholders such as Heads of Department (HoDs) and the researcher. The goals of the meeting were principally of three-folds. First, to formally, introduce the study; bringing everybody involved in the research on board and individuals to familiarize themselves with one another for effective teamwork. Second, to set common objectives (based on the principle of specific, measurable, achievable, realistic and time-bound (SAMRT) approach), taking care not to disrupt other clinical services in the facility and at the same time, being

cognizant that the study is time-bound. Third, to elect measures to ensure a steady supply of research commodities to avert any kind of breakdown or interruption during the study period.

The principal investigator made a presentation of the study and the study plan. Members seized the opportunity to ask questions and to make suggestions before the final study plan was adopted. The CMD assured of maximum cooperation and appealed to other staff to be supportive. He directed that in the event of stock-out of commodity, items should be borrowed from the neighbouring health facilities for which an arrangement has been made. He consequently appointed one of his staff to oversee and give weekly updates of stocking levels.

6.5.2 Training of Midwives

Five midwives who work directly in the ANC were trained. Each of them had more than 30 women booked for ANC during the study period. Six other midwives who occasionally participated in the booking process were not considered as formal research staff because their presence was minimal considering their contributions. This group made a minimal number of bookings (range, 1-6 ANC bookings). Most of them were temporary staff (*ad-hoc staff*) while others were borrowed from other units when the existing staff member(s) were on off-duty or failed to turn up for duty. We, however, trained all the eleven midwives. At the onset, we had agreed with the management of the facility to retain these core research midwives in the ANC unit throughout the study period to help maintain uniformity of service delivery, ease monitoring of their performance, as well as ease administering proper pieces of training and updates.

The training sessions were conducted over three half days (after work hours) to avoid disruption of clinical services since the nurses involved in the training were the same staff

who render services to patients during busy rush hours of the day. In the first training session of the first half day, a public health practitioner made a slide presentation in which he highlighted the basic virology of HIV, the transmission routes with emphasis on heterosexual and mother-to-child transmissions, including interventions to reduce infection. There was questions and answers session at the end of the presentation. Handouts were given to participants to study at home, appendix H.

The researcher anchored training on the second half-day. The session started with the rapporteur of the previous day training session. Participants were encouraged to contribute and ask questions during this period. Questions were randomly asked participants to assess the level of understanding.

The day's training started with reviewing the existing intervention before introducing the main activity. The idea was to start from the known to the unknown. After these preambles, the main topic was introduced. The discussion focused on the aim of the research, nature of the experiment, research questions and the role of the midwives in the study. The distinctive differences between the two approaches for offering HIV (client-initiated VCT and routine opt-out) were highlighted and the protocols for delivering the two introduced and discussed in detail. At the end of the training, the women were given training materials including the discussion protocols to study at home. A rapporteur was elected for the next training session.

On the third half training day, the principal researcher led the training, which concentrated, on role-play. After the rapporteur presentation, participants were divided into four's and each participant taking a turn to conduct both individual and group counselling, using the written discussion protocol while the rest members watched and critiqued performance. The main researcher participated in the role-play, making corrections when necessary especially on the

discussion protocol. After the training sessions, and during the study period, the team members organized occasional meetings to tackle unforeseen circumstances, to assess the general progress of the study, identify problems with the discussion protocol and provide support. Additionally, during the study, the main researcher conducted periodic monitoring of the performance of all the research midwives to ensure uniformity in the delivery of the discussion protocol and giving feedback when necessary. Each midwife was observed for no less than twice during the client-initiated VCT and routine opt-out regimes.

6.6 Data Collection Procedure

6.6.1 Overview

There was no randomization of women into groups; however, all research participants booking for ANC from July to September 2016 were categorized as the comparator group and received the standard intervention. Consequently, those who booked from October to December 2016 were categorized into the experimental group and received a routine opt-out model. During the booking, each woman was allocated with a group identifier code, which marks the formal entry into the study. Only those women who consented to participate in the study received this code.

On the clinic days, the midwife concealed the participant's code on a specific location known to the clinic midwife. The code numbers indicated that the woman was a research participant and specified which cohort she belonged to. The six midwives who had received training for offering HIV tests (see the next section) conducted most of the bookings. Women who belonged to the comparator group were not routinely offered an HIV test unless they requested it on self-motivation. If this happened, the midwife followed the standard protocol for client-initiated counselling and testing as contained in the discussion protocol.

If the woman accepted the test, an explanation of the procedure for delivering both positive and negative results will be given. Equally, she was required to give active consent through the signing of consent form before the blood sample is drawn for HIV testing.

On the other hand, the women in the experimental group were arranged into 5-6 women and they were offered group counselling by the midwife. For the two cohorts, the corresponding pre-test and post-test HIV discussion protocols were printed in a handbook and kept in the ANC consulting rooms for ease of reference. Midwives were instructed to refer and to follow the protocols during counselling sessions. For provider-initiated testing HIV test was discussed as well as the other antenatal screening tests. In this group, a blood sample was drawn unless the woman actively declined to test. Women who did not enrol in any study group received all other clinical services, including HIV test, for those who requested for one.

For all individuals, blood samples for testing for either HIV or other relevant investigations were clearly identified by the laboratory technologist with the identifier code number, which was assigned to each client. Samples for the HIV test were boldly labelled HIV on the body of the container before delivery to the laboratory for testing.

For every woman who received one of the interventions, the midwife completed a checklist and entered the relevant information, including the socio-demographic information into a specially designed ANC record book. The tests were performed in the laboratory and the results delivered to the research midwife who maintained strict confidentiality of the results by entering them into an ANC record book, which was kept locked in the office. All tested women received the same day test result, involving post-test counselling.

6.6.2 Pre-intervention (Client initiated VCT) Procedure

During the three-month controlled-trial period or the comparator group (July-September 2016) women received client-initiated VCT. All the five core research midwives who received training were involved in offering voluntary counselling and testing to the women who sought HIV tests on self-referrals. Throughout the pre-test counselling, the midwife counsellor followed the discussion protocol contained in the handbook. The individual pre-test counselling was conducted, focusing on the following:

- Proper identification of the client with the coded number and assuring the client of confidentiality.

- Provision of information about HIV-test, benefits and the implications, including PMTCT.

- Modes of and risk factors for transmission, particularly MTCT and measures for prevention.

- Benefits of knowing one's status in the context of PMTCT.

- The test procedure and meaning of a negative or positive test result in an explicit term.

- The availability of antiretroviral drugs for PMTCT.

For the mothers who voluntarily indicated interest to have an HIV test, the midwife offered HIV counselling and testing services involving detailed pre-test counselling and subsequently post-test counselling. The one-to-one pre-test counselling session is normally followed by active consent from the woman (either verbal or signed) before a blood sample is drawn for an HIV test. This procedure is in line with the national algorithm for HCT in which the midwife performs risk assessment after pre-test counselling, obtained informed active consent before

the blood sample is drawn, and ensures that the blood sample is clearly labelled for an HIV test and other ANC investigations for this group of women. For other women who have not specifically requested for HIV test, blood samples were still obtained from them for other routine ANC investigations (Haemoglobin-HB, venereal disease research laboratory (VDRL), Hepatitis B and blood group).

The samples were sent to the laboratory for the investigations. The patient was asked to return for post-test counselling within an hour of obtaining the blood sample. Patients who declined HIV screening were tested for other routine ANC investigations. Women who came with their partners received couple counselling or individual counselling depending on their preference. The laboratory conducted the test and returned the results to the counsellor for post-test counselling on the same day.

Women were post-counselled by the same individual counsellors who conducted pre-test counselling. The main objectives were to make the women understand the implication of their test results; how it affects them and their unborn child and steps to be taken based on the test result. For the women with HIV-negative test results, the emphasis was stressed on the need for prevention of sexual HIV transmission. For HIV-positive women, the emphasis was on PMTCT interventions, single-dose Nevirapine (sdNVP) for the baby, counselling for exclusive breastfeeding of the baby for six months as prescribed by WHO and national guidelines (FMOH/NACA, 2015; FMOH, 2016) and mother-infant follow-up. Women who had sexually transmitted diseases other than HIV were treated for the infection.

6.5.4 Intervention (Provider-initiated opt-out testing (Routine HIV testing)

Following the introduction of routine testing from October to December 2016, the research midwives prescribed the HIV test after holding a 10-15 minutes group discussion and health

education with the pregnant women, using a handbook discussion protocol as a guide. Testing was recommended to all pregnant women. The discussion emphasized HIV transmission, PMTCT services (ARV drugs for the mother and sdNVP for the baby) and details of how the result will be given. The midwife informed women that testing was voluntary and with the right of refusal. In addition, it was emphasised that whether an individual undertook the test, this would not diminish the quality of other care the woman would receive. Women who came with their husbands received couple counselling if they opted for that while those who arrived late when group sessions had been concluded received individual counselling. A blood sample was drawn, labelled and sent to the laboratory for HIV tests and other ANC investigations such as syphilis, hepatitis, haemoglobin, blood group, etc. Women who declined testing had other ANC investigations done for them. They also received individual counselling, which focused on addressing their reasons for opting out of HIV testing. This was further reinforced in subsequent prenatal care visits. Women were guaranteed the confidentiality of the test result and the need for partner counselling. Test results were delivered to the women the same day after extensive post-test counselling. Emphasis was made on mechanisms to remain negative for the women with the seronegative result. HIV positive mothers received counselling on coping strategies, referral to PMTCT clinic and care and support services and the need for exclusive breastfeeding. Also, the counsellor highlighted the need for promotion of other safe infant feeding practices and family planning as well as a conversation of their families, their own, and their child's survival and the possible exposure to stigma. Figure 6.3 below, shows the algorithm for routine HIV counselling.
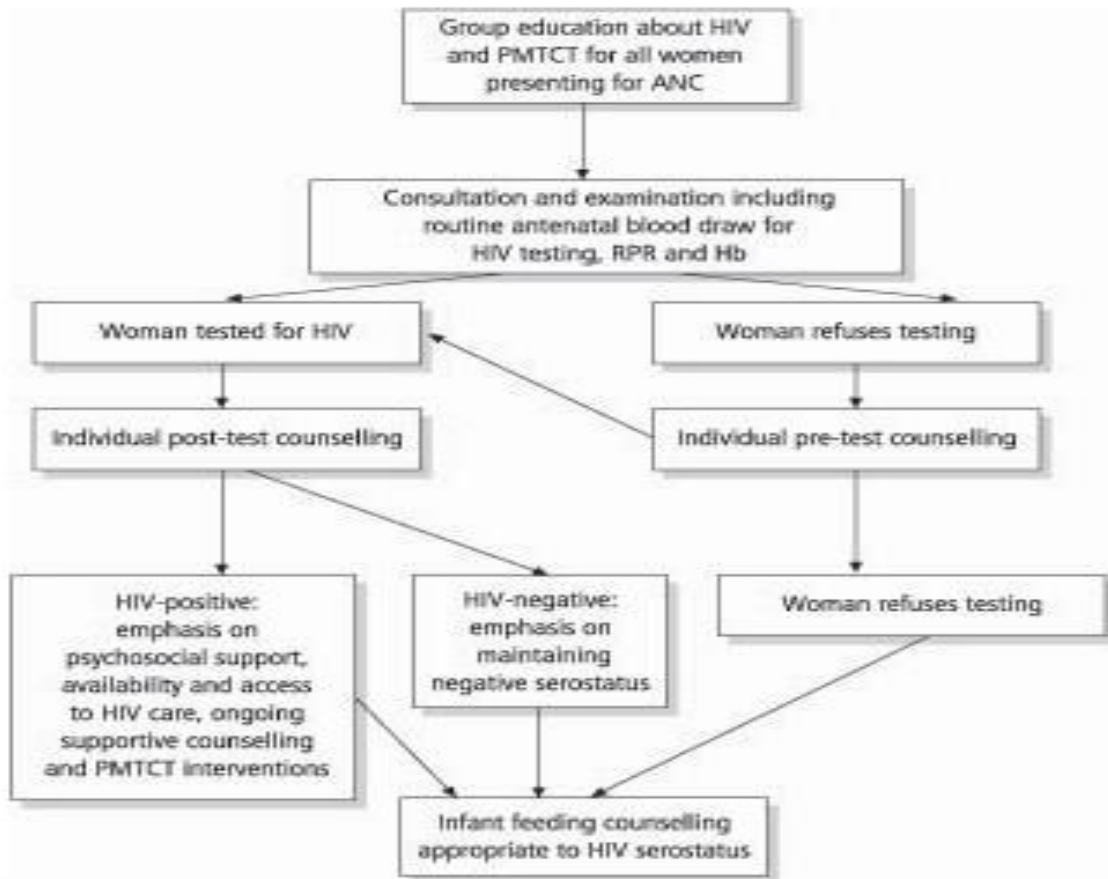
Figure 6-3 Illustrates the vital steps for provider-initiated routine opt-out testing

6.5.5 HIV Testing Procedure.

The HIV test was conducted on-site in the hospital's laboratory using the current national testing algorithm, which is based on serial testing. A serial test using the first line kit (Determine HIV/1/2 test, Abbott Laboratories, USA) was used to determine the serostatus of each blood sample. A non-reactive test result to Determine rapid kit is recorded as seronegative, which means that the individual is negative to HIV antibodies (HIV test result= Negative). A reactive test result (with Determine HIV1/2) was sequentially tested for confirmation using the second line rapid HIV test kit (Uni-Gold Test, Trinity Biotech, and the USA). If the test was reactive, a seropositive test result (HIV-positive) was recorded. However,

any discordant test result between the 1st line and the 2nd line test kits was resolved using a tie-breaker rapid test kit (Chembio HIV1/2 STAT-PAK, USA), Figure 6.4.
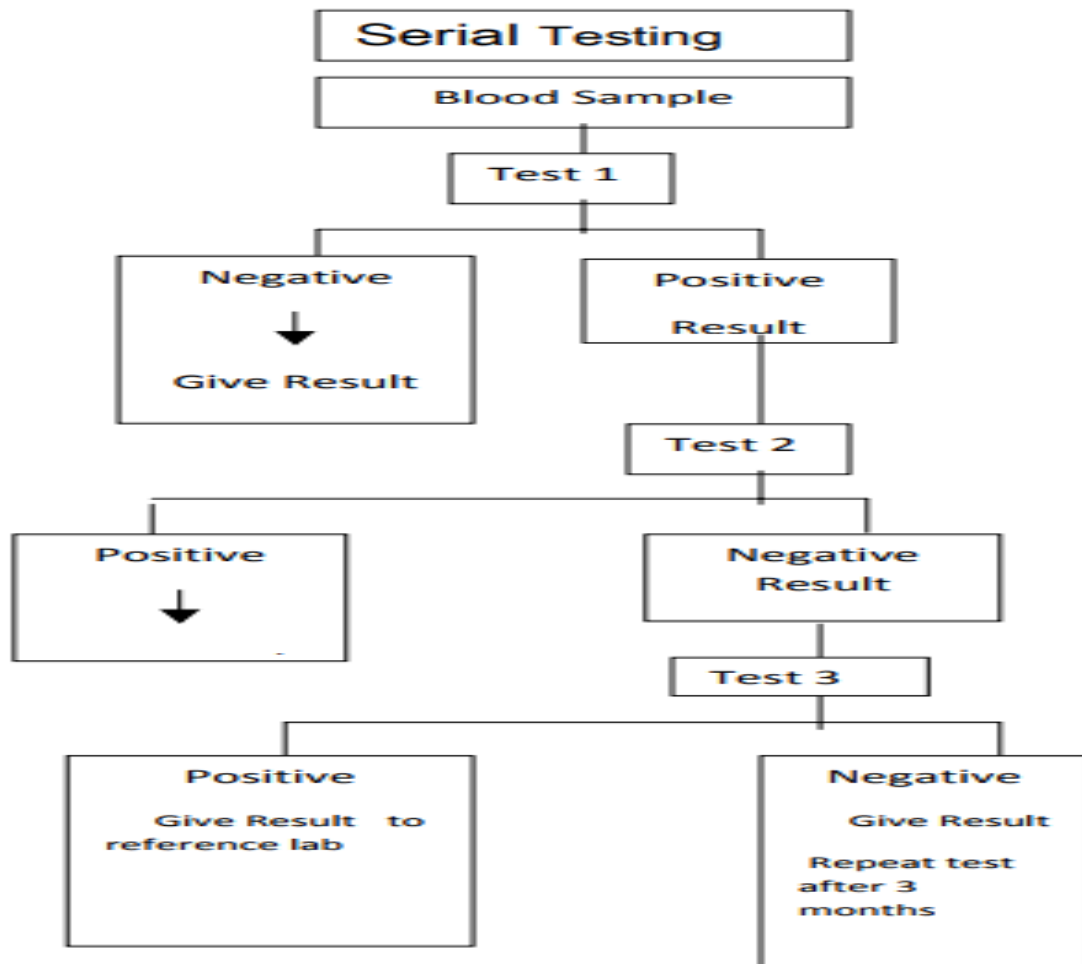
Figure 6-4 National HIV testing algorithm based on serial testing

6.6. Data collection and analysis.

6.6.1 Data collection.

Quantitative data collection was undertaken. Data were analysed descriptively following the six months covered by the study. The uptake of ANC HIV testing and the testing outcomes were compared between the policy changes introduced during the study period (Client-initiated VCT versus Provider-initiated routine opt-out). Specifically, data regarding HIV testing rate case detection rate and treatment for PMTCT were collected. In addition, categorical data were collected.

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6.6.2 Data analysis.

Quantitative and categorical data were enumerated and analysed using software Statistical Package for the Social Sciences (SPSS). Statistical analysis involving descriptive statistics and bivariate analysis of chi-square test. A p-value of 0.05 was considered significant for all computed comparison. All differences are recorded with the *P*-value of X^2 tests or the phi-correlation test reported with a 95% confidence interval. Results were presented in statistical formats using absolute numbers tabulated on tables, graphs, and percentages, histograms and bar charts.

6.7. Ethical Consideration.

6.7.1 Ethical Approval.

The conduct of credible research requires both diligence and expertise. However, other considerations such as honesty and integrity are paramount and hallmark of reliable research. They are the umbrella under which the rights of human participants are protected from abuse. To uphold the ethical conduct of this study, the rights to self-determination, anonymity, confidentiality and informed consent were adequately preserved. The study obtained formal ethical permissions from Manchester Metropolitan University Research and Ethics council. The study was also granted ethics approval by Research and Ethics Committee SHMC, Abuja Nigeria where the study was conducted (see appendices I and J). Verbal consents were obtained from the gatekeepers of the patients in the facility (State House Medical centre) as well as the ANC section.

6.7.2 Confidentiality and anonymity

Measures were appropriately taken to preserve and maintain the confidentiality and anonymity of participants. According to (Sweeney, 2002) "A release provides k-anonymity protection if the information for each person contained in the release cannot be distinguished from at least k-1 individuals whose information also appears in the release".

In this study, participants were identified using coded numbers rather than their names. Patients' names were only used when the principal researchers did trace information. All

records containing patients' information were locked in a filing cabinet. The computer files with sensitive information were all password protected. The analysis of the data was conducted using coded identifiers in appropriate, secure, research surrounding. The researcher with minimal contribution from external individuals performed the data analysis in the strictest anonymous environment. The personal identifiers or features that may link individuals with the data were completely removed in situations where an external person was involved. Conversely, confidentiality explains situations where data or information from research participants are handled in ways that preclude exposure of such personal data in the public domain in a manner that does not protect the individual's identity. In this study, unauthorized individuals were not allowed access to data with traceable identifiers. In situations where the publishing of the research findings is undertaken, personal identities will be removed. Moreover, the principle of self-determination was also enforced. This is because the research participants were treated as autonomous agents who volunteered based on informed consent.

6.7.5 Chapter summary

This chapter has clearly explained in details the research methodology, including the population, sampling process as well as data collection instruments and strategies employed to uphold sound ethical standards, reliability, and validity of the study.

The next chapter 7 presents the economic dimension of this study and method for the evaluation.

Chapter 7 : Methodological approach to the economic evaluation of health care

intervention: A focus on HIV testing strategies in antenatal care service.

7.1. Introduction

The chapter discusses the rationale for conducting economic evaluation; starting with

background information. Some sections of the chapter were dedicated to outlining the main

concepts of economic evaluation in medical decision making: the main framework, including

the rationale and theory underlying economic evaluations. The second aspect is to outline

guidelines for best practices in conducting economic evaluation and criteria for incorporating

the findings into medical decision-making. In addition, the methodological approaches for

conducting this evaluation was well-discussed, paying deep attention to the issues of

interpretation of results, especially those elements with direct bearing with this study. These

aspects pertain to the choice of health outcome of interest; selection of analytical framework

that is compatible with the data from the fieldwork and representative of the scenario for the

study; comparison of current testing approach with the new intervention and choice for ANC

based population-level study.

7.1.2 Synopsis of prevention of mother to child transmission (PMTCT) of HIV

The ideal way to reduce perinatal HIV transmission is via the prevention of HIV in pregnant

women (Stein., 1993; Mantell et al., 2006). However, this is not always possible and PMTCT,

often referred to as vertical transmission is the alternative measure for doing so. This involves

a series of interventions geared towards preventing HIV acquisition from an infected mother

to her baby during pregnancy, labour, delivery or breastfeeding (McGowan and Shah, 2000).

Among these interventions is the diagnosis, which centres on the need to identify as many

infected mothers as early as possible. Undiagnosed status heightens the susceptibility of

vertical HIV acquisition from an HIV infected mother (McGowan and Shah, 2000). The woman also risks developing AIDS in the absence of proper treatment (Drake et al., 2014). Under an ideal situation, comprehensive PMTCT can reduce MTCT to less than 1%, even in breastfeeding environment (Wettstein et al., 2012; Fowler et al., 2016)

Apparently responding to low testing rates associated with client-initiated VCT, WHO endorsed the use of provider-initiated antenatal HIV testing approaches to all member states. The goal was to tackle the challenges of time constraints, the lengthy requirement for written informed consent and competing demands with physicians' roles.

Many countries both developed and LMICs have already adopted this program and routine testing is now the mainstay of HIV screening in these settings (Yazdanpanah et al., 2010; Leidel et al., 2015). As with any new intervention, the policy-maker is faced with the challenge of identifying which intervention that addresses the health needs of the population at 'value for money'.

Several recent studies particularly in the United States of America (Paltiel et al., 2006; Alverson and Alexander, 2009; Shah et al., 2016) and Europe (Yazdanpanah et al., 2010; Deblonde et al., 2010) have shown that routine HIV testing is both clinically and economically effective. Clearly, it is not ideal to extrapolate studies from another country to another country such as Nigeria. This is because different epidemiological, economic conditions and cultural variations between settings warrant a country-specific understanding of the economic impact of such intervention before adopting it.

Hence, based on the need to re-evaluate the HIV testing policy in Nigeria, the current study focused on assessing the costs and cost-effectiveness of provider-initiated routine HIV testing in an antenatal setting.

Globally, the number of new HIV infections is declining, however, countries like Nigeria continues to witness high rates of infection. The reports suggest that provision of antiretroviral medicines to pregnant mothers living with HIV has so far averted 1.6 million paediatric infections since 2009 (UNICEF, 2016b). However, Nigeria witnessed the highest new MTCT of HIV in the world, in 2016, and only a third of HIV-positive pregnant women have learned their HIV status. (UNAIDS., 2017). WHO recommends a four-pronged approach to containing MTCT and these include primary prevention among women of childbearing age, prevention of unintended pregnancies among infected women, prevention of paediatric infection from infected mothers and appropriate treatment, support, and care for women living with the virus, their children and families.

For countries seeking to expand HCT coverage, integrating HCT services into existing services through provider-initiated testing and counselling (PITC) approach, it is necessary to evaluate the economic impact of this program prior to the adoption.

Regarding Nigeria, the government and their implementing partners are working closely to implement the consolidated WHO guidelines on PMTCT program(NACA, 2017). Nigeria is currently exploring the alternative option for HIV testing in line with the new recommendation. Besides, clinical impact expanding HIV testing in ANC has other consequences from an economic viewpoint. This is more so amidst the current economic crisis in which renewed interest in achieving 'value for money' has become the focus of policy-makers who would want to implement the most efficient HIV service without compromising quality. For a country seeking to expand HIV testing coverage, provider-initiated opt-out testing may potentially present an opportunity for an effective HIV testing strategy.

7.2. The concepts of health economics.

7.2.1 Framework for economic studies

The goal of this section is to describe the framework underpinning economic evaluations in the medical decision process. The section explains relevant health economic principles; rationales for performing economic evaluation of health care interventions; types of economic evaluations as well as evaluation designs, in this case, trial-based costing.

Generally, economics is a branch of science that deals with resource allocation. Health economics, on the other hand, is a subset of economics that deals with resource allocation within the health sector (Kernick, 2003). In both cases, resources (labour, capital, and land) are viewed as scarce. Based on the premise that societal resources are finite, meaning that resources are limited to produce enough goods and services to satisfy every demand, choices must be made between competing alternatives; hence the need for a prudent way of resource allocation. Making an economic choice results in sacrifice because the available resources must be channelled to a program that benefits society the most. Given this situation, organizations and indeed the society must make choices concerning how goods and services should be allocated to meet the important societal demands in a manner that maximizes health care spending (Eddama and Coast, 2009). From this point of view, the reality of scarcity engenders the need for evaluating alternative mechanisms for resource allocation in a way that promotes efficiency. One of the strategies employed to select wisely from a range of interventions to achieve efficient resource allocation is to determine cost-effectiveness. Cost-effectiveness is a form of economic analysis, which compares the relative costs, and outcomes of various courses of action to ensure value for money. Broadly, health economics evaluation

is applied to contain costs and manage demands within the health institutions (Eddama and Coast, 2009).

For clarity, at this point, the frequently used economics terms and concepts about this study will be described. Central in the heart of a health economist is the efficiency of resource allocation knowing fully well that human wants such as health care services (laboratory investigations, neuro-surgery, dental surgery, plastic surgery and so on) are unlimited but the resources to achieve them are limited. This means tight budgetary allocation does and always exists and therefore one service or a health care program must give way (forgone alternative) for the other to be implemented (best alternative) (Vollmann, 2013). However, it is natural to expect the service with better outcomes (efficiency) to take precedence over the other (Izetbegović et al., 2013). This relationship is expressed as an opportunity cost: a situation where the value for the next best alternative is forgone. Efficiency implies that the resources are being channelled to interventions (goods or services) where they produce the best results or generate better outcomes at minimal cost (Vollmann, 2013). In this context, as will be discussed in detail in a later section, the selection or adoption of a particular testing technique, for instance, routine opt-out HIV testing to improve testing coverage and uptake in ANC facilities would mean that the next best alternative, which is client-initiated VCT, is forgone.

 Health economics is the branch of economics that deals with resource allocation in the healthcare settings is therefore vested with this obligation. This unit follows the framework of economic concepts in health and healthcare spending to provide bargaining power with suppliers of health care services. In the words of great scientists in a study, health economics means inculcating economic principles in like manner philosophy to which conventional

goods are during the decision-making process of purchasing or allotting resources to health interventions by policymakers or individuals (Morris, 2012). This concept highlights the fundamental framework for which health economics conceive the same analytical principles that guide the economic allocation of resources of general goods and services. Fundamentally, economics is traditionally premised on the disbursement of limited and scarce resources (e.g., raw materials, capital, and labour) for which choices must be made (Izetbegović et al., 2013). However, human wants are vastly unlimited and rarely satiable due to inadequate resources. An economic evaluation of health care interventions, therefore, aims at guiding the policy-maker with the arduous task of judicious allocation of health care resources, detecting priorities and refining health policies (Izetbegović et al., 2013).

Health economics view healthcare as economic goods with finite resources from which the society must make choices in resource allocation. Lack of enough health care resources impede the adequate supply of health care needs that people would want to access; and to this extent, choices and opportunity costs (The forgone best alternative) must be made. Health care services are hardly enough in any society (Health Knowledge, 2010). Under this circumstance, health interventions must be adopted based on relative efficiency, which describes the resource use and the potential net benefit of the intervention.

The opportunity cost of health interventions can be examined using cost-effectiveness evaluation. When two programs are compared using cost-effectiveness analysis the opportunity cost of the alternative uses of the resources becomes explicit (Vollmann, 2013).

Health care interventions are deployed to improve health with the available preventive measures, medical proceedings, and treatment. The variations in the quality of health care provision across the country as well as rising costs of expenditure warrants the need for

effective utilization of health care resources. These factors in addition to scarce resources accentuate the necessity to choose the most effective intervention through the conduction of cost-effectiveness analysis (Dang et al., 2016).

 Essentially, economics, in general, focuses on the allocation of limited resources among competing programs, health economics specifically deals with the allocation of resources for improving health (van Nooten et al., 2012). Health economics plays distinct roles: examines and evaluates issues related to effectiveness, efficiency, and value of resources in health and health care settings (van Nooten et al., 2012; Dang et al., 2016). Prospective uses of economic evaluation include price negotiation, communicating with prescribers and development of clinical practice guidelines (Yothasamut et al., 2009). Such evaluations are relevant in understanding the economic aspects of health and the challenges that impede the procurement of adequate health care (Mishra and Nair, 2015).

A health care service often depends on the deployment of complex interventions to deliver medical and public health goals. The adoption of these interventions is expensive in terms of cost of service delivery, which has led to a rise in health care service. In fact, the most visible and distinct difference between the rich and the poor is access to health interventions (Teerawattananon et al., 2009). The economic evaluation that is embedded in health intervention assessment has gained credence as a strategy to compare and determine the health benefits and costs of alternative programs (Kobelt et al., 2013). This approach is extensively used to prioritize interventions that represent the most effective use of resources among the competing alternatives in the developed countries (Dang et al., 2016)

Any new intervention that is being considered for adoption in a society usually undergoes predetermined phases of evaluation to ascertain its worth vis-à-vis outcome and cost.

Normally, for health care programs, health economists provide guidance on which intervention should be adopted, both in resource-constraint and in resource-rich countries (Wang, 2013). This mechanism has emerged as a global-level standard, which does influence a fruitful priority setting and is generally considered a mechanism to handle the health care priority setting (Glassman et al., 2012).

Scarce resources limit the number of health care interventions that can be adopted in many circumstances, and therefore choices must be made among the competing interventions. The decision to implement one program should be based on the economic sense (Glassman et al., 2012). Health economics seeks to assist the decision-making process by offering an unequivocal decision-making framework premised on the principle of efficiency (Kernick, 2003). Hence, to prioritize and efficiently allocate resources, an appropriate analytical tool is employed to put the cost and benefits of the interventions into a proper perspective.

In line with the above framework, the introduction of provider-initiated routine HIV testing over the existing client-initiated HIV testing in Nigeria warrants an economic evaluation. Presently, pregnant women do not routinely receive HIV testing during ANC visits. Hence, a great number of HIV infected children are born that could be averted had a program for diagnosing all infected women been implemented. This study evaluated the additional costs to the health care system and the additional health benefits accruable from adopting routine HIV screening program compared with client-initiated VCT during ANC plus the implication for the health care policy. The clinical effectiveness of an intervention describes the degree or extent to which the health care intervention improves quantity and quality of life (Long et al., 2015). Given the tight budgetary allocation for health care in Nigeria and globally, it is unacceptable and unethical not to put the available resources to the most efficient use.

7.3. Rationale for this study

7.3.1 Reasons behind the Study

An important public health strategy for PMTCT is to reduce new HIV infections in women of reproductive age. For the women who are already infected with the virus, transmission can be reduced by initiating antiretroviral treatment during and after pregnancy. However, only those who are identified before delivery can decide whether to take up this intervention (Nicoll et al., 1998; Tookey et al., 1998; Wohlgemut et al., 2012). Most health centers in Nigeria only provide HIV screening at the direct request of an individual client or to a population of women who are classified as being at higher risk (FMOH/NACA., 2015). This has led to most HIV infected women being undiagnosed at delivery and many women in Nigeria remained unknown of their HIV-positive status. Pregnant women unaware of their infection carry a greater risk of transmission; resulting in over three-folds chances of transmitting the virus to their babies than those who know their HIV-positive status (Faghih and Secord., 2012).

In 1999, HIV testing policy changed from client-initiated to routine testing in the United Kingdom (Townsend et al., 2006). Statistics from national surveillance and unlinked anonymous survey HIV prevalence provided evidence of the impact of the policy change. Testing rates increased from less than 25% in 1997 to more than 90% in 2001 (Keane et al., 2002). During this period, an estimated 380 children were born to HIV infected mothers (Brown et al., 2004). With the rapid increase in the number of HIV infections and with the highest prevalence rate in the UK among the heterosexual population, it was certain that MTCT of HIV was set to rise (Dean et al., 2001). Certainly, if a large proportion of women: 90%

or more rather than 25% know their HIV-positive status and receive the standard preventive measures for PMTCT, avoidable cases of MTCT would have been enhanced.

For instance, in 2000, an estimated 450 HIV-positive women gave birth in the UK (Brown et al., 2004). Based on the on-request testing approach (client-initiated VCT), it is expected that about a quarter of these mothers learn their HIV-positive status (Nicoll et al., 1998). Knowing that transmission rates with appropriate preventive measures for PMTCT reduce the risk of infection to around 2% and that in the absence of these interventions, to approximately 20%. Hence if 25% of these 450 pregnant women learn their HIV status and accept treatment while 75% do not it would be estimated that 70 of these children would become infected with HIV. On the contrary, if 90% of the 450 women tested and accepted treatment, it can be predicted that only 17% of these children born to these HIV infected mothers may become infected.

The above scenario mirrors the current situation in Nigeria (NACA, 2017). Asymptomatic mothers do not routinely receive HIV testing and most testing is based on self-referral; hence, a large proportion of HIV infection in children, which could be averted if a program for frequently testing their mother, is introduced.

However, this amount of information, which focuses on the clinical outcomes alone, is not enough for a decision-maker who is charged with implementing an HIV prevention program. Attaining the finest or most 'efficient' level of HIV testing technique requires evidence-based information on resource use associated with individual HIV testing approaches, and the level of benefit derived by the target population. Hence, the policymaker would require scientifically cogent yet appropriate reports concerning the costs and benefits of alternative methods of delivering the intervention. The policymaker must know the various interventions that are in existence, the ones that have proven to be effective, the cost of implementing it,

and whether it can be adapted to the local community (Holtgrave et al., 1996; Yothasamut et al., 2009). The policymaker needs to balance the need for the resources required by the different HIV interventions with the potential benefits, avert the maximum number of MTCT of HIV within the available resources and reflect on other vital factors such as access.

Following the 2007 WHO and CDC revised recommendations supporting the adoption of routine HIV testing for all pregnant women; the Nigerian government has begun to make frantic efforts to implement this policy.

The routine offer of HIV differs in important ways from client-initiated VCT. Among the salient differences is the abolishment of written informed consent: consent would now accrue from the general medical consent. Other differences are task shifting of counselling and testing from physician to midwives, and replacement of comprehensive pre-test counselling with streamlined information. Women would also have to receive counselling in groups.

The purpose of this study is to evaluate the additional cost to the health care system and the additional health outcomes associated with introducing routine HIV testing among pregnant women who are receiving antenatal care services in a tertiary health facility, compared with the current scenario of client-initiated HIV testing. To the best of my knowledge, no studies have examined the cost-effectiveness of routine HIV testing in Nigeria.

7.4. Justification for economic evaluation.

7.4.1 General economic concept

Resources in the health care system are infinite, coupled with continuous demand to maximize health benefits to clients within the available resources (Higgins et al., 2010). The rising cost in the provision of health care compared with other sectors due to the availability

of a wide range of new and expensive technologies as well as labour-intensive nature of health care provision have culminated to mounting pressure on health care budget (Higgins et al., 2010; Holtgrave et al., 2012). Besides tight budgetary allocation, health care resources are on her own limited by total funds available in the atmosphere of competing for health programs with other sectors, such as housing, education and other societal infrastructures (Kernick, 2003). This is more so with rising demand for services and reliance on very expensive and complex technologies. Evidence shows that intensive care units represent up to one-third of all hospital costs due to new technologies or new interventions that are being introduced (Halpern et al., 2004). New interventions are often considerably costlier, and concerns are being raised about the financial impact of such interventions. Expensive technologies do not necessarily translate to better service or service that is commensurate to the cost (Higgins et al., 2010), hence the need for economic evaluation.

As a new program, it is essential to understand its clinical impact concerning resource requirements before a decision for switching from client-initiated to provider-initiated routine opt-out strategy. This ensures that funds are channelled to the best health programs and in the most judicious manner. Economic evaluation makes it possible for the clinical impact relative to resource use of health care interventions to be explicitly examined and understood thus aiding decision about which intervention to adopt in an atmosphere of heightened cost consciousness and heightened competition for limited resources (Halpern et al., 2004). The goal is to implement health care interventions with maximal health outcomes at a net economic benefit to society.

Attaining the finest or most 'efficient' level of HIV testing technique requires evidence-best information on resource use associated with individual HIV testing approaches, and the level

of benefit derived by the target population and the society in general. In Nigeria, there is growing consciousness that decision-makers should prudently allocate resources; individuals, groups and civil societies are beginning to hold the government accountable for equitable and prudent resource allocation. Thus, demanding to know how increment in resource allocation drives benefits in clinical outcomes. On their part, the government is beginning to respond by creating agencies charged with regulating and provision of quality service at a low cost. For instance, the service compacts of Nigeria (SERVICOM) established to monitor improved service delivery of ministries, departments, and agencies (MDAs) and in conjunction with the ministry of health created a dedicated department whose responsibility is to recommend health care interventions on behalf of the Government based on cost-effectiveness. However, the application of this policy is being hindered by the dearth of economic evaluations of health interventions. The cost benefits of interventions must be evaluated against the alternatives and information regarding the findings made available to the policy-makers.

As an essential part of the provision of quality clinical service based on value for money, this study examines the cost-effectiveness of two interventions for HIV testing namely the provider-initiated routine opt-out and client-initiated opt-in VCT approaches.

7.5. Economic Evaluation Design

7.5.1 Evaluation Designs

Economic evaluation outlines the framework for examining the cost and consequences of competing programs or interventions. In the context of health care, the goal is to establish a combination of human and material resources that maximize the health benefits or other indicators of social welfare (Olsen and Smith, 2001). Economic evaluation has increasingly gained relevance in the health sector across the world and has become the backbone for

informing health care decision-making process (Cuijpers et al., 2005; Glasgow et al., 2006). A common vehicle often regarded as a gold standard for the conduct of economic evaluation is trial-based study. This is evidenced in the quantity of trial-based economic evaluations reported in the literature (Ramsey et al., 2015). For example, in the United Kingdom, data extracted from the National Health Scheme (NHS) Economic Evaluation Database showed that more than 30% of economic evaluations released of late were performed through trial-based studies (Tacconelli, 2010a).

Designs for economic evaluation could be structured through primary or secondary data collection. However, there is a common consensus that clinical-based trial (primary data collection) are the best vehicles for performing such evaluation. First, this is conducted because there are no existing data or evidence on the intervention, and therefore provides the initial and many opportunities to generate reliable evidence of costs concerning effectiveness. Second, trial-based economic evaluations are more likely to have lower marginal cost as against alternative study designs, which the benefit linearly improves with cost (Kernick, 2003). Notably, they provide access to considerable individual participant's data of which numerous statistical computations and econometric techniques evaluating relationships regarding clinical and economic factors of interest can be calculated. On the contrary, some experts suggest that trial-based economic evaluations are inter alia, truncated by time horizon, limited comparator, lack of relevance to contemporary contextual circumstance, and inability to incorporate other relevant information from both trial-based and observational studies (Sculpher and Drummond, 2006). These have waged a heightened debate between the opponents and proponents of trial-based economic studies, when, the two should be complementary rather than alternatives or disparate approaches (Buxton et al., 1997).

The USA Panel of health economists, as well as the International Society for Pharmacoeconomics and Outcome Research (ISPOR), proclaim that primary data collection is the most appropriate and robust source of data (Ramsey et al., 2015). Clinical based trials give the researcher the ambiance opportunity to evaluate the cost-effectiveness of intervention under the natural world settings (Edwards et al., 2008; Glick, 2015). In this way, the participating study participants are the representatives of the caseload, through which the comparison of the new intervention with the standard practice is made with a follow-up under real world. In the absence of trial-based design, modelling studies using data estimation are conducted. In such circumstances, the generalizability of the findings may be compromised due to the application of stringent criteria and treatment protocols. These defaults are difficult to control, although to a certain level they are normally accounted for during the computation of the economic evaluation (O'Sullivan et al., 2005). Trial-based studies enhance opportunities for upholding internal validity during the rigorous process of collecting patient specific-data (Edwards et al., 2008). Moreover, the marginal cost of gathering economic data alongside clinical data is classically modest.

For these reasons, this study on economic evaluation followed a trial-based approach for the data collection. Specifically, data relating to costs of resource use variables for delivering the interventions was imputed alongside the clinical data.

7.5.2 Choices in Methods for Economic Evaluation

The economic evaluation compares two or more interventions in terms of healthcare resources, costs and consequences to achieve efficiency. Efficiency is the optimal utilization of scarce resources so that everybody in society benefits from it (Kernick, 2003). Applying efficiency in the healthcare industry demands priority setting aimed at achieving high-quality

and low-cost services. Efficiency is achieved through productive and allocative frontlines. Productive efficiency involves the optimal utilization of available health inputs (resources), avoiding wastes and maintaining high-quality services to the society without altering or compromising the quality of other services (Hollingsworth, 2008). Similarly, allocative efficiency addresses the concerns of the society by prudently allocating resources to the right mix of health interventions in a manner that addresses the adequate supply of all relevant societal health care and welfare (Hollingsworth, 2008). Technical efficiency is about the mixture of the technically efficient resources to minimize cost and at the same time achieve a good outcome (Palmer and Torgerson, 1999; Shiell et al., 2002; Ravangard et al., 2014). The goal of all frontiers of efficiency is to use programs that deliver high-quality care at minimal cost for society (Ravangard et al., 2014)

Comparative health economics are classified based on the kind of comparison of costs and consequences. Depending on the type of evaluation, the reporting of outcomes varies from non-monetary, naturalistic units to monetary assessments (Drummond, 2005). Generally, there are four main categories of full economic evaluations, that is, evaluations that consider both costs and outcomes (Angjellari-Dajci et al., 2013). The four categories of this kind of evaluation are; cost-minimization analysis, cost-effectiveness analysis, cost-utility analysis, and, cost-benefit analysis.

A cost-minimization analysis compares the costs of alternative interventions while conceiving all relevant outcome measures as equivalent (i.e. equal patient quality of life or equal effectiveness) (Newby and Hill, 2003). This method is used in calculating intervention costs to project the least costly intervention modality. Cost-minimization can only be used to compare two interventions that have been proven to be of equivalent, in both dose and therapeutic outcomes (Newby and Hill., 2003). A common application of cost minimization analysis is the

comparison of generic equivalents of the same intervention entity. Thus, if client-initiated VCT and provider-initiated screenings are known to have an equivalent effect in testing rates then cost minimization could be used to determine the least costly modality. However, few interventions can exhibit these characteristics. Although the simplest of the four categories of economic analysis, only limited interventions can be evaluated using cost-minimization analysis.

Cost-benefit analysis is performed to measure both incremental outcomes and costs in monetary terms (Brent., 2011). This enables a direct computation of net monetary cost for delivering a health outcome such as a survival gain (gain of life-year) which is commonly translated to the cost of productive value to the society (Brent., 2011). In other words, the life-year gained is typically monetized to be equivalent to regular income. The strategy for measuring gains in quality of life includes techniques such as willingness to pay. Individuals (occasionally family members, policy-makers or even service providers) are vetted for the amount they are willing to pay for a quality of life benefit. However, the method through which the health outcomes are measured in monetary terms is somewhat debatable (Neumann and Weinstein, 2010). This has limited the wide application of cost-benefit analysis in the health care industries.

Cost-effectiveness analysis performs a more comprehensive evaluation of intervention costs. Cost-effectiveness analysis compares alternatives and measures outcomes in natural units (Chambers et al., 2015). Precisely, costs are measured in monetary units, whereas effectiveness is reported in terms of clinical outcomes such as complications prevented, life-years saved, cases of infections averted, or diseases cured. Cost-effectiveness analysis, therefore, evaluates the incremental cost of delivering an incremental health gain (ICER) expressed in accordance with a particular health outcome, which varies based on the

indication of the intervention (Chambers et al., 2015). However, it does ignore some important information about the intervention (Hill., 2012). For instance, it fails to report the quality of life or degree of injury incurred during the given period. More so, cost-effectiveness is unable to compare alternative interventions that have different natural benefits. For instance, an intervention, which increases life years, cannot be compared with another, which enhances physical fitness. In addition, the results of most cost-effectiveness analyses are quite context-specific that they can hardly be extrapolated to inform the decision in other populations. This is reflected in the debate concerning the use of league tables containing the results of studies using a variety of approaches, which were performed to understand a variety of context-specific questions (Pinkerton et al., 2001; Mauskopf et al., 2003).

An important analytical tool of cost-effectiveness analysis is the incremental cost-effectiveness analysis (ICER), computed using the difference in costs (incremental cost) of the alternate health care interventions and dividing it by the difference in health outcomes (incremental health effect) between the new intervention and the comparator (Yothasamut et al., 2009). This yields the extra-cost for an additional unit of health effect. ICER is typically a summary measure depicting the economic value of a program relative to the comparator. In the United Kingdom, for instance, the most frequently measured indicator of health effect is quality adjusted-life year. This makes it possible for ICER values to be compared across diseases ranges; however, in other health care settings, different measures of health effect might as well, be used ICER is predominantly suitable when the decision to implement a more expensive intervention, which generates a better health outcome, is being considered. For a decision to be taken, ICER value is compared to a pre-determined threshold to determine whether adopting the new intervention will bring an efficient use of resources. ICER is calculated thus:

$$\frac{\text{Cost}_{\text{intervention}} - \text{Cost}_{\text{control}}}{\text{Outcome}_{\text{intervention}} - \text{Cost}_{\text{control}}}$$

Another important economic evaluation method is called a cost-utility analysis. This is used to measure cost concerning utilities, especially the degree of quantity and quality of life. However, this approach is moderately unpopular due to difficulty in quantification or putting a value on health status or improvement in health status as perceived by different societies (McGregor, 2003). In contrast to cost-benefit analysis, cost-utility analysis is used to measure alternate interventions whose benefits may be different (Rios-Diaz et al., 2016). It measures the outcome value directly from the patient in a generic format such as quality-adjusted life-year (QALY). This method captures the survival time (extra-life years) plus changes in quality of life into one measure. An appreciated quality of life is expressed as utility measured on a scale of 0-1, where 0 represents dead and 1 represents perfect life. With this, a comparison across various types of health outcomes could be made, yet this requires value judgment regarding increases in quality of life (utility) concerning different health outcomes (McGregor., 2003). Using an incremental cost-utility ratio enables the cost of achieving a health benefit with an interventions to be measured against similar ratios computed for other intervention. This approach is employed when there are several purposes of an intervention, particularly when both quality and quantity of life are of an utmost important outcome measure of interest. The main advantage of a cost-utility analysis is that the outcomes present broader measures, and this is helpful when a comparative analysis of merit for various types of health care interventions are made (McGregor., 2003). In general, it provides a generic context through which decision about value for money of introducing an intervention. In circumstances where the health-related quality of life is the important expectation of the research, a cost-utility analysis should be performed (Earnshaw and Lewis., 2008). However,

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if this is not identified as an imperative health effect of the intervention studied, a cost-effectiveness analysis is the preferred form of economic evaluation (Hill., 2012; Chambers et al., 2015; Earnshaw and Lewis., 2008). Ultimately, the choice for any of these methods in a given study must be justified in relation to the research questions and goals. In this study, a cost-effectiveness analysis was performed because this is the most suitable approach in addressing the research questions. Cost-effectiveness analysis is most appropriate in evaluating different interventions with varying degrees in the outcome, as well as costs but they both have common outcomes. This attribute is typical of the current study, which focuses on examining the economic impact of client-initiated versus provider-initiated HIV testing. Besides, it incorporates a comprehensive view of costs and benefits, including indirect impacts, reflecting the interest of all stakeholders who may be affected by the intervention. Furthermore, from the scientific point of view using the guidelines for conducting an economic evaluation, summary outlined in table 7 .1 below. In this context, the goal is to identify the most efficient intervention option regarding cost per unit effect (such as cost per infection averted) rather than the cheapest intervention *per se.*

Table 7-1 Criteria for choosing appropriate evaluation method (Klarenbach et al., 2014)

Type of evaluation	Cost considered	Health consideration	Strengths	Important issue
Cost-minimization (subset of Cost-effectiveness)	Health care costs for both the patient and the disease state are compared for every intervention	Assumption is not made in relation to health status attributable to disease or intervention	Easy to assess with minimal data for the cost. Opportunity to determine the technical efficiency of each technique	Healthy analysis, assumption of same outcomes of disease and the treatments compared
Cost-effectiveness	All necessary health care costs for the patient and disease condition are matched with each of the intervention	It is generally used for regular health outcome e.g. blood pressure, renal function (eGFR), and serum LDL levels	Matches costs of treatment with therapeutic effectiveness based on health outcomes that are readily available from clinical trials	Values of results from this technique are difficult to interpret and comparisons between populations and diseases are not possible. Effectiveness outcome may not capture all relevant health outcomes
Cost-utility	All necessary health care costs for the patient and disease condition are matched with each of the intervention	Health status is transformed into a quality-adjusted life-year score based between 0=death and 1= Perfect health. Every aspect of disease and its treatment is contained in one metric	The unit comprehensively analysis health, with limits to and comparisons of outcomes among different populations and diseases	Although more rigorous, requires lots of data collection. Inferences when estimating health-related quality of life
Cost-benefit analysis	Monetary units	Monetary units		

7.6. Evaluation Method

7.6.1 Data collection

This study performed an economic evaluation following a non-randomized trial-based (NRCT) prospective study approach in an urban health facility in the Federal Capital Territory, Nigeria. An estimate of health and economic impact of HIV screening and receipt of test results using NRCT supported with decision modelling. The guidelines of the panel on cost-effectiveness in health and medicine were used in computing and reporting findings. The study was performed from a health care provider's perspective, which includes salaries of personnel, cost of medication, equipment, and consumables.

Patients were followed for three months using one of the following two methods of HIV screening: (i) client-initiated VCT with comprehensive counselling. (ii) provider-initiated HIV testing and counselling with streamlined counselling information.

The study was structured to understand the health benefits starting with a pregnant woman entering into contact with the health system for ANC, and receiving a continuum of care for PMTCT, details of the study protocol has previously been discussed in chapter 6 section 6.4 of this thesis.

The risk of MTCT depends on background HIV transmission rates during the periods of parturition, labor, and delivery. Because this study did not extend beyond the point at which delivery occurred due to the passage of time in relation to the Ph.D. program some of the relevant data could not be obtained directly. Women were only followed-up for three months in each of the study arms. This time horizon was adequate to capture vital data to measure the effects of the immediate treatment and to examine child survival outcomes associated with the interventions. A decision tree was also performed to complement study analysis.

Where not provided from the study, probabilities are obtained from data from existing literature.

Women received a particular HIV testing strategy depending on their group. HIV positive women were given ART using the Option B+ approach. The babies also received ART for prophylaxis immediately after birth, and up until six weeks. The primary outcomes of interest were the cases of HIV infections identified by screening, number of infant cases averted and cost per averted cases. Cost valuation, where possible, were imputed directly from receipts or purchasing documents. In some circumstances, costs were derived from Nigeria's fiscal commission as well as from high quality published articles when the data could not be obtained from the study. Costs are expressed in the United Kingdom Pounds, where the study was designed. The costs of HIV testing kits were inputted directly from the purchasing receipt. The additional overhead cost was equally imputed. The ART regimen evaluated is a combination therapy of zidovudine and lamivudine plus either efavirenz or nevirapine. Costing for ART prophylaxis using Nevirapine was also included. The study is based on the payer's perspective since the cost would fall on the Ministry of Health and her agencies. Figure 7.1 below is a schematic representation of the decision tree model. Healthcare payers utilize health research data to support the decision-making method, while the method in which such evidence is being used may vary among payers. From the perspective of the Nigerian healthcare agency, there is a necessity for real-world data to complement the outcomes of clinical trials and apprise negotiations on pricing. Evidently, healthcare payers are using health outcomes data in different ways to reach decision-making. The extensive databases available to payers may be used to enhance and to obtain real-life information that augments clinical trial data and economic models of outcomes and costs, and to aid the targeting of programs.
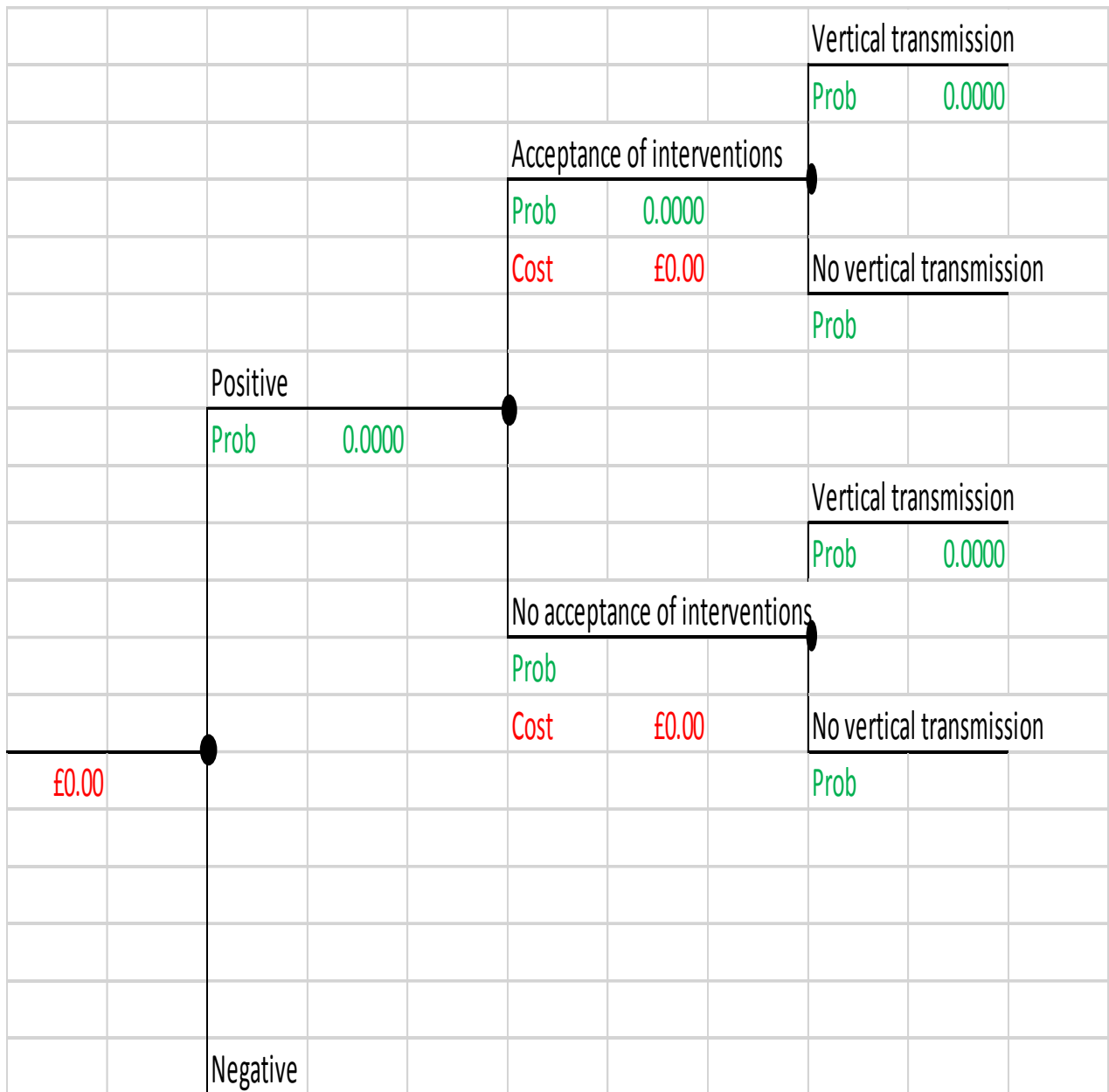
Figure 7-1 A schematic diagram showing decision tree model. The tail end at the left represents the initial decision to access HIV testing through any of the two strategies (client-initiated VCT and provider-initiated). Patients in each model decides whether to test or not to test. All the women, regardless of testing outcome enters the decision tree. Once a woman is tested for HIV, she may receive post-test counselling or may not. In all the strategies, women who declined testing during their initial contact with the physician or midwife may elect to be screened at a later period.

7.6.2 Essential considerations for economic evaluation

Trial-based economic evaluation involves the collection of resource utilization during an ongoing clinical trial (Sculpher. et al., 2006). To perform an economic evaluation, specific costs are accounted for depending on the perspective for which the study is undertaken (Drummond. et al., 2008). A particular cost may be accounted for in one perspective but may not be needed in another(Forbes et al., 1987). For instance, patients fare (travel costs) is a form of cost from patients and a societal perspective but does not necessarily constitute a cost from payer's or health care provider's perspective. Hence, the need to describe the perspective for which an economic evaluation is being performed. Therefore, it is essential to specify the study perspective, which clearly describes the basis of the analysis and determines the important costs that need to be considered.

In general, there are three main types of study perspectives on health economic evaluation. They include the perspective of health care provider, patient and societal perspectives. In respect to health care provider the cost of health care service delivery, which involves the salary of healthcare professionals, cost of medication and equipment are all accounted for (Jönsson, 2009). On the other hand, from the perspective of the patient, this amounts to different costs borne by the patient for seeking healthcare services. For example, patient-specific resource utilization may include the cost of tests; the cost of travels to health care, time off duty, and duration of hospital stays and level of community services during the period of follow-up. Conversely, the perspective of society accounts for all costs incurred by the society in delivering the health care intervention, which is the cost to the patient and the health care provider such as loss of productivity for the employee taking medical leave.

Conduction of health economic evaluations from the context of societal perspective has additional measuring costs and benefits associated with the relevant stakeholders in the society (Jönsson, 2009). For example, an expensive medication, which relives pains and reduces sick leaves, might not be cost-effective from the perspective of the patient. However, from a societal perspective, the drug might be cost-effective because it increases productivity and reduces loss to absence from sick leaves. However, the reality of performing a societal perspective is that it is complex and often expensive to measure every person in the society who may be affected. Because of this, many health care evaluations in contemporary literature were performed for the perspective of health care providers (Gavaza et al., 2010). However, the choice of perspective in the economic evaluation should ideally be influenced by national methodological guidance. In this case, Nigeria's blueprint guidelines on economic evaluation align with international standards, of which most studies predominantly followed the health care provider's perspective (payer's perspective), (Gavaza et al., 2010). As a result, this study was conducted using a health care provider's perspective and the resource use involving personnel cost and supplies were measured concurrently during the clinical trial (refer to chapter 6).

Normally, an economic evaluation is set against a particular time horizon. Only the health outcomes that emerge and the costs incurred during this period are considered in the evaluation. All the interventions are evaluated under the same period. The reference case analysis recommends a time horizon that is durable enough to involve all potential changes in costs and health impact across the alternate interventions. The considerations used in calculating this is based on the natural history of the disease, the sequence of the interventions, the occurrence of the health impact in addition to the costs associated with the interventions being compared. A lifetime horizon is used as long as one of the interventions

under study has a long-term impact, usually a lifetime impact on the patient, perhaps in terms of length of life, costs, health-related quality of life or other chronic or disabling conditions (Tschaut, 2006; Earnshaw and Lewis, 2008). Nonetheless, the shorter horizon is suitable if the changes in costs and health outcomes are not followed beyond the study horizon (Gravelle and Smith, 2001). Regarding this study, the principal goal is to determine the comparative economic impact associated with cases of averted infections in children born to HIV positive mothers during a three-monthly pre-and post-intervention phase. Although limited by the duration of the Ph.D. program, a long-term follow-up period for this clinical trial was impossible and unnecessary since a short time horizon was sufficient to collect relevant study data. Besides, computing costs and health impacts over the patients' lifetime can be both extensive and expensive adventures: the extra information can be extrapolated, using modelling of short-term clinical data (Victora et al., 2004).

Sensitivity analysis is aimed at explaining the procedure for evaluating the robustness of an economic evaluation by looking at the uncertainty. Every economic evaluation is characterized by a certain level of uncertainty parameter (Briggs and Gray, 1999; Darba and Albacar). Sensitivity analysis enables the researcher to vary systematically the inputs, for any variable of interest, substituting them with high or low values or both (for example, the costing or prevalence rate). If the outcome remains the same, that is unchanged after re-analysis, then the results are considered robust. On the contrary, if the outcomes are not robust, sensitivity analysis can point at which level where the intervention will be most useful.

Likewise, international consensus suggests that all costs for effectiveness evaluation should be valued using a single and constant currency (Walker et al., 2010). Cost measured at different periods should be adjusted such that the monetary value is uniform (Claxton et al.,

2006). Experts suggest using gross domestic product (GDP) deflector to make the conversion.

A purchasing power parity (PPP) is also advocated in performing economic evaluation (Kim et al., 2015). A PPP rate indicates that a currency equivalent of $1, for instance, may purchase more or fewer services within a setting than what US$1 can purchase in the USA. This study followed all these guidelines except the PPP. PPP was not possible because the medical supplies used in this study were purchased from outside Nigeria.

7.6.3 Dimensions and Estimation of Outcome.

Because economic evaluation compares the cost and benefits of alternative interventions, a program is considered cost-effective if it provides greater health gains than investing the resources in alternative interventions (Harwood, 2008). The likelihood of a patient gaining additional benefits for the potential mobilization of additional resources needed for the intervention is expressed in the cost-effectiveness plane.

Evaluation of costs, health outcomes, and ICERs give clear guidance to policy-makers under three circumstances: (i) when the policy-maker has stated a predetermined health effect and the goal of effectiveness measure is to minimize cost. (ii) When because of budget constraint the aim is to maximize benefit within the available resources. (iii) When the policy-maker explicitly defined standard or threshold for what should be regarded as cost-effective (Marseille et al., 2015). In any of these three scenarios, the researcher evaluating the cost-effectiveness is unable to objectively provide a direction to the policy-maker without first, gathering pertinent information regarding health effect, cost targets or thresholds. The challenge is how to ascertain with certainty that implementing an ICER result would represent good 'value for money'. A few approaches are used to tackle this problem, among which are threshold based on per capita national incomes, benchmark intervention or use of league

tables. However, for LMICs, the most common and of course, the WHO recommended approach is the use of threshold based on per capita gross domestic product (GDP). Under this context, costs less than three times the national annual GDP is viewed cost-effective while costs less than one national GDP is viewed very cost-effective (Marseille et al., 2015).

An analysis of the cost-effectiveness plane shows that when the cost is plotted against the outcome, the benefit to the patient with additional resource investment in the intervention can be measured in relation to the associated cost. Starting from the South-East, an intervention can be both less costly and more effective. In this scenario, the new intervention is regarded as 'dominant' and therefore recommended for adoption. Switching to the North West indicates that the new intervention is both expensive (costlier) and less effective. In which case, the intervention is dominated, and an outright rejection of the new intervention is strongly recommended. From the Southwest axis, it shows that although the intervention is less costly it is less effective. Similarly, from the North-East, the intervention costs more and equally more effective. In these two scenarios, the rule of thumb is predicated on what one is willing to pay to gain an additional unit of effectiveness or willing to save to forgo a unit of effectiveness. A cost-effectiveness plane (CE plane) was originally planned for this study; however, it emerged that the dominant intervention can be determined using ICER. Because of this, there was no need to plot a CE plane. Figure 7.2 below is a cost-effectiveness plane (Dowie, 2004).
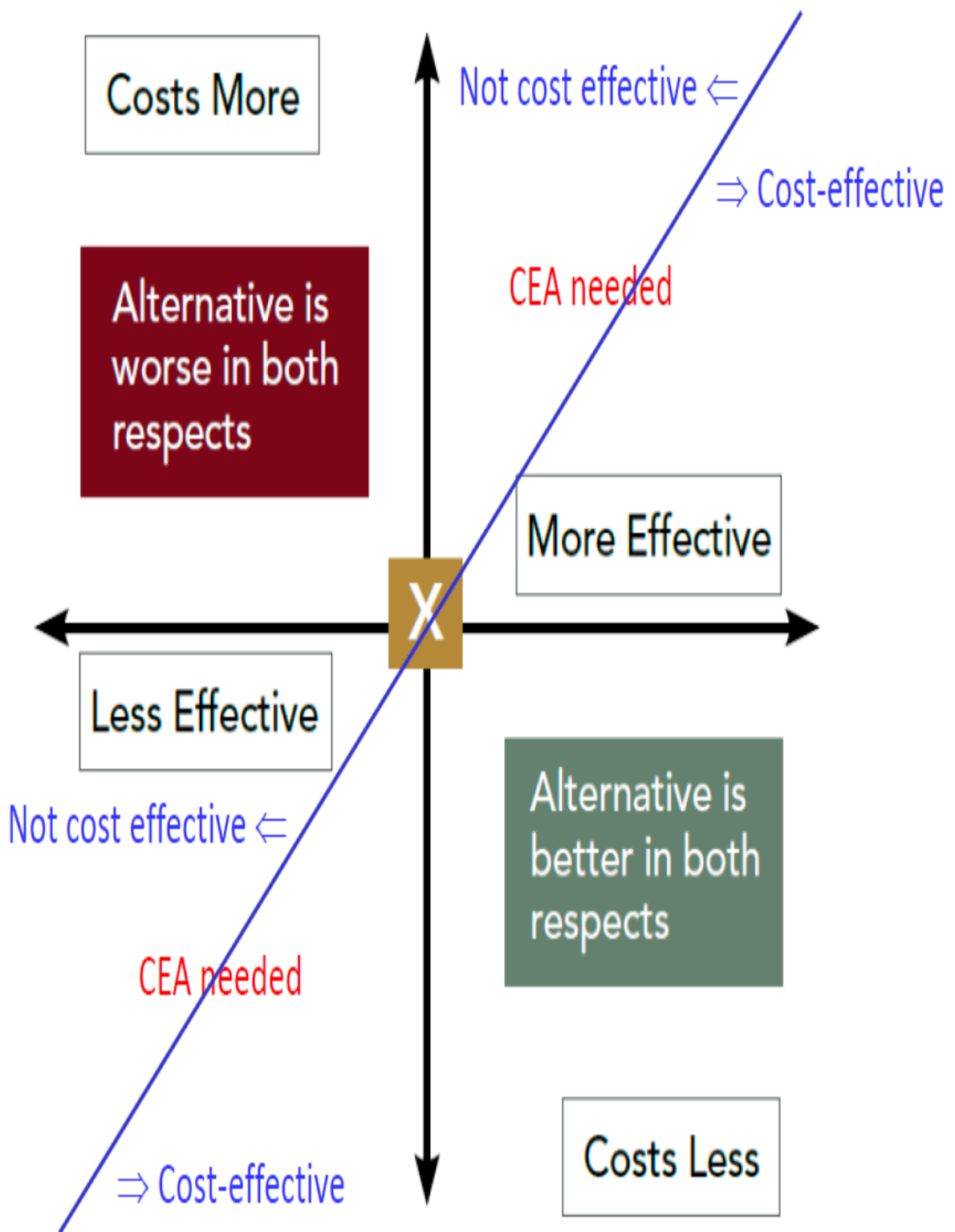
Figure 7-2 Cost effectiveness plane for priority setting in low-middle-income countries (Cohen and Reynolds, 2008).

7.7 Chapter summary

7.7.1 Conclusion

This chapter has highlighted the key concepts of health economics: how they relate to effective resource utilization within the healthcare sector. Health care decision-making requires information from multiple angles including economic values. Of the four economic evaluation strategies, cost-effectiveness is an outstanding and the most appropriate approach for this study based on the nature of the outcome of interest. The methodological approach to conducting cost-effectiveness in a trial-based study involves accurate enumeration of resource utilization, which is determined based on the perspective of the economic evaluation. The incremental cost-effectiveness ratio is a statistical analysis used to summarize the cost-effectiveness of a health care intervention. Although different methods are used to determine ICER's thresholds (point of 'value for money'), threshold based on per capita national gross domestic product is commonly used in LMICs.

In the next chapter 8, the results of both clinical and economic evaluations of this study will be presented.

Chapter 8 : Result

8.1. Introduction

This chapter presents the results of the study findings. The chapter is divided into two sections. The first section presents the clinical outcomes of the study findings, which included the demographic information of the study participants. The second section presents the results of the economic evaluation of the study data. A summary of the study findings is also presented at the end of the chapter.

8.1.2 Section 1: Result from clinical data

8.1.3 Background

Of the 700 pregnant women approached (registered for ANC during the study period) by study staff, 615 representing 87.6% accepted to the study inclusion. Two women were initially excluded from participation due to their known HIV-positive status and three others because they declined the offer to participate after consulting with their partners. Others did not participate (80 women) because they did not return their consent forms, and therefore were not enrolled in the study. Overall, 615 pregnant women were enrolled and all of them participated in this study. Table 8.1 below presents the sociodemographic of the women who participated in this study. Data from the study show that the two groups are largely similar (homogeneous) in characteristics. The mean age of participants in both groups is 26 years. Most of the participants in both arms are married (approximately 99%). The proportion of participants regarding tribe and religion is equally relatively the same. Regarding religious affiliation, with client-initiated, more Muslim women 188 (61.44%) compared with Christian mothers 133 (36.92%) while 5 (1.63%) belong to other religions. With the provider-initiated

approach, the proportion of Muslim participants - Christian participants was relatively equal to 152 (49.19%) against 149 (48.22%). Other religions retained 8(2.58%). Almost all the participants in the two groups are married: 303 (99.01%) and 305(98.7%) for client-initiated and provider-initiated, respectively. The rest women are either single or widowed.

Table 8-1 A comparison of demographics between the two interventions

Table 8.1 A comparison of sociodemographic variables between the two interventions							
		Client initiated	Provider initiated			Client initiated	Provider initiated
Tribe				**Age group**			
	Ibo	71 (23.20%)	68 (22.0%)		15-19	23 (7.51%)	36 (11.65%)
	Hausa	106 (34.64%)	104 (33.66%)		20-24	30 (9.80%)	39 (32.03%)
	Yoruba	86 (28.10%)	82 (26.53%)		25-29	92 (30.06%)	93 (30.09%)
	Other	43(14.05%	55(17.98		30-35	113(36.9	96(31.06
Religion					35-39	42	42(13.59%
	Christian	113 (36.92%)	149 (48.22%)		≥40	6 (1.96%)	3 (0.97%)
	Muslim	188 (61.44%)	152 (49.19%)	**Parity**			
	Others	5 (1.63%)	8 (2.58%)		0-2	73 (23.85%)	97 (31.39%)
Occupation					3--5	209 (68.30%)	124 (40.12%)
	Full house	78 (25.49%)	108 (35.95%)		≥6	24 (7.84%)	88 (28.47%)
	Farmer	54 (17.64%)	47 (15.21%)	**Marital status**			
	Trader	66 (21.56%)	62 (20.06%)		Married	303 (99.01%)	305 (98.70%)
	Apprentic	12 (3.92%)	63 (20.38%)		Single	3 (0.98%)	3 (0.97%)
	Civil serv	77(25%)	15(4.8%)		Divorced	0 (0.00%)	1 (0.32%)
	Others	19 (6.20%)	14 (4.53%)	**Type of marriage**			
Education					Monoga	226(73.8	102(33%
	No educa	59 (19.28%)	38 (12.29%)		Polygamy	77 (25.16%)	203 (65.69%)
	Primary e	105 (34.31%)	117 (34.86%)		others	3 (0.98%)	4 (1.29%)
	Secondar	99 (32.35%)	88 (28.47%)				
	Tertiarry	43 (14.05%)	66 (21.35%)				

8.2. Result

8.2.1 Impact of interventions on test acceptance.

Table 8.2 depicts HIV testing uptake rates according to the two study groups. The average testing rate for the two interventions is 70.6%. The new method of directly offering the test (routine testing) led to a higher testing rate than the traditional VCT method. Of the 309 participating women during the 3 months (October to December 2016) of routine opt-out HIV testing, 292 (94.5%) tested and post counselled, whereas 142 (46.4%) of 306 pregnant women during the initial 3 months study (July to September 2016) based on self-referral VCT study, tested and post counselled (p = 0.05). The unadjusted difference of 48.1% represents an absolute change in percentage between changes in default interventions. There was a significant change in HIV test uptake between the two interventions. Figures 8.1-2 are the pictorial depiction of testing rates for the two intervention groups: the shorter blue-shaded bar illustrates uptake of client-initiated VCT while the longer blue-shaded bar depicts uptake of routine offer of HIV test. Overall, the method of directly offering HIV tests to all the women resulted in a higher uptake than the standard client-initiated VCT. The test acceptance rate is higher for women of the Ibo extract than other tribes. When the religious effect is put into consideration, Muslims tend to dominate under the routine offer of testing. A Chi-squared test score of 308.5 was obtained, with p-value (p<0.01) which is less than the chosen significance level of p= 0.05 indicating that the null hypothesis should automatically be rejected. In other words, there is an association between testing strategy and uptake of HIV tests. The Phi correlation report of 0.528 also indicates a strong correlation between the type of offer and test acceptance. Typically, Phi-values between 0.3 - 0.7 are considered the strong association between type of test offer and uptake of the test.

Put together, 149 pregnant women tested under the client-initiated testing approach. As shown in Table 8.2, seven women (2.3%) who tested under this approach did not receive their HIV test result and post-test counselling. It is unclear whether the women intentionally avoided receiving their test results as attempts to contact them proved abortive. Although, there have been reports suggesting that logistics challenges such as transportation, long waiting time and counsellor absences contribute to women not knowing their HIV status. In routine testing, all the 292 women (100%) received their results and post-test counselling.

Table 8-2 Impact of interventions on testing outcomes

The impact of the interventions and demographic on test acceptance			P-value
	Client-initiated	**Provider-initiated**	
Tested	149(48.7%)	292(94.5%)	0.0005
Recived result	142(46.4%)	292 (100%)	0.08
Tested not post-counselled	7 (2.3%)	0	
Significant test X^2 =308.5[*]	**Phi-coeficient=0.528**		
Marital status			
Married	432/601 = 78.9%		
Single/Divorced	9/14 = 64.3%		
Significant test X^2 = 28.9*			
Religion			
Christianity	215/305 = 70.50%		
Muslim	226/308 = 73.40%		
Other religion	2/3= 66.67%		
Education			
No education	71/133 =53.38%		
Primary education	120/174 = 68.96%		
Secondary education	180/229 = 78%		
Tertiary education	70/78 = 89%		
Significant test X^2 = 15.3	**Phi-coeficient=0.328**		

Age GP	15-19	20-24	25-29	30-34	35-40	41-45
Testing rate	25/54 (46.3%)	35/65 (53.8%)	165/181 (91.2%)	133/212 (62.7%)	38/82 (46%)	6/9 (66.6%)
Significant test X^2 = 6.93*						

*P< 0.01. Phi-coefficient value between the ranges of 0.3-0.7 indicates strong association.
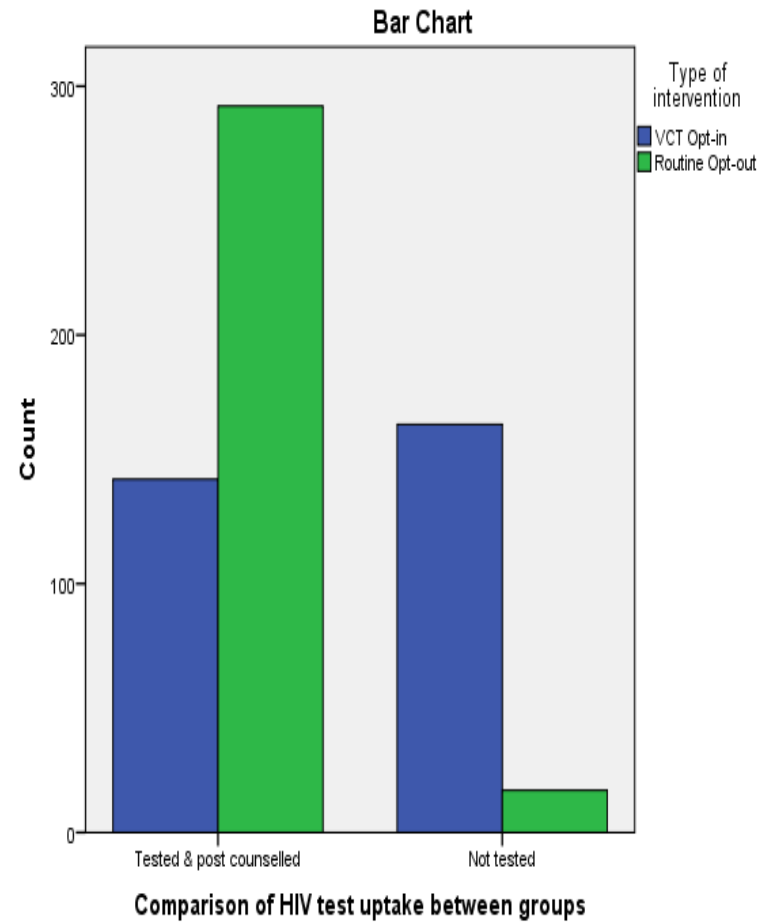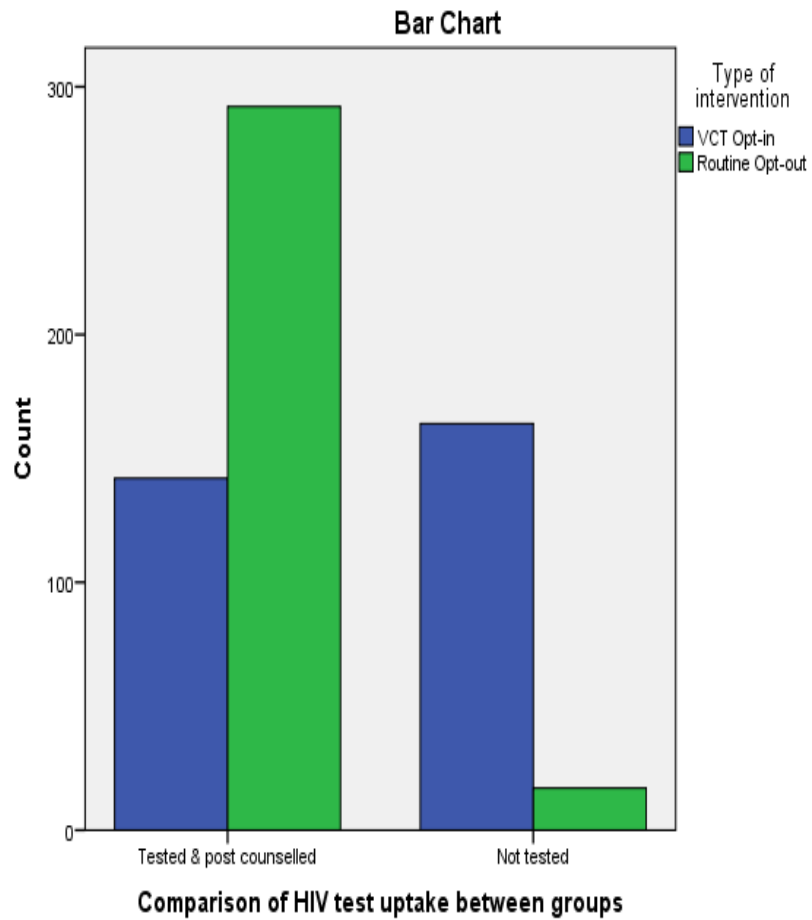
Figure 8-1 & 8-2 Graphical representation of impact of different interventions on HIV testing uptake rate in each group. Significantly, more women tested and received their HIV result under provider-initiated routine opt-out testing compared with active choice VCT.

8.2.2. Test Acceptance Based on Demographic Information.

Table 8.2 presents data from crosstab analysis on HIV test acceptance according to demographic data of the women. Women who were considerably more probable to accept HIV tests were the younger mothers (<30 years), married women and those with higher educational background. HIV testing increased progressively as the educational level increased. Nearly only half of the mothers with no formal education (53.38%) accepted testing whereas 89% of women with tertiary level education accepted testing. Religion did appear to have an effect on the uptake: however, the type of religion (Christianity or Muslim) did not show stronger influence over the other. Test acceptance among Christians and Muslims were 70.5% and 73.40% respectively.

8.2.3 Detection of HIV Positive Cases among Participants.

Below in Table 8.3 is a summary of the crosstab result output. During the routine antenatal testing regime, more HIV-infected pregnant women were diagnosed (44 cases compared with 15, p<0.03). In terms of a percentage point, the case detection rate rose from 4.9% in client-initiated VCT to 14.2%, almost triple the active consent strategy. Equally, there is a significant association between HIV case identification and mode of offer of the test (X^2 =4.73). All the HIV infected women in both arms received their test results and post-test counselling.

Table 8-3 HIV case detection and uptake of antiretroviral treatment

HIV test result.	Type of intervention		P-value.
	VCT Opt-in	Routine Opt-out.	
HIV-negative.	134/149 89.9%	248/309 84.9%.	p< 0.01
HIV-positive cases.	15/149=10.1%	44/292=15.1%	P< 0.03, X² =4.73

	165/306	17/309.	
Declined testing.	51.30%.	5.5%.	P< 0.01.

8.2.4 Uptake of antiretroviral treatment for PMTCT.

Overall, of 59 HIV positive cases identified during the study period, 54 (91.5%) accepted ART treatment for PMTCT. 10(66.7%) of the 15 HIV cases identified under client-initiated testing-initiated treatment while the rest 5(33.3%, p<0.009) refused treatment. Among the 44 identified HIV cases under routine testing, all the women in this group accepted ARV treatment 44(100%) (p<0.03, X^2 = 6.057). The phi-value, however, shows a strong correlation between treatment and intervention. Table 8.4 and figure 8.4 depict the study findings.

Table 8-4 Acceptance of ART treatment based on intervention.

	Seropositive		p-value
	VCT Opt-in	Routine opt-out	
Receiving ARV	10 66.7%	44 (100%)	0.03
Not Receiving ARV	5 (33.3%)	0.00%	0.009
X^2 = 6.057 Phi-correlation 0.389			

Figure 8.3 Uptake of ARV for PMTCT during VCT and routine testing periods
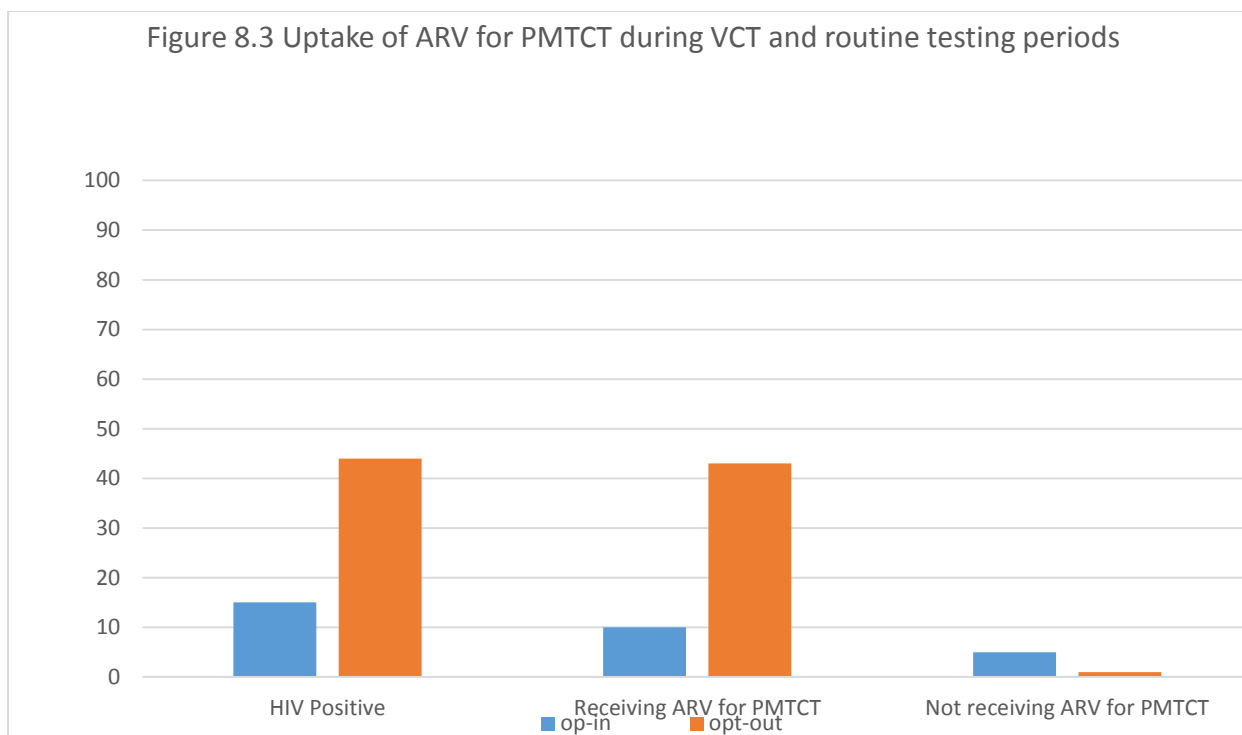
Figure 8-3 Uptake of ART treatment among the HIV-positive cases in the two arms.

8.2.4. The Effect of Midwife Characteristics on Test Acceptance during Antenatal.

One of the most important aspects of this trial is to understand the relationship between test acceptance and midwife characteristics. Data from this study suggest that midwife background is influential in HIV test acceptance. Table 8.5 below shows that HIV test acceptance improved with midwives along the line of educational level and experience. Of 615 study participants, 441(71.7%) elected to undergo an HIV test. The five regular (core) midwives booked a median of 73.5 women (range 50 -120). Midwife with up to five years' work experience booked the minimum at 50 representing 11.34% while the midwife with ten years of work experience and master's degree booked 120 women representing 27.21%. Three midwives who worked occasionally (ad-hoc staff) in the O&G department booked 39 (8.84%) women but were not analysed individually.

Table 8-5 Association between midwife characteristics and test acceptance.

Midwife characteristics		Proportion of women taking HIV test	Significant test $X^2 = 101.1$	
0-5yrs with primary education		50/441 (11.34%)		
0-5yrs with secondary		64/441 (14.51%)		
5-10yrs with first degree		78/441(17.68%)		
6-10yrs with first degree		90/441 (20.40%)		
10yrs with masters		120/441 (27.21%)		
Ad-hoc staff[**]		39/441 (8.84%)		
Median booking[*]		73.5		

[*]Five Midwives who are regular staff in the Obstetrics and gynaecology department (O &G) of the study centre. [**]Ad-hoc staff who represent a group of four casual midwives who were not analysed individually as they made less than 20 bookings each. The core midwives made a minimum of 50 bookings.

8.4. Section 2 Result of Economic Evaluation.

8.4.1 Background Information.

The demographic background of the study participants has already been shown in section one of this chapter, table 1. The two cohorts were enrolled in a study comparing the clinical and cost-effectiveness of routine HIV testing against client-initiated VCT HIV testing conducted in a busy ANC health facility in North-Central Nigeria. Characteristics in the two groups did not differ. Overall, 615 pregnant women participated in the study. Participants were drawn from

all the local tribes of the country, 22.6% Ibo, 34% Hausa, 27% Yoruba and 15.8% other minority tribes.

During the study, 292 out of 309 participants enrolled under the routine offer of HIV tested under this model representing 95.7% while 149 participants out of 306 who registered under VCT opt-in tested, of whom 142 received post-test counselling while seven women absconded from post-test counselling. Among the women who tested under routine HIV testing, 44 (14.2%) of the women were newly diagnosed with HIV compared to 15 (4.9%) newly identified cases under the client-initiated strategy.

8.4.1 Study Findings.

Table 8.6 below shows the HCT activities with their unit costs. Table 8.6 presents a comparison of the testing outcomes summary for the two interventions (Routine testing against client-initiated testing). Aggregate costs for routine opt-out HIV testing amounted to £38183.50 whereas the total cost for VCT was lower at £20204.80. Mainly, routine testing has a higher aggregate cost than costs for client-initiated testing. The unit cost for testing HIV also varied between the two interventions £130.70 versus £136 routine opt-out and client-initiated VCT, respectively. Cost per client counselling and testing using client-initiated VCT are generally more expensive than the cost per routine HIV testing and counselling.

Table 8-6 the unit costs of HCT activities.

Activity	Rountine opt-out	VCT opt-in
Hourly wage for pre-test counseling	24.77	30
Hours for each pre-test counseling	0.12	0.2
Hourly wage for blood sample collection	25	25
Hourly wage for adminstrative work	21.07	21.07
Hours for technologist conducting a rapid test (first line)	1.5	1.5
Hour for drawing blood	0.04	0.04
Hours for technologist conducting a rapid test (first line)	1.5	1.5
Unit cost of first line rapid test	5	
Total no. of Rapid test	292	149
Unit cost of 2nd line rapid test	5	
Total no. of Repeat test	44	15
Unit cost for rapid test (tiebreaker)	15	15
Post-test councelling		
Hourly wage for post-test counseling	24.77	24.77
Hours for post-test	4.582	4.582
No of negative cases	248	134
No of positive cases	44	15
Unit cost of ART medication, 6months($)	45	45
Unit cost infant nevirapine(6wk)	16	16
Hours for post est counselling	0.5	0.5
Unit cost, post-test counselling	12.385	12.385

Table 8-7 Decision tree output and outcome summary

Inputs	
Probability (vertical transmission, routine testing approach mother accepts	0.2200
Probability (vertical transmissionClient-initiated, mother accepts intervent	0.2800
Probability (mother accepting intervention)	1.0000
Prevalence (undetected HIV in antenatal population)	0.0300
Cost of routine test	£130.70
Cost of vertical transmission mitigation	£61.00
Cost of client initiated HIV testing	£136
Outputs	
Increamental cost of Routine test	-£0.90
Probability of vertical transmission (routine testing)	0.2200
Probability (Vertical transmission|Client tseting)	0.2800
Reduced veritical tranmision (additional perinatal case averted)	-0.0600
Additional cost per case averted=	£15.02
Cases averted, routine testing	34.32
Cases averted, client-initiated VCT	10.8
Outcome difference	**23.52**
Cumulative cost, routine testing + treatment	38183.54
Cumulative cost,client-initiated + treatment	20204.75
Cost difference	**17979**
ICER	**764.4**
Cost per new diagnosis, routine testing	806.7623
Cost per new diagnosis, client initiated testing	1285.314
Total cost of HCT, client testing	19279.71
Total cost of HCT, routine testing	35497.54

Note: Probabilities of vertical transmission are computed from a combination of the results

of this trial study as well as data from high-quality literature.

Regarding transmission averted in children, more cases were averted during the 3-months study period of routine testing strategy compared with client-initiated VCT (34.32 versus 10.8); resulting in more than three-fold improvement over standard client-initiated VCT.

A breakdown of the average cost of new HIV infection identified is also shown in Table 8.7. The cost per new diagnosis under routine testing is valued at £806. 76 whereas the cost per new diagnosis using client-initiated opt-in costs £1285.31, indicating the substantially lower testing cost per new diagnosis with routine testing. The introduction of routine HIV testing would require an additional cost of £15.02 per case averted. This included costs for ART for the woman during the period of pregnancy, prophylaxis for the baby and a follow-up visit for the HIV positive women who refused treatment for PMTCT.

Routine counselling also has a more favourable incremental cost-effectiveness ratio, resulting in an ICER of £764.40. Largely the provider-initiated counselling is a dominant model compared with the client-initiated testing, and the ICER outcome is well below the acceptable threshold. Figure 8.3 below displays the decision tree-modelling cascade of this study.
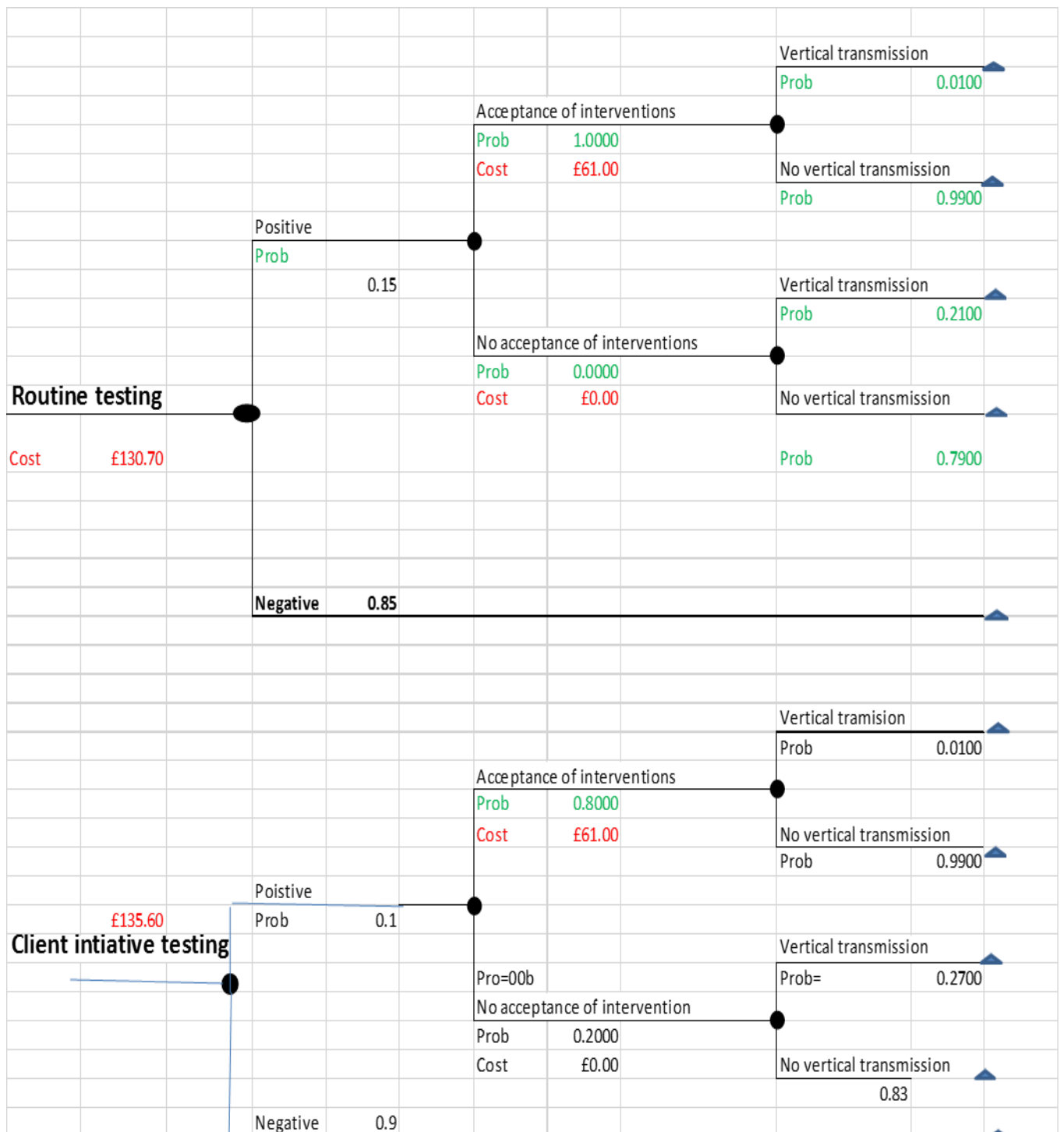
Figure 8-4 Decision tree modelling for routine opt-out and client-initiated HIV testing in FCT, Abuja.

8.4.2 Sensitivity analysis

A one-way sensitivity analysis was performed to account for important epidemiological assumptions and uncertainties. The HIV epidemiological burden was varied to represent the

current national prevalence among pregnant women in Nigeria since trial rates were significantly higher than the prevailing situation-15percentage against 3 percent.

Thus, if the prevalence of undiagnosed HIV during pregnancy were adjusted from 15% to reflect the prevailing national rates of 3%, the cost-effectiveness of routine testing would still be favourable with the benefit of reduction in transmission rates. Additional cost for adopting routine testing per case adverted would be £398.42, Table 8.8.

Table 8-8 One-way sensitivity analysis using national prevalence rate.

Inputs	
Probability (vertical transmission, routine testing approach mother accepts	0.2200
Probability (vertical transmissionClient-initiated, mother accepts interventi	0.2800
Probability (mother accepting intervention)	1.0000
Prevalence (undetected HIV in antenatal population)	0.0300
Cost of routine test	£130.70
Cost of vertical transmission mitigation	£61.00
Cost of client initiated HIV testing	£136
Outputs	
Increamental cost of Routine test	-£23.91
Probability of vertical transmission (routine testing)	0.2200
Probability (Vertical transmission|Client tseting)	0.2800
Reduced veritical tranmision (additional perinatal case averted)	-0.0600
Additional cost per case averted=	**£398.42**

The probabilistic sensitivity analysis as shown in Table 8.9, demonstrates that at a prevalence rate of 0.03, routine testing remained cost-effective at an ICER score of £152.88. The probabilistic analysis allows the decision-makers to determine various epidemiological situations in the given population at which routine testing is cost-effective in relation to the client-initiated testing approach.

Table 8-9 Probabilistic analysis deducing ICER in relation to epidemiological situation.
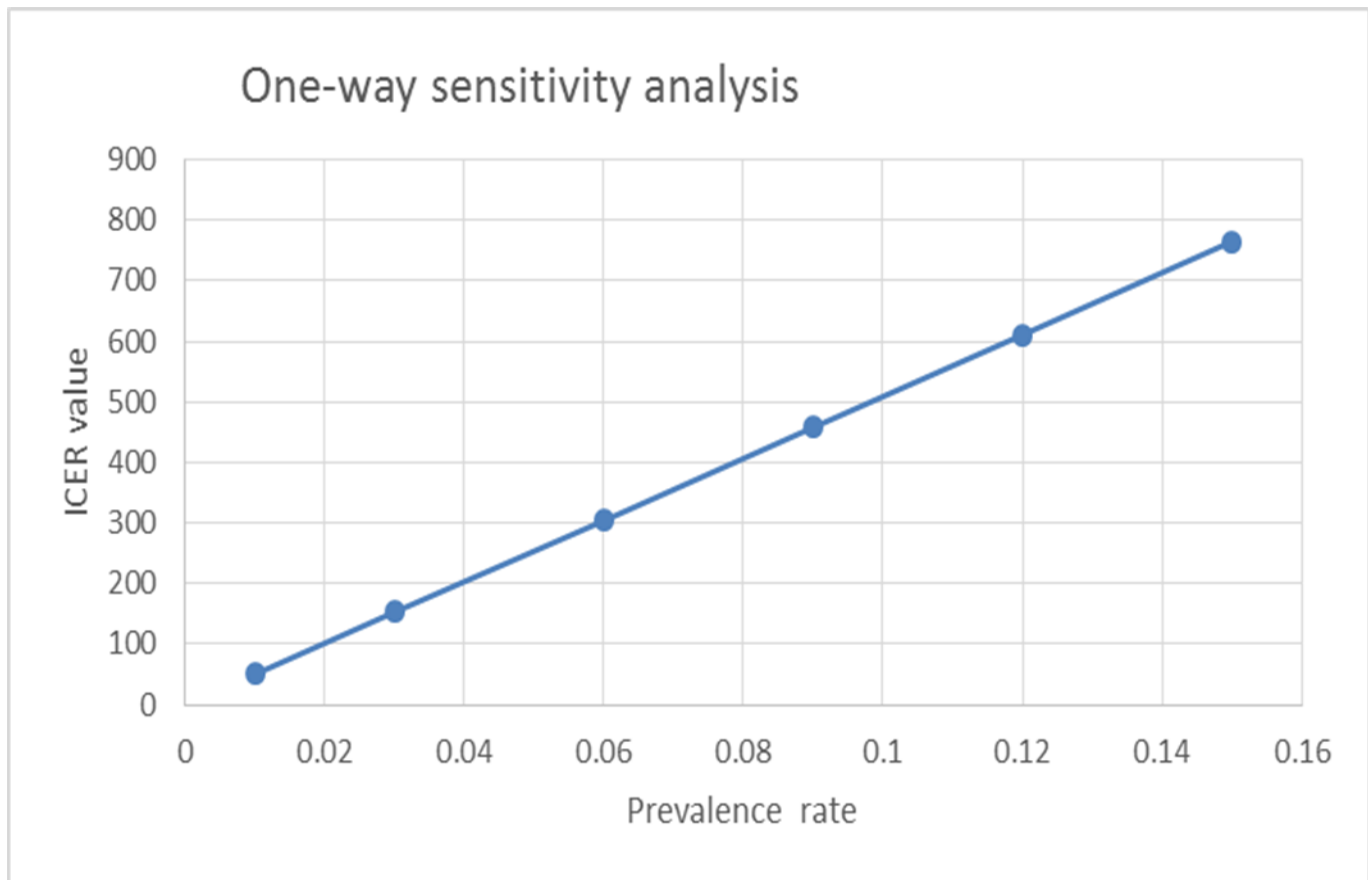
8.5. Summary

8.5.1 Conclusion

Data from this study show that most women who received offers for HIV testing through routine testing strategy accepted the offer (94.5%), and all were post-counselled. This is in contrast with the client-initiated counselling strategy where only 48.7% accepted testing and 46.4% received post counselling. Test acceptance was highest among women aged 20-29 and among women with higher education. Significantly, more women were identified with HIV 44 (15%) and initiated with ART treatment under routine testing compared with 15 (4.9%) identified women with only. Routine HIV testing is cost-effective at various epidemiological scenarios in this setting. The next chapter focuses on the discussion of the findings: relating it to the literature, demonstrating how it affects the original hypothesis and its implication in practice.

Chapter 9 : Discussion of Study Findings

9.1. Introduction

As a guide to the reader, this chapter is dedicated to discussion on the clinical and economic findings of this study. First is the overview of the research findings followed by the discussion in relation to the intervention outcomes, the strength of the study and the limitations therein. The verse part of the chapter is, however, dedicated to the discussion of the study findings. The purpose is to draw together, compare, contrast and discuss the outcomes of the two interventions and interpret them in relation to the literature in this field. The chapter will also identify the commonalities as well as the emerging issues from the study as a whole. The last section of the chapter is the summary signposting to the next chapter.

9.1.1 Summary of the Study Problem

This study compared two approaches to HIV screening during pregnancy among women attending the antenatal clinic. A pre-post non-randomized controlled trial was conducted to understand both the clinical and the cost-effectiveness of provider-initiated routine opt-out versus client-initiated VCT models of testing to aid the decision-making process. The findings provided useful information about PMTCT service activities and utilization including test acceptance, uptake of ART for PMTCT among the infected pregnant women as well as cost and cost-effectiveness of the interventions.

MTCT is considered the predominant mode of HIV infection in children of which approximately 90% of the infections occur through this mode (Magoni et al., 2005; Drake et al., 2014). Treatment with combination ART drugs can reduce transmission rates to less than 2%. However, before a woman is enrolled in treatment for PMTCT, she must first learn her HIV-positive status. Yet, the relatively simple service required to make such a decision is

lacking in settings like Nigeria where MTCT rates are high, thus hindering access to treatment options for PMTCT. MTCT of HIV has virtually been eliminated in some countries that adopted rationale steps such as readily availability and accessibility of HIV testing and treatment services.

While provider-initiated HIV counselling and testing is the dominant approach for offering HIV in most developed countries and is being recommended by WHO (Simpson. et al., 1998), its impact has not been fully evaluated in the Nigerian context. Knowing the impact of such an intervention may assist in developing and adopting the appropriate testing technique to increase HIV test acceptance across the country.

9.1.2 Summary of the Key Study Findings

Put together, this study recorded a remarkable acceptance rate of routine opt-out HIV testing among antenatal women in a country that is facing unprecedented rates of perinatal infection. Routine testing considerably increased testing rates, case detection rates and access to treatment for PMTCT among pregnant women. Specifically, a facility-based antenatal screening for HIV that is premised on routine opt-out principle closed the gap of 'missed opportunities' to screening compared to VCT. Likewise, the study identified an association between sociodemographic of the women with test acceptance. One plausible interpretation of the positive association between test acceptance and educational level is that women who have less formal education may fail to understand the real value of maternal and child health. Perhaps these women have less access to health care services as well as health education and services in the real sense of it. Aside from the lower level of education, test decline is predominantly among married and unemployed mothers. The probable reason is that these women are unable to make decisions on their own, as they are financially

dependent on their partners. The routine opt-out strategy is both cost-saving and cost-effective as demonstrated with the ICER value that is well below the threshold of 1-3 times the gross domestic product (GDP) of Nigeria.

9.2. Discussion

9.2.1 Discussion on Study Findings

Antenatal care is a unique opportunity for a pregnant woman to receive excellent lifesaving care from health care professionals to improve the outcome of pregnancy for both the mother and the unborn child. Part of this care is the exchange of sensitive information about the health of the woman and the unborn baby, and additional new HIV testing techniques must not undermine the overall aim of this encounter. This, in addition to the complex nature of HIV, including the controversy surrounding HIV testing, has provoked concerns among experts on the rationale for implementing routine HIV testing in antenatal care. The findings of the present study contradict this notion and clearly support the introduction of this strategy. The adoption of routine testing in ANC is feasible and increased HIV testing rates among women who sought antenatal services. Furthermore, routine testing presented opportunities for early diagnosis of HIV infection in women who are asymptomatic but attending ANC (filling the gap of missed opportunity), and therefore the likelihood of reducing morbidity and mortality as well as onward transmission to others particularly their unborn babies.

9.2.3. Methodological consideration

Voluntary counselling and testing has been the standard of care in Nigeria before this study. Because of the nature of this study, it would be neither feasible nor ethical to introduce any form of randomization to a potentially lifesaving intervention of this kind. In order to be

definite without any form of ambiguity about the impact of the new intervention, the current intervention, which is client-initiated VCT (active consent VCT), was measured as the control arm (comparator intervention). The post-intervention arm or routine provider-initiated opt-out was evaluated as the new intervention group. This arrangement helped to minimize bias from asymmetric information since none of the arms knew their treatment prior to the experiment. Hence, there was no prior sensitization of participants about treatment allocation in terms of allocation into a particular arm of the intervention. All participants had equal opportunities to access the advertorials in form of posters, health leaflets, and banners that are typically found in and around the study facility, including in the antenatal unit, where the study was conducted. Following this concept, the changes in testing uptake could clearly be attributed to the impact of the introduction of the new technique (routine HIV testing opt-out) for offering an HIV test. Essentially, the present study was proposed to establish women's preference in terms of testing uptake of a superior HIV testing strategy. Although the sample size was a good representation of the population, a significant proportion of women who attended antenatal services in this study facility during the study period were not involved in this because of logistic problems. While some of the women were discretely booked others, who were unbooked presented while already in labour. Additionally, it is difficult for this study to determine the accurate number of pregnant women from this catchment area who never sought for ANC in the first place, nor understand, what the HIV status of this group might be. ANC is a strategic place for gathering relevant data on issues that concern maternal child health for the planning and implementation of important programs such as PMTCT.

9.3. Impact of Interventions on Testing Outcomes

9.3.1. The Impact of the Different Testing Approaches on Testing Rate.

An essential component of PMTCT is the determination of the pregnant woman's HIV serostatus during the antenatal care, however, after decades of offering HIV screening using the traditional on-request VCT, Nigeria program was unable to realize high testing levels (Nigeria Federal Ministry of Health (FMoH), 2013). This study found that switching from client-initiated VCT (opt-in) to routine provider-initiated HIV testing approach in antenatal clinics extensively improved test acceptance rate among pregnant women, in an urban health facility in Nigeria. The percentage of women who knew their HIV test result more than doubled from 46.4% in the era of client-initiated VCT to 94.5% using the routine opt-out testing technique. The dramatic improvement in HIV test acceptance did not result in any noticeable adverse effect. Data from this study profoundly favour the implementation of the routine opt-out testing technique, at least in the FCT, Abuja, where test acceptance has so far been dismal. This result of high acceptance of routine opt-out strategy recorded in this study is indeed in agreement with many other evaluations of opt-out strategy performed in different parts of the world, such as in the USA, Canada, Europe, and Africa. In these settings, sustained increases in rates of prenatal test acceptance have been recorded after the implementation of universal HIV testing in the ANC. This approach has also become the mainstay of national screening strategy in the USA for nearly two decades (Roome et al., 2002) and the United Kingdom has had it in the national program for many years (Townsend et al., 2006). Moreover, this study finding is in agreement with studies conducted in Botswana (Creek et al., 2007b) and Zimbabwe (Chandisarewa et al., 2007), countries with high HIV prevalence similar to Nigeria, which recorded increases in testing rates above 95% after the policy change. The

Botswana data showed increases in acceptance rate and post-test counselling. In comparison, the testing rate rose from 75.5% to 90.5% (p<0.001) during the policy change from client-initiated testing to provider-imitated respectively. In addition, a similar study in Malawi demonstrated that after the implementation of routine HIV in ANC, HIV test acceptance among pregnant women rose to 78.7% from the initial testing rate of 52.6% during the VCT opt-in (Kasenga et al., 2009b). Likewise, high testing coverage was reported when routine HIV testing and PMTCT were concurrently introduced in a large African program in rural Cameroon (Matovu and Makumbi, 2007), a country with much lower HIV prevalence. Nigerian experience illustrates hope that a successful paradigm shift could be achieved even in an intervention that has long been tied to self-referral VCT.

The significantly higher testing rate could be related to different factors. As the main information provided to the women during the discussion session focused on the risk of MTCT and the capacity of ART treatment to considerably reduce vertical transmission and improve the health of an infected woman, understanding these benefits may explain the reason for high testing rate. Therefore, effective communication of the benefits of prenatal HIV screening using carefully worded unambiguous information in contrast with information overload may be crucial to test acceptance among the expectant mothers. This suggests that the training, which the midwives received prior to the study and the strict adherence to specific discussion protocols, may be strong predictors of testing uptake among these women. In other words, prolonged discussions during HIV pre-test counselling may not be essential; rather only, the key benefits of testing should be emphasized during the group discussion class prior to testing. Next, the significantly higher uptake of the HIV testing rate during the routine opt-out offer of HIV test may be associated with in-group loyalty, which is typical of Nigeria culture (collectivist society). This is because the women who received 'routine offer'

were grouped, addressed and received the brief health discussion as a unit, perhaps they would have viewed this arrangement as an act of 'oneness', that is, a state of being united and following one another's footstep, including in decision making. Another possibility may be that the women were too daunted to decline the offer from the midwife counsellor. Maybe too naïve to refuse a piece of medical advice from the midwife who is charged to recommend health instructions for a successful pregnancy. A survey regarding routine testing in Botswana suggested that despite the majority of the respondents accepting that routine testing was beneficial, 68% reported that they could not reject a test offered by their provider (Weiser et al., 2006). This may be an indication that the midwives have unique influence over the pregnant women that lured them into accepting to test. This, in addition to the dispassionate presentation of concise and easily comprehensible information on the benefits of HIV testing in pregnancy, may have contributed to the improvement in the uptake. Furthermore, there is a likelihood that the women were perhaps less apprehensive in participating in routine HIV testing because the community, including their partners, families, and friends perceived routine testing as standard antenatal care delivered to all pregnant women, rather than test offered to isolated individuals at higher risk. In other words, routine testing is socially acceptable in the community. Apparently, this minimizes the risk of stigma and discrimination that are often associated with HIV testing. Another reason may be that the awareness about the benefits of HIV has generally grown over time within the community. Perhaps, women are actually knowledgeable in the epidemiology of HIV and genuinely needed some form of reassurance from reliable sources such as health professionals, that HIV testing and access to treatment could indeed result in a reduction in MTCT cases. In line with this, the Ministry of Health has sponsored programs, which included jingles in televisions, and radios about the efficacy and availability of ARV for PMTCT.

However, it is crucial that this program does not result in complacency regarding women who decline to test. Clearly, this specific population may require additional support and provision of sufficient HIV discussion tailored to meet their specific individual needs. One long-term effect of antenatal HIV screening is the general notion among women that HIV testing is a one-off event. Thus, women who have had an HIV test in the past may refuse to test on this basis. Ongoing exposure to the risk of HIV acquisition as demonstrated in the current pregnancy indicates that repeat testing should be encouraged at all times, particularly in subsequent pregnancies. Policy and midwifery training to address this challenge may be required.

overall, the circumstances that influence an individual to undergo an HIV test is complex and enmeshed in multiple factors including individual beliefs and values, cultural, available information and societal view towards an HIV-positive test result (Gruskin et al., 2008). Stigma, discrimination and partner violence are some of the consequences of a woman's HIV-positive result (Maman and King, 2008). These adverse consequences could deter women from learning their HIV status. Thus, implementing routine testing should concurrently be followed with community mobilization focusing on encouraging the members to develop positive attitudes to people living with HIV.

9.3.2 The Association between Test Acceptance and Woman's Socio-Demographic Characteristics.

Socio-demographic characteristics have been demonstrated to be an influential predictor of health-seeking behaviour all over the world, including Africa (Akwara et al., 2003; Rajaraman and Heyman, 2007; Tenkorang and Owusu, 2010): the less educated and the poor being less likely to utilize health care services or to engage in preventive behaviours (Tenkorang et al.,

2009). In terms of screening for HIV, several studies conducted in different countries suggest that test acceptance increases with higher educational status (Fabiani et al., 2007; Gbadegesin, 2004; Cockcroft et al., 2007; Ben-Natan and Hazanov, 2015). The findings of the current study are consistent with these data. Women with higher formal education are likely to use rational rather than traditional approaches to health decisions, making them more aware and willing to be guided by public health recommendations such as HIV test acceptance. Rajaraman and Heyman (2007) pointed out that formal education ignites the confidence to negotiate for health care services and even to dialogue with the health care provider. Although primary education is free in Nigeria, the 'almajiri syndrome' means that over 5.5 million girls are out of school(UNESCO, 2014). Socioeconomic barrier coupled with early marriage may explain why test decline is high among a certain group. Although the ethnic differences in HIV test acceptance may be a reflection of socio-economic disparities, other reasons are probably social activities and lifestyle factors. The finding that education plays an important role in health-seeking behaviour further demonstrates how socioeconomic disadvantage may pose a challenge to disease prevention efforts. This requires an urgent solution from the policymakers.

The association of age, marital status, ethnicity and religion with HIV test acceptance has been well studied by various authors (Pignatelli et al., 2006; Perez et al., 2006; Mahmoud et al., 2007; Dahl et al., 2008).

Religion has been an instrument for the dissemination of HIV/AIDS information, including issues relating to preventive strategies. Regarding HIV testing, a certain religious denomination has made it mandatory for prospective couples to undergo one before solemnization. Although relevant experts are underscoring the human rights implication of such guidelines, this step has unarguably encouraged many of the religious faithful to undergo

testing. Data from this study found that Christians and Muslims alike are more likely to undergo an HIV test compared with others who are not affiliated with any of these religions. This result is similar to the study in Ethiopia, which reported a strong association of testing uptake among the Christian folks compared with traditional religions (Wringe et al., 2008). However, this finding contrasts with the study conducted in Sudan, in which the authors reported that being a Christian was significantly associated with lower test acceptance compared with being a Muslim or other religious group (Mahmoud et al., 2007). Though the studies were conducted in settings that were predominantly Muslim dominated, and this could explain the direction of the study findings. Overall, this result appears to highlight the contribution of religious institutions in building a healthy society. This finding probably indicates that religion profoundly shapes the attitude of its members regarding how they respond to health issues such as HIV testing uptake. The Muslim population in this study appeared to dominate with testing under routine HIV testing approach, perhaps due to their long-held value of in-group loyalty in their day-to-day lifestyle. This positive attitude should be considered in programmatic planning for effective HIV testing.

Many researchers have reported an association between the ages of patients and HIV test acceptance (Pignatelli et al., 2006; Mahmoud et al., 2007). Mohammed and colleagues (2007) in a study in Sudan found that HIV test acceptance was higher among women older than 26years. Likewise, several other studies also suggest that the age of an individual woman is associated with HIV test acceptance. This study found that testing uptake increased linearly with age and peaked at ages 25-29.

Another important influencer of test acceptance among this group was being married followed by being a full housewife and educational level of the woman. Other variables such as ethnicity and occupation of the participants did not play any statistically significant role in

test acceptance. Although most of the participants are either married or in a long-term partnership, the study finding shows that 70.7% accepted testing compared with 44.4% of single women while all (100%) of divorcee underwent testing. This study result is in agreement with previous studies conducted Ghana (Tenkorang and Owusu, 2010) and in South Africa (Venkatesh et al., 2011) where testing rates increased with being in long-term intimate partnership as well as having a higher educational level (Venkatesh et al., 2011). Since being married is associated with HIV testing, this may suggest that women who are married feel more protected in terms of exposure to HIV, and with higher education, they tend to understand the benefits of being tested.

9.3.3 Receipt of test result

The study also found that the introduction of routine testing led to an increase in receipt of test results compared to VCT opt-in. In this study, nearly 100% of the women who tested for HIV during the routine offer received their results, including those who are seropositive. This is an improvement from the low return rate, which was recorded in self-referral VCT where a substantial proportion of the women, failed to claim their result, most of whom, however, tested negative to HIV. Highly trained and very skilled midwife counsellors who provided well-tailored group education about the benefits of routine antenatal HIV test, the availability and effectiveness of ARV for PMTCT, in addition to the use of rapid test kits with on-site test result may have contributed to this change. In contrast to this finding, Botswana and Kenyan studies reported that a substantial proportion of pregnant women, 29% (Creek et al., 2007b) and 31% with 41% of seropositive (Creek et al., 2007b; Seipone et al., 2004) did not receive their test results after the adoption of routine testing. However, the study reported that testing was conducted in a different place outside the antenatal facility; hence, the results were not

immediately delivered to the clients. In our case, the tests were conducted in the side-laboratory, which is located in the antenatal unit, and test results were delivered to the clients on the same day. The result of this study agrees with a previous similar study in Zimbabwe, which reported that almost all the pregnant mothers (98%) received their results, including those who were infected with the virus (Chandisarewa et al., 2007).

The present study also showed that offering antenatal testing for HIV that followed the principle of routine opt-out testing identified more infected women (14.2%) compared with 4.9% during the self-referral active consent VCT. Thus, nearly three-fold increases in the number of identified women who were infected with the virus were diagnosed during routine opt-out testing compared with active consent VCT. Overall, HIV prevalence among the parturient women during the routine testing period of this study is higher than the official estimate for the region (North Central) 5.8% as well as the National rates of 3.0% for pregnant women (Nigeria Federal Ministry of Health (FMoH), 2013; FMOH/NACA, 2015). In addition, by comparison, this rate is higher than estimates in states most burdened with HIV (such as Akwa-Ibom 10.8%, Anambra 9.7% and Imo 7.5%) except Benue state, which has 15.4% (FMOH/NACA, 2015).

This finding is consistent with a study conducted in antenatal settings in Botswana, which reported that the introduction of routine HIV testing increased the case detection rate among pregnant women from 47% in VCT opt-in to 78% (Creek et al., 2007b). Likewise, in the Netherlands, a significantly higher rate of cases was recorded 80.3% after the adoption of routine antenatal HIV testing against 33.7% during the implementation of VCT opt-in (Boer et al., 2011). A study in Malawi did not show any significant variation in terms of statistical significance in case detection rates between the two interventions (17.7% versus 16.5%) however, in terms of case detection rates in absolute numbers, routine testing identified a

much higher number (148versus17) of HIV positive women (Kasenga et al., 2009b). The reason for this difference could be due to many asymptomatic but infected women who, perhaps never viewed themselves as being at risk and would normally not have taken the test under client-initiated VCT but are now being encouraged to have a test under routine testing approach. Hence, many more women are being tested and many of them are being identified as being infected, unlike the active consent approach where many of the women who undergo testing are mostly those who experience HIV symptoms. Therefore, the initial gap of 'missed opportunity' to test women in ANC is being closed-up using the routine testing approach.

In general, the differences in this study finding could be due to variations in both the HIV risk factors as well as the cultural practices among the study population. In particular, the unexpectedly high rates of infection recorded in this study is most likely a result of the study setting and study population. First, FCT as a whole, where the study was conducted is one of the largest HIV epidemic cities in Nigeria (Bashorun et al., 2014). This means that a large proportion of people living in this city may be undiagnosed careers. Second, the study population is significantly composed of armed personnel and women who are in partnership with armed personnel. This group of individuals apparently faces a greater risk of HIV infection than the general population. Armed forces on deployment are constantly exposed to the risk of HIV infection through their 'risk-taking' adventures with sex workers (Singer et al., 2010). They also engage in illicit sex as a means of evading the solitude that is often associated with migration. However, the unexpectedly high rates of infection in this study may not reflect the actual burden in the general population. Nevertheless, identification of asymptomatic but infected pregnant mothers certainly will reduce the incidence of HIV transmission in this group, especially cases of vertical infection (Bayer and Oppenheimer, 2013). In addition, as a

referral centre providing free services for PMTCT, the ANC unit at State House Medical centre receives clients from other neighbouring health facilities within and outside the city.

The study also found an association between seroprevalence and age of pregnant women. The highest proportion of HIV positive pregnant women was within two sub-groups: those between the ages of 40-45 and those between the ages of 25-29, similar to what was reported in the 2014 HIV seroprevalence survey of ANC attendees in Nigeria (FMOH/NACA, 2015). This pattern is of concern because older women may have had previous pregnancies (multiparous) with undiagnosed HIV-positive serostatus, which could have increased the risk of transmission to their babies. That are babies born to their previous pregnancies would have an increased probability of HIV acquisition since the woman did not take risk reduction measures; depending however on the point at which the woman became infected herself. In the absence of appropriate PMTCT services, the likelihood of vertical transmission increases from less than 2% to 45% (Bassett et al., 2008; Becquet et al., 2009). Again, in terms of the younger age group, it is worrisome because young women aged 25-29 who are new entrants into motherhood are being infected at a disproportionate rate. This population is often used as a proxy to measure the incidence rate in the general population as they represent new entrants into reproductive age as well as engagement in a formal and stable relationship. A factor that could be predisposing young women to HIV infection might be prior unstable premarital sexual relationship since HIV transmission in Nigeria and indeed Africa is predominantly through heterosexual contact (Pybus et al., 2003). In this study, HIV prevalence was highest at 40.7% among women between the ages of 25-29-year-old, mirroring other similar studies (Glynn et al., 2001; Galadanci et al., 2008). These findings suggest that HIV infection predominantly occurs among relatively young women and peaking at the later ages of 20-29, probably after few years of first sexual debut (Dellar et al., 2015; Naicker et al., 2015). An

immature genital tract during defloration and cervical ectopy might accentuate the risk of HIV transmission in this population (Bouvet et al., 1989; Murdaugh, 2005). Existing sexually transmitted infection exacerbates susceptibility to HIV infection (Ward and Rönn, 2010). Additionally, young women tend to have an intimate male partner who is older than them in their first sexual encounter or later, hence they may experience a higher risk of infection by being exposed to men who may already be infected from previous multiple sex partners (Dunkle et al., 2004; Mocumbi and Amaral, 2006). The PMTCT service and HIV/AIDS prevention should focus on young women: educating them on how to delay intimate partnership until they are ready to get married and empowering them on negotiating skills, especially in circumstances where condom use may be handy. Partner testing and disclosure should be an ongoing slogan that should be highlighted during any counselling and testing sessions with young women. They should also have abundant access to information, which helps them to reduce the risk of infection. This is particularly important for women from the northern part of Nigeria, who due to cultural reasons, do not have the freedom to negotiate terms for sexual engagement within the union.

9.3.4 Uptake of ARV Treatment for PMTCT

Another significant finding of this study was that routine opt-out HIV testing of this study demonstrated that identifying HIV infected women led to effective referral and linkages with PMTCT treatment and care services. Significantly, more women were linked to PMTCT services to access treatment and care for the reduction of MTCT. The study result shows that enrolment into antiretroviral treatment increased from 67.7% in VCT opt-in to 97.7% after the adoption of routine opt-out HIV testing. This finding concurs with a similar study conducted in Botswana, which reported an increase from 29% during VCT to 56% in routine

opt-out, an almost two-fold increase in the proportion of women receiving treatment for the prevention of vertical transmission of HIV. The impressive linkages to PMTCT services and access to treatment of this study could be associated with the presence of an existing PMTCT service structure in this facility, increased knowledge of the benefits of PMTCT and the skills, which the midwives gained through the training. These findings underscore the need to integrate routine HIV testing into antenatal service as a standard of medical care for all pregnant women.

The most worrying aspect of the research observation is that some women did not subscribe to participate in the study, yet they failed to access HIV testing and counselling on their own, of which counselling and testing are available free of charge to all pregnant women. Moreover, some women did not seek ANC despite being eligible for the free use of the health facility rather this group arrived in the hospital once they were in labour. The hospital is however yet to develop an HIV testing and counselling protocol for women in labour. This population may therefore not benefit optimally from PMTCT service.

Nevertheless, the findings of this research raise optimism that with concerted effort and renewed commitment, Nigeria can achieve the ambitious goal of 90% testing uptake in pregnancy as well as virtual elimination of paediatric HIV in the near future. This is because antenatal service presents a well-organized system for diagnosing pregnant women, managing those who are infected through a rapid referral to PMTCT services as demonstrated in this study. These are all necessary for the timely commencement of antiretroviral treatment for the reduction of MTCT.

9.3.5. Impact of Midwife Characteristics on Test Acceptance.

This study also evaluated the impact of midwife characteristics on HIV testing uptake. The midwife counsellor plays an important role in testing uptake. The results of the current study indicate that test acceptance varied within this group of midwives ranging from 27% to 41.2%. This non-uniformity of uptake rate could be due to factors associated with individual midwife counsellor or with the pregnant woman. From the findings of this study, the variations in test acceptance are associated with the individual midwives' characteristics relating to educational level and experience or length of professional practice. Two of the midwives who have less than five years of work experience plus a diploma degree both achieved 27% test acceptance (n=117). A midwife with more than five years of professional experience with a first degree recorded 31.6% (n= 137). However, the midwife who has a master's degree with more than ten years' experience performed the highest test acceptance of 41.2% (n=179). The performance of the midwives improved with professional experience and educational background. This finding is in agreement with previous studies, which measured similar characteristics in different settings. In one of the studies, testing uptake among pregnant women varied between 3% and 82%, depending on the individual midwife's characteristics relating to knowledge of HIV, how she conveys counselling message and the manner in which the content was delivered (Meadows et al., 1990). In another study, there was a wide range of uptake rates of 15% to 48% among ten midwife counsellors. The current study mirrors the findings of these studies. The previous study was conducted in the USA while the latter was performed in London, UK. Regarding the study in the UK, the midwives received the same level of training and followed a written uniform counselling instruction, yet they recorded wide degrees of test acceptance. However, midwives have different levels of education and work experience. While the findings of the current study mirror the above literature, it is not

in agreement with the earlier notion that the performance of health professionals is predicated entirely on the level of medical knowledge (Johns., 2010). In this study, aside from medical knowledge, other factors such as experience played a vital role in test acceptance. According to Meadows and colleagues, (1990) successful test acceptance depends on a conglomeration of factors, which includes communication and counselling skills as well as good knowledge about HIV/AIDS disease.

The necessity to undergo an HIV test affects the individual's psychosocial well-being. More so, knowledge of HIV positive status during pregnancy is a traumatic experience not only to the woman but also to the entire family.

As with any other clinical investigations, the health care professional should under rationale condition buttress cogent reasons for HIV testing and benefits therein. Because the midwife is the gatekeeper of pregnant women, it is, therefore, her primary responsibility to take steps to ensure that they understand the likely advantages and disadvantages of HIV antibody test. She must highlight that knowledge of the HIV serostatus empowers the woman to make an informed decision concerning her health as well as that of her unborn baby. Accordingly, depending on the test outcome appropriate care is given to the woman following PMTCT service guidelines.

The midwife should perform this task in a manner that is convincing and rich for the woman to accept testing through the perspective of informed decisions. However, the results of this study suggest that providing the midwives with the same work condition did not guaranty they are performing the same way. This raises a concern about the possible attributes of the counsellors in making health information appealing to their patients.

Clearly, midwife's attitude, behaviour, and knowledge are important attributes that must be considered when designing a program to increase HIV testing. In general, the likelihood for a woman to accept an HIV test largely depends on which of the midwife that is offering the test. The qualitative study could helpfully explore the quality of midwife's counselling attitudes and approaches that best attract ANC HIV-testing uptake. Besides, continuous refresher training of the midwife could enhance their understanding and update their knowledge on recent advances in the field to ensure that women receive encouraging current information about the benefits of HIV testing.

9.4 Using the Theory of Planned Behaviour to Understand HIV Testing

9.4.1 Overview

In the absence of an effective cure or vaccine for HIV, behavioural change remains a critical HIV prevention option. As part of the HIV prevention strategy, prevention of mother-to-child transmission of HIV (PMTCT) aims to reduce vertical transmission. Being an important PMTCT intervention, increasing uptake of HIV testing in ANC is part of the core focus of this study. HIV testing aims at timely identification of HIV positive pregnant mothers for onward PMTCT interventions. This study compared the testing rate of routine opt-out approach to client-initiated approach of HIV testing in ANC. Findings from this study showed a substantial increase from 48% to nearly 95% in the testing rate after a switch from client-initiated to routine opt-out. Several empirical studies concerning routine opt-out testing are primarily focused on the tension between increasing HIV testing rate and the potential violation of values such as ethical and legal doctrines. Yet, a few research (Mirkuzie et al., 2011; Mtenga et al., 2015) have considered this debate using health behaviour theory. This section of the thesis examined from a theoretical point of view, how the mode of the offer (routine opt-out

or maybe group offer versus client-initiated individualized offer) and test acceptance may be explained using cognitive-behavioural theory.

9.4.2 The Concepts of Health Behaviour in HIV Testing

The dominant cognitive behaviour models that shape intervention development have their origin in psychological theory **(**Fowler and Christakis., 2008**).** There are several elements of behaviour change at each level of the socio-ecological stance relative to behaviour change interventions, including HIV prevention. At the individual level includes issues from the micro-levels, such as individual's view, emotions or beliefs. At the level of the individual's network includes family influences such as kind of relationship, level of satisfaction or social support (Kaufman et al., 2014). Regarding larger group level includes culture, community norms while the institutional level involves factors within the healthcare system such as quality of care, confidentiality, and adequate resources. Theoretical models conceptualize how these variables impact and interact together.

The most noticeable theories are the Health Belief Model (Quah, 1985), the Social Cognitive Theory (Bandura, 1994; Safren et al., 2010), The Theory Of Reasoned Action and Planned Behaviour (TPB) (Icek Ajzen, 1991) the Trans-theoretical Model and the information motivation (Brug et al., 2005) as well as behavioural skills model (Rongkavilit et al., 2010). Each of the theories is concerned with how individuals make behavioural choices. The general notion is that individuals elect to make a course of action based on the degree to which they view that their preferences will result in what they value. Hence, the characteristics of the theories are premised on factors that reflect values.

HBM is a psychological model that attempts to describe and predict health behaviours. This is done by aiming at the attitudes and beliefs of individuals. The HBM is premised on the view

that an individual will take a health-related action (i.e., accept HIV test, for instance) if the individual has a favourable expectation that by taking a suggested action could prevent a negative health condition. For instance, taking an HIV test will be effective in preventing HIV. The principal framework of HBM are the perceived threat and net benefits: apparent susceptibility, perceived severity, perceived benefits, and perceived barriers. These conceptions were proposed as accounting for an individual's "readiness to respond". This model does not recognize structural factors as such that is the contribution of socio-economic and organizational environment.

Social cognitive theory (SCT) opines that portions of an individual's knowledge acquisition are directly related to observing people within the context of social interactions and experiences. SCT defines the impact of individuals' experiences, environmental factors and the effect of others on individual health behaviours. This model premises that preventing HIV transmission necessitates both reinforcing safe behaviours and changing unsafe ones. SCT provides prospects for social support through communicating expectations, self-efficacy, and using observational learning and other reinforcements to attain behaviour change. Again, this framework negates the structural framework in terms of the institutional factors.

The Multiple Domain Model (MDM) was expanded from the Theory of Planned Behaviour, substituting perceived behavioural control with self-efficacy. MDM posits that there are several domains of influence on health behaviour (Tiller, 2001). These influences are listed thus in the order of relevance: situational/contextual variables, preparatory behaviours, behavioural intentions, normative, attitudinal and self-efficacy beliefs. Others are personality and social environmental factors and social structural variables. In essence, the MDM combines several individual-level theories including factors such as sociological sense (social

class, race, gender), and variables that influence personality social environment (family relationships) and social situational variables (relationship status). Thus, factors that are distal to an individual are explicitly modelled as elements that shape one's behaviour.

The Network-Individual Resource Model (NIRM) theorizes about considerable reciprocal Interconnectedness of individuals within their critical social-networks during their lifespan. However, this tie does not negate that harm (HIV transmission) could also arise through this social-network (Johnson et al., 2010). Networks create structural realities that may have a direct or indirect positive or negative influence on risk behaviour. Dynamic Social Systems Model (DSSM) conjectures that resources, science and technology, formal, and informal social influences, social bonding and environments are conditions that vigorously intersect to create structural realities at all levels that influence HIV prevention and detection. Structural influences are likely to affect risk behaviour in one way or the other. Another model, the Transmission Reduction Intervention postulates explicitly on the fact that HIV transmission is mainly through the exchange of body fluids, typically by community sexual and injection exchange (Friedman et al., 2014). The position of this model focuses on the need to concurrently intervene at higher levels such that the caregiver resolves power imbalance with the patient, ensuring that they understand the patient's social and economic realities. Organizations possess resources that promote or impair individual behaviour.

In general, several of these models contain ideas that are very related (or identical) but use diverse terminology, creating the impression that they are dissimilar. The lack of agreement regarding what to call certain constructs has led to fragmented literature that could be better integrated if a common set of terminology were agreed upon.

Overall, health behaviour is fundamentally influenced by the cultural contexts from which an individual was nurtured. Decision-making as an aspect of life is a rational universal practice in human behaviour, as people of all cultures have opportunities and challenges that necessitate making choices from among alternatives (Taras et al., 2010). The impact of cultural values on human behaviour have been a strong theme in recent debates. Culture is a value that give order and guidance to people in their reasoning and actions as they contend with common human challenges and problems (Oyserman et al., 2002). Through understanding of the philosophies that different social groups apply in their thoughts and actions, researchers have been able to deduce the values shared by several social groups. Societies can then be characterised and linked based on commonly shared values.

Societies are branded as either individualist or collectivist according to affiliation between individuals and their relationship to groups (Triandis, 1986). Collectivism is described as the relegation of personal interest to the goal of the group with a prominence on sharing and group harmony. Conversely, individualism involves a state of individual's self-orientation that highlight self-sufficiency and control that anchors on self-accomplishment. Nigeria is a collectivistic culture where individuals are integrated into groups. The individualism-collectivism construct has been used widely to understand social conducts, especially in efforts to predict health behavioural tendencies. For example, Osyerman and colleagues (2002), reported that the individualism-collectivism concept have considerable impact on psychological processing, and that cultural variances in the dimension provide a strong explanatory means for appreciating the variability in the behaviour of individuals in different parts of the world. Therefore, to put health behaviour regarding HIV testing in context, the theory of planned behavior provides a practical framework to discuss the study outcome.

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9.4.3 Using the Theory of Planned Behaviour to Understand HIV testing in Nigeria.

The Theory of Planned Behaviour (TPB) represents a plausible and favourable theoretical framework for explaining and predicting social behaviour. TPB framework theorizes that individuals intending to act safely do so in accordance with commonly shared values. This concept could be applied as a practical tool for understanding and interpreting HIV testing behaviour in ANC settings relative to Nigeria culture. It can also aid in understanding the barriers and facilitators to behavioural modifications relative to HIV testing uptake.

According to TPB, the desire to undertake a specific behaviour is directly associated with three important elements- the-so called antecedents of intention namely personal attitude, subjective norms and perceived behavioural control. Personal attitude (the answer to the question: what are the benefits and am I willing to do that?), subjective norms (the answer to the question: Do other people expect me to do that?) and perceived behavioural control (the response to the question: Do I have the required ability to do that?). Typically, behavioural intention is a reflection of attitude and subjective norms (Sheeran, 2002; Molla et al., 2007). Here, subjective norm refers to perceived social pressure to accomplish the behaviour. This reflects the belief that an important person or group of individuals will recommend and support a particular behaviour. Subjective norm is, therefore, perceived social pressure from others for an individual to act in certain ways and the willingness to adhere to the views of these individuals (Molla et al., 2007). Perceived behavioural control defines the ease or difficulty in performing a particular behaviour. Subjective norms perceived behavioural control and attitudes are reinforced by behavioural, normative and control beliefs, respectively. In combination with TPB, variables such as past behaviour and descriptive norms have a magnificent impact on intention and behaviour. Descriptive norm refers to the

perception of the women concerning what their colleagues (other ANC attendees, friends, and neighbours, sisters) do with respect to HIV testing. In other words, a descriptive norm means an expectation that the woman will behave according to her perception of the pattern of behaviour in the group (are other women accepting or refusing to test?). The possibility of expressing any of the behavioural response at any given time and in a particular context has been described as a 'behavioural potential' (Kelly and Barker, 2016). The drivers of behavioural potential include perceived rewards of present behaviour, self-efficacy, normative belief, perceived consequences of not changing behaviour and motivation. For example, women in power-imbalance (e.g. patriarchy) are vulnerable to partner's influence-who may choose to be supportive or show negative influence (harm by poor care). In parallel, a network of the interconnectedness of the women could strengthen health gain when more women actively participate and support one another (Spring et al., 2012).

Now, focusing on the testing outcome of this study, it would suffice to note that the astounding testing rate witnessed in routine opt-out was most probably influenced by subjective norm (perceived social pressure). In other words, the subjective norm meant a woman's perception of substantial others' attitudes on whether one should or should not accept testing. In this case, group members acted as normative norms to engage in HIV test acceptance. Perhaps, receiving group-counselling made women feel socially obliged to accept HIV testing. The finding in this study (substantial increase in test acceptance under routine opt-out) mimics a study in Ethiopia, where attitude and subjective norms were reported as the strongest predictors of intended condom use among young adults (Molla et al., 2007). Similarly, subjective norms and attitudes were found as predictors of college students' motivation to learn about HIV/AIDS prevention (Gebreeyesus Hadera et al., 2007). This added to perceived behavioural control (the ease to either accept or reject testing), might have

enhanced test acceptance. This finding suggests that the decision to accept HIV testing in ANC was largely under the influence of subjective norms and behavioural control. Probably, under routine testing, pregnant women underwent HIV testing if they perceived normative pressure.

From a practical point of view, the current finding suggests that in order to encourage HIV testing in antenatal, it is critical to motivating non-intenders as well as focus on women who have positive intentions but still do undergo testing. However, the overarching principle of HIV testing is to ensure that informed consent is not violated.

In general, reception to HIV testing is contingent on how various individuals, groups and organizations relate in the immediate and wider settings: that is social interconnectedness. This aspect was well emphasized in the current intervention as the women received pre-test information in groups and an environment that encouraged social bonding. This might have played a significant role as women viewed participation as being non-discriminatory resulting in the huge success recorded in the present study. Cultural context proved to be an essential component in a previous study on intentions.

As highlighted earlier in chapter 4, section 4.6.3 of this thesis, the cultural background of Nigeria lays emphasis on the in-group lifestyle (collectivism). Individuals coming from more collectivistic countries (Nigeria for example) appear to experience stronger pressure from a significant other and are more eager to comply with their opinions (Frank et al., 2015). Likewise, individuals born and raised in predominantly individualistic societies may have a stronger inclination toward certain behaviours and may pay less attention to what other people think or do. Hence, the HIV group discussion forum administered to the women probably influenced test acceptance, despite Nigeria being a patriarchal society. The findings

of the present study agree with the principle underlining planned behaviour theory (Icek Ajzen., 1991). Also, consistent with this, is a study on binge drinking among university students, which found that a combination of attitude, subjective norm and self-efficacy strongly predicted desires to binge-drink, providing support for the theory of planned behaviour (Johnston and White., 2003). The study found that the norms of a behaviourally relevant reference group were a strong predictor of individual member's intentions to binge-drink, especially for those who strongly identified with the group. Data from the same study further suggested that focusing on individual students' attitudes, perceptions regarding pressure from significant others to drink and elements of internal motivation and control may be valuable strategies to either reduce or encourage the frequency of excessive alcohol consumption.

Also, TPB constructs exist at the institutional level. Since individual and structural variables are pertinent to HIV risk reduction that is transmission prevention, therefore appropriate interventions should focus on the linkage between the two levels. The institutional level involves factors within the health care system (Johnson et al., 2010). This includes factors (control beliefs) such as quality of care: confidentiality, protection from stigma and discrimination and the quality of patient–midwife interactions. Institutional trust accrues to the extent that healthcare providers have the responsibility to facilitate coping mechanisms for clients seeking care since such an act promotes service users' sustained existence. Individuals infected with HIV are often concerned that healthcare providers may disregard confidentiality. However, health professionals have legal, professional and ethical obligations to keep all patient information confidential (Sauka and Lie., 2000). Confidentiality was identified as a critical prerequisite for building trusting relationships between the health care provider and an HIV-infected individual within the counselling process, right from the first

visit up to the follow-up counselling. It is also one of the most important elements for the formation of trust and proper functioning of the midwife-patient relationship. Trusting relationships cannot be established in situations where the health care provider ignores or fails to understand the needs of an HIV-infected in the context of his/her HIV status (Sauka and Lie., 2000). Breaches of confidentiality can act as a catalyst to distrust and disincentive to test acceptance, which diminishes the overall public's trust in health care. Therefore, HTC should be sensitive to the cultural, historical traditions as well as prevailing public health practices, social norms/values and political differences in attitude toward the importance of treating a woman as a private individual. Health providers whose members act in defiance of safe health norms present abundant evidence that clients' trust and acceptance play extremely significant roles in health behaviour.

In the case of the current study, practical measures were tactically designed to maintain confidentiality. Although standard confidentiality practices applied to both control and experimental groups such as the use of a coded identifier (totally anonymized) and women volunteered to test in privacy (opportunity to decline to test in the midwife's office if they wished to do so) without the knowledge of others, additional measures were taken during routine opt-out. For instance, women who opted-out of testing were not discriminated against. In fact, before the intervention, the midwives received special training from a team of experts on HIV prevention and control focusing on how to address confidentiality issues as well as stigma and discrimination. The training also emphasized the significance of treating all women at risk or living with HIV with respect as well as the need for stringent adherence to confidentiality for all other sensitive information. Moreover, women had the choice to accept, defer or elect to conduct the test elsewhere. Besides, test results were entered into computer and password protected. The password was private, and the computer locked secured in an

office where only the researcher and the midwives have access. Information was only made available to other healthcare providers on the need-to-know principle. Perhaps, these extra measures engendered the needed confidence to encourage improved testing as witnessed in routine opt-out. Confidentiality concerns also included accessing other ANC services such that no woman was discriminated against due to her refusal of the offer to test or in relation to the HIV-positive result. Women who declined the offer received all other ANC services and HIV infected women were treated like normal patients. Consistent observations were also reported in the previous study in Latvia (Sauka and Lie., 2000). In the study, confidentiality was reported to be a cornerstone for shaping trusting relationships between the health care providers and the patients.

Another dimension of TPB relates to whether the woman anticipates more benefits than negative outcomes (personal attitude) in response to testing. As demonstrated in the current study, women who received group pre-test information (95% uptake) were more likely to test for HIV compared to those who received individual pre-test counselling (44% uptake). For group counselling, the content of the pre-test information was simplified, easily comprehensible and clearly highlighted the benefits of testing. Simpson and colleagues (1999) pointed out that simplified and concise pre-test information delivered to women in a routine opt-out strategy was instrumental in ensuring that women understood the benefits of testing and this stimulated test acceptance. The finding of the current study using the routine opt-out approach concurs with the result in the UK (Simpson et al., 1999) as well as the result of a review study that evaluated barriers to HIV testing (de Wit and Adam., 2008). In the review study, the perceived benefits of testing were a vital test-promoting factor (de Wit and Adam., 2008). More evidence from Sub-Saharan Africa suggests that the pre-test information delivered to the pregnant women in the opt-out strategy varied and, mainly focused on

encoding women to get tested without the key benefits for having an HIV test (Ujiji et al., 2011; Njeru et al., 2011). This appears to highlight the need for concise and quality educational messages as currently applied in routine testing of this study. The message should focus on beliefs women hold about the consequences of HIV testing. This would aid women's understanding of the core benefits of testing and subsequently increase the mother's motivation to accept testing. Related to the above, is an aspect of TPB constructs bordering on one's attitude (Spring et al., 2012). This concept suggests that attitude towards HIV testing plays a significant role in the use of HCT services and that women within marital unions are likely to accept HCT services if they cultivate a positive opinion towards the ideals of HCT services. The reason for this may be that married women may have the impression that they are safer since they live in a dyadic committed relationship. Although most women that participated in this study were married, being married might have influenced test acceptance based on the notion that a stable relationship (being married) confers some safety net. Women may also have optimistic prejudice about their susceptibility to contracting HIV infection such that the incentive to testing may be based on their perceived benefits rather than their predisposition to HIV infection. As stated above, the significantly higher proportion of those who received routine opt-out model accepted testing, since the benefits of testing were emphasized. In agreement with this data, is a review that assessed barriers to HIV testing in which perceived the benefit of taking an HIV test was reported as a critical test-promoting factor (de Wit and Adam., 2008).

9.5 Economic Impact of the Intervention

9.5.1 Cost-effectiveness of the intervention

Data from this study support routine HIV testing for all pregnant women in this study site, even at a 3% prevalence of undiagnosed HIV among pregnant women. This study evaluated the cost-effectiveness of two approaches for offering HIV tests in pregnancy. Data inputs involving testing and counselling costs as well as costs associated with receipt of test result outcomes were used as key inputs for this analysis. The data was gathered mainly from this non-randomized controlled trial evaluating cases of HIV infection averted in children born to the participating HIV-infected mothers. An additional source of data was high-quality literature. This method enabled the computation of cost-effectiveness of the two screening approaches in line with guidelines for the conduct of cost-effectiveness in health (Sanders et al., 2016).

The main finding is that provider-initiated routine HIV testing of all women attending ANC is cost-effective relative to the traditional client-initiated counselling and testing. The improved effectiveness and the subsequent cost-effectiveness happened because this method led to higher rates of testing and receipt of test results. Routine testing, at £764.40, met the conservative threshold for cost-effectiveness in comparison with the alternative client-initiated testing. When the benefit is viewed from the angle of the additional unit cost of case averted, routine testing yielded a much more favourable outcome, requiring only £15.02.

Although WHO and CDC recommend that countries should implement routine HIV testing in antenatal settings, Nigeria is yet to integrate such a program into ANC services. Probably, three elements of routine testing would have contributed to its success. Among the reasons is the idea of task shifting-using non-physicians, in this case, the midwife counsellors

extensively increased test acceptance rate. This finding is in agreement with a large body of literature, which recommends the use of task shifting in the provision of preventive medicine (Cargill et al., 1991; Atri et al., 1997; Stone et al., 2002). For example, a systematic literature review consisting of 81 articles reported that the most successful approach to improve preventive health care services was an organizational adjustment, whereby non-physician staff performs specific preventive tasks (Stone et al., 2002). Aside from this point, the use of non-physician personnel has the additional potential benefit of lowered cost by substitution of cheaper personnel. In this study, the aggregate costs of testing were higher for the strategy that employed a provider-initiated approach; however, the increase in cost was because of higher rates of testing which counterbalance the gain of lower time and personnel costs.

Another important component of the provider-initiated routine testing approach is the streamlined counselling strategy unlike the comprehensive counselling approach of the client-initiated testing method. In comparison, the traditional testing and counselling approach has higher counselling costs during the pre-test counselling session, lasting an average of 20minutes. This is in contrast with the provider-initiated counselling approach, which lasts an average of twelve minutes. This finding mirrors a randomized trial in which the pre-test counselling session of traditional self-referral VCT lasted for 20 minutes whereas the provider-initiated testing approach lasted an average of 7minutes, resulting in almost 65% reductions in counselling costs. The trial did not report any difference in HIV knowledge between the two populations -client-initiated versus provider-initiated (Anaya et al., 2008).

The next important aspect of routine testing was the use of rapid testing and dedicated midwife counsellors. Although both approaches utilized the rapid testing technique, enabling test results to be ready within 20minutes and the women to receive post-test counselling the same day, nurses who performed client-initiated testing had another patient load to attend.

This resulted in long queues and forcing most women under this strategy to make two visits since they had important domestic tasks to perform. However, in this trial, the test costs were similar for routine testing versus client-initiated testing, although receipt of post-test counselling differed in the two arms. The finding of this study is consistent with several other pieces of literature, which suggest that rapid HIV testing significantly increases the receipt of post-test counselling (Kassler et al., 1997; Hutchinson et al., 2006; Lyss et al., 2007; Spaulding et al., 2015). Recent trials have also reported the potential economic value of rapid HIV testing techniques (Mehta et al., 2008; Farnham et al., 2008; Spaulding et al., 2015).

9.5.2 Link between Interventions and Cost-effectiveness

Cost-effectiveness analysis helps to identify a program that has the prospect to substantially reduce disease burden and at the same time at a reduced cost. Routine opt-out screening using rapid HIV testing and brief counselling information was cost-effective compared with standard HIV testing and counselling strategy, because of increased rates of testing, case identification, receipt of the test result and access to treatment. The current study found that more women learned their HIV status under routine testing and more HIV positive cases identified early in the pregnancy and initiated with ARV, thus reducing MTCT to <1%. Because the clinical benefits to those linked to care are so dramatic, linkage rates need only be 10% for the intervention to remain cost-effective. This study highlights the WHO's recommendation emphasizing the need for positive HIV-test cases to be accompanied by timely linkage to relevant prevention, treatment and care services (World Health Organization., 2009). Infected mothers who are adherent to treatment live a healthy normal life like the uninfected persons with the additional benefit of long-term infant HIV-free survival (Chisholm and Saxena., 2012). The sensitivity analysis suggests that a policy of

universal screening remains cost-effective at a prevalence of 3%, which is equivalent to the national rate. Reports from urban slum show much higher prevalence among who do not register for ANC services (Adedimeji et al., 2007), implying that the benefits could probably be more exponential had the program coverage, been extended to this sub-population.

Additionally, advances in the management of HIV, using combination efficacious, tolerable, and durable HAART have led to reductions in secondary HIV and opportunistic infections (Coenen et al., 2008). HIV counselling improves condom usage and encourages safer sex practices at the community level. Emerging evidence from LMICs shows that accessing HIV testing is associated with a reduction in unprotected sex (Denison et al., 2008). The impact of HIV counselling on the horizontal transmission of HIV in the community during antenatal visits may prevent cases of HIV among adults, therefore, making the choice of testing more attractive to decision-makers. Data show a reduction in sexual risk behaviours among HIV infected mothers after they have been enrolled in ART treatment programmes (Aboki et al., 2014). This study did not consider the additional prevention benefits inherent in universal HIV testing in pregnancy or additional costs of HIV orphaned.

9.4. Discussion- Clinical and Economic

9.4.1 General discussion

For many years, a few data were available on prevention of mother to child transmission of HIV. Lately, however, many successes have been recorded in developing effective and affordable strategies to reduce the probability that a woman will pass the virus on to her child. Among the most important interventions to PMTC are the provision of antiretroviral treatments to all HIV-positive pregnant women and avoidance of breastfeeding, where possible. However, these interventions require that a woman knows her HIV status. Yet in

many low-middle-income countries, where 95% of MTCT occurs, there are many 'missed opportunities' to counsel and test a woman to identify her HIV status.

HCT during pregnancy provides a voluntary testing session for both the healthy and asymptomatic pregnant women, including their partners to learn their HIV status. The antenatal setting is an important avenue for delivering this important service to all pregnant women. Because this intervention has been, slow to gain acceptance in many countries, particularly in settings where HIV is deeply stigmatized, hence the need to identify an alternative strategy to increase uptake.

 Before the advent of effective treatment for HIV, testing was reduced to a mere diagnostic tool used for confirming suspected symptomatic AIDS patients. However, with the growing efficacy and availability of ART treatment, testing has transformed to become a crucial intervention in the pathway of HIV treatment and management. A recent study involving many countries on the efficacy of HCT showed the critical role of HIV testing as an effective HIV prevention strategy (Coates et al., 2000). Given this positive outcome, support for HCT and other preventive activities is now the dominant issue in this discourse. The expanded availability of ART in LMIC, particularly among pregnant women demands a corresponding level of HCT activities on a level not yet experienced. MTCT related cases continued to increase in HIV endemic areas. In FCT Abuja, for instance, the increasing number of postnatal admissions from HIV-related complications in previously undiagnosed HIV women accessing services in health facilities (Okechukwu and Abdulrahaman, 2008) such as State House Medical Centre, one of the six earliest VCT centres in Nigeria, and the site where this study was conducted, is an indication of the growing demand for HCT. When the centre was designated HIV/AIDS centre in 1999, an average of 12 new clients was seen per month. During

the last two years from 2016, the number of new cases has grown to an average of 83 per month.

HIV/AIDS-related stigma and discrimination are probably the factors that affect seeking for HCT. A stigmatizing environment about AIDS and their concomitant fears for discrimination can discourage women from seeking testing and HIV treatment services (Chesney and Smith., 1999; Golub and Gamarel., 2013). Findings from this study may be interpreted in the light of the above reason, indicating that routinizing HIV testing reduces stigma.

These novel findings become more significant when it led to more women having access to other PMTCT interventions, such as early diagnoses and linkage of the infected women to PMTCT program like what is obtainable in many developed countries. There are two dimensions to this, firstly, early diagnosis and treatment in pregnancy results in dramatic reductions in transmission rates, essentially MTCT rates, and secondly, an improved prognosis for the mother.

However, it is pertinent to understand that a one-off time antibody testing does not entirely preclude infection throughout the pregnancy. A woman, who initially tested negative to HIV antibodies early in pregnancy might still seroconvert or become infected with HIV at the later stages of the pregnancy. This finding is common in countries with a high burden of HIV and had been documented in developed countries (Johnson et al., 2012). Studies in different parts of the world such as in Northern Alberta and the UK showed HIV seropositivity rates ranging, from 0.1-0.3% due to seroconversion among pregnant women who previously tested negative to HIV antibody test (Hughes et al., 2009; Moses et al., 2008; Klein et al., 2014). Also, a recent study in South Africa found a seroconversion rate of 3% during pregnancy with four-fold transmission rates higher than women who were infected before the pregnancy (Moodley et al., 2009). Likewise, in North Carolina, studies showed that 3.4% of MTCT cases occurred due

to the seroconversion or new infection after a negative antibody test results in pregnancy (Patterson et al., 2007). An infection could occur after the initial screening during the first trimester or could be missed because of seroconversion (window phase) period. This omission could be resolved through retesting of the mothers in the third trimester of the pregnancy or through pooled testing of HIV-negative specimen for ribonucleic acid using polymerase chain reaction (PCR) to detect HIV (RNA-PCR). However, a more prudent and perhaps cost-effective approach would be testing of male partners alongside their pregnant women preferably using RNA-PCR. In the case of women who did not receive antenatal care and who present to the hospital in labour, a rapid test kit may be enough to initiate ARV treatment as soon as possible. These measures are critical in formulating an effective nationwide PMTCT program. Essentially, adopting a universal nationwide HIV testing strategy for the prevention of MTCT requires improvement in the process of counselling and testing for HIV.

The overall goal of prenatal screening of women for HIV during antenatal care is to identify those who are infected with the virus. This is to enable them to receive medical and psychological care to improve their health, decrease the incidence of MTCT as well as decrease the risk of horizontal transmission to their sexual partners. Decreasing the incidence of MTCT also involves the administration of antiretroviral prophylaxis to the exposed infants and subsequently conducting early infant diagnosis to establish the infant's HIV status. This study did not focus on this critical area. A population-based retrospective study, which evaluated the number of infants who were prenatally exposed to HIV and who received timely antiretroviral prophylaxis and early infant diagnosis showed abysmal low rates (Coplan et al., 1995). Coplan and colleagues (1995) demonstrated the importance of follow-up medical care to identify HIV seropositive infants born to infected mothers. In that study, only 56% of the HIV exposed infants received some level of follow-up care, of whom 28% of the infected

infants received a proper evaluation for treatment within the first three months of life. Delay in detecting HIV infected infants result in delay in the start of appropriate care. Aside from increased morbidity and mortality (de Martino et al., 2000); this may lead to neurocognitive delays and psychiatric symptoms (Antinori et al., 2011). Optimal care during the early life of the neonatal period, especially for infected ones ultimately enhances survival rate (Ciaranello et al., 2011).

Overall, the experience of this study suggests that routine offer of antenatal HIV testing led to substantial increases in PMTCT service demand due to rising rates of HIV testing. More HIV positive women were also identified, and antiretroviral treatment initiated. Similarly, there was a moderate rise in demand for other clinical services from the women because of the improved HIV testing rate, irrespective of HIV testing outcome. The overall consequence is a likely higher benefit for maternal child health; however, coincidentally there is considerable resource implication. Going by the projected scale of resource requirements concerning the provision of complete coverage of PMTCT services to at-risk group in sub-Saharan Africa, particularly in Nigeria, then it is assumed that no resource-poor setting can bolster the capacity (in terms of staff, consumables, and drugs) for the implementation of this magnitude. In concrete terms, the thorough implementation of PMTCT may become, in a way, a demand for holistic expansion of health services rather than developing PMTCT services along with horizontal programs. Several studies have documented numerous barriers to assessing PMTCT services ranging from socio-cultural to infrastructural decay (Lindgren et al., 2005; Thorsen et al., 2008). Although the above scenario represents a sound approach, it is, however, viewed a long-term method, and therefore may not be feasible, as urgently needed. In the interim, the plausible and perhaps pragmatic approach would be to embark on the massive strengthening of PMTCT structures by investing more broadly in maternal and child

health, intensifying education on HIV/AIDS prevention, safe delivery and safe infant feeding practices as ways of forestalling HIV/AIDS-related stigma. PMTCT services should also be extended to women who deliver at home or those who utilize the services of traditional birth attendants, encouraging them to exploit antenatal services in subsequent pregnancies. This should certainly be done in a way that preserves their autonomy and privacy. Health care personnel who are directly involved in providing these services should be retrained to meet the idiosyncratic landscape of the new role in dealing with the dynamic nature of HIV.

Undoubtedly, the results of this study have established that routine testing is more effective compared with client-initiated VCT: increased the proportion of women testing for HIV, identified more women who are living with HIV and enrolled in PMTCT services, and most importantly decreased the risk of vertical transmission. However, notwithstanding these proven benefits of routine HIV testing, in several settings, the policies to introduce this strategy have raised several ethical concerns, particularly in settings engrossed with human rights abuses, gender inequality, illiteracy, poverty, weak health care infrastructure and inadequate supply and poor access to antiretroviral treatment (Anderson, 2006; Rennie and Behets, 2006). In a study in South Africa, Abdool and colleagues (1998) demonstrated the degree to which informed consent in a medical setting was not actually voluntary, rather tacit coercion. The study reported that in the survey of the study participants, 88% expressed that they felt compelled to accept HIV testing while another substantial proportion of the women felt obligated not to quit, as doing so may result in negative consequences (Abdool Karim et al., 1998). Whereas the need for women to have an HIV test is undeniably crucial, any mode of doing so must conform within the confines of human rights and justice-the one that respects the right of a woman to accept or refuse to be tested. All stakeholders should

understand that this is an inalienable right of every human being that should never be violated.

Another concern is that the offer of an HIV test based on routine testing approach necessitates impromptu decision-making to accept testing. There is hardly any opportunity for the woman to deliberate or reflect on the consequences of a possible HIV positive test result nor does she strategize on how to overcome the challenges that follow it. In many circumstances, managing the ensuing outcome presents overwhelming difficulties, starting from the disclosure of a positive HIV test result to her male partner to denial. Of which, the consequences are often fear of abandonment, loss of economic support from the male partner, accusations of infidelity, violence, stigmatization and discrimination, isolation in addition to the attitude of angry family members for being infected with HIV. All these coupled with the psychological trauma of positive serostatus drive the woman into an unresolvable dilemma, which may eventually jeopardize the overall goal of the screening. This situation combined with guilt, shame, depression and internalized stigma, which is often associated with HIV infection compromises compliance with treatment. Empirical findings showed that lack of partner disclosure of HIV infection is a barrier to access to PMTCT services including treatment (Medley et al., 2004). Studies also show that stigma and discrimination are key reasons why infected women fail to access treatment (Sayles et al., 2009; WHO, 2011). The result is that the woman may not adhere to the care and treatment plan, resulting in drug failure and possible complications to the woman and infection to the unborn child.

Likewise, intimate partner violence is an important concern often associated with women whose partners have not consented to an HIV test. Studies in India and the United States reported that between 30-40% of women who underwent an HIV test experienced some forms of violence from their partners (Satyanarayana et al., 2009; Nasrullah et al., 2013). The

need for a male partners and indeed wider family involvement cannot be overemphasized. There is a general view that PMTCT services are excessively female-focused and this has negatively affected the effectiveness and overall success of the program. As documented in studies in Burkina Faso and Cote d'Ivoire, male partner involvement in maternity services that included couple counselling contributed to significant improvement in service delivery (Sarker et al., 2007; Desgrées du Loû et al., 2007). Additionally, studies from both developed and developing country settings found that partner testing for HIV has important public health benefits. Wamuti and colleagues (2015) and Cherutich and associates (2017) showed that male partner or couple testing for HIV resulted in social support of the woman, improved access to medical care and effective consensual risk reduction plans.

Therefore, to achieve the optimal use of routine opt-out testing, it is important that the midwife counsellors highlight the objectives, risks, and benefits of testing and ensure that women understand their right of refusal. The women with a positive tests result or those who refuse test should be treated with dignity and should not be denied any prenatal care nor discriminated against in other ways. Those who refused testing should, in addition to access to other medical care be offered one to one counselling to allay their fears for refusing the test at the first instance.

Generally, several lessons emerged from these findings. Firstly routine testing closed the gap on 'missed opportunity' to screen women who attend antenatal care for HIV. All the participants irrespective of their socio-demographics, age, education tribe religion or marital status accepted this strategy. Routine testing helped women to learn their status early in pregnancy, including those who were asymptomatic. Individuals who are diagnosed and treated in the early stages of the infection have a higher prognosis and the risk of transmission to others is minimized with the initiation of ARV (Anderson, 2006). Importantly, although

there were low levels of male partner involvement in this study cases of intimate partner violence were equally low, which is often a major concern of HIV infected women, when they disclose their status to their partners (Medley et al., 2004). Only one such case was recorded in this study. Second, the study's experience provides assurance that a successful paradigm shift is possible in Nigeria in programs that appear so interwoven with VCT practices. Despite the well-entrenched VCT program in the life of HIV testing in Nigeria, this study recorded a staggering paradigm shift. Moreover, the exclusion of client-centred, comprehensive counselling did not seem to contribute any adverse effect, at least, not in terms of testing uptake rate. A formal qualitative study would be handy in establishing the exact opinion of pregnant women regarding routine testing, in this setting. This result supports previous studies, which reported the effectiveness of short, clear-cut information on the use of condoms for sexual risk reduction. In their finding, the researchers reported that a survey showed 98% of the participants correctly used a condom to minimize the risk of sexual infections (Kamb et al., 1998). Likewise, studies in two settings in the United States and the United Kingdom found no significant benefit with comprehensive counselling for risk reduction, and this is in line with the findings of this study (Metsch et al., 2012; Kennedy., 2014). In contrast, a study reported an improved testing uptake following comprehensive pre-test counselling (Colpin., 2006).

Furthermore, the exclusion of comprehensive counselling seemed not to have contributed any adverse effect, at least, not in terms of testing uptake. Many women still assented to testing without any form of hesitation after receiving the short group information during the discussion period with the midwife counsellor. However, a formal qualitative study would be handy in establishing the exact opinion of pregnant women regarding routine testing, in this setting. Nevertheless, previous studies reported the effectiveness of short, clear-cut

information on the use of condoms for sexual risk reduction. The researchers conducted a survey among the sexually active population, which showed that after receiving short counselling sessions, 98% of the participants reported that they correctly use a condom to minimize the risk of sexual infections (Kamb et al., 1998). Likewise, studies in two other settings in the United States and the United Kingdom found no significant benefit with comprehensive counselling for risk reduction, which seems to support the notion of this study (Metsch et al., 2012; Kennedy, 2014). In contrast, a study reported an improved testing uptake following comprehensive pre-test counselling (Colpin., 2006).

The study also found that the removal of a separate consent form for HIV testing, a requirement for the VCT opt-in approach (HIV exceptionalism) might have paved the way for enhanced testing. As demonstrated in this study the bureaucratic requirement to sign a consent form, explicitly for HIV seems to constitute a hindrance to HIV testing uptake. With the implementation of routine testing, there was no need to obtain additional consent form from the women before performing an HIV test. Although women still have the right of refusal, the consent that accrues from general medical care was enough to conduct the test. Women that had some concerns about certain issues such as confidentiality were given the opportunity to privately discuss with the midwife counsellor for clarification before their blood was drawn for the test. Treating HIV like other diseases is likely to reduce the stigma that follows an HIV test and encourage more people to go for one.

9.4.2. Strength of the study

There are many strengths to this study. Participants with close similarities were used in this study. This is in addition to a multi-ethnic diverse community of participants. All the diverse cultures, relevant age groups and different socio-demographic characteristics (married,

single, widowed and separated) typical of Nigeria structure are well represented in the population of participants in this study. Another strength is the measure taken to ensure and maintain the quality of the findings. For instance, no group received undue information about HIV testing during the recruitment of participants, nor was there any preferential community awareness campaign encouraging people to have HIV tests, throughout the study period. Other strengths include its prospective in nature, its large sample size and its conduct within a stable uninterrupted facility. There was no time-based difference between the conduct of the two interventions, VCT opt-in versus routine opt-out. All the interventions were performed relatively within the same period. Another strength of this study is that the study facility is well established in the management of HIV, having been among the earliest few centres that started PMTCT service in Nigeria. With its wealth of experience, the facility has the necessary structures for offering and maintaining an uninterrupted PMTCT service. The facility is also a referral centre for managing complicated cases of MTCT. For instance, there is a dedicated team of HIV specialists comprising paediatricians, nurses, and dieticians, which is attached to the PMTCT unit. Thus, this attribute may act as both strengths and weaknesses as the study was conducted in near to ideal situation, however, this ideal situation may not be available in other facilities, making it difficult to generalize the study findings. Furthermore, there has never been any known study in Nigeria comparing routine antenatal HIV to client-initiated VCT at the facility level; therefore, this is the first attempt to undertake this task.

9.4.3. Challenges of the study

Several challenges were identified during the study period of this provider-initiated testing program. First, the health facility is grossly understaffed, especially in terms of midwives' staffing levels. Midwives often receive training on counselling for HIV, but the rising patient

population resulting in increased workload had left most of the staff members reluctant to committing to taking extra or additional tasks of counselling. Besides, the shortage of funds has led to the inability of the management to employ and train a new set of full-time nurses. Therefore, during this trial period, midwife counsellors were often borrowed from other sister units to complement the efforts of the existing staff. Second, the prevailing economic hardship in Nigeria, as well as high-level nurse, turn over (Due to search for greener pasture abroad) demands that more resources should be provided for training. This is particularly of the essence for effective communication of the program of routine HIV testing: highlight the benefits of HIV testing, dispel the notion that routine HIV testing is mandatory as well as misconceptions about HIV.

Third, this study did not cater for women who arrived in labour and those who booked late. Although data shows that this group is more probable to refuse to test, there are several reasons for them to be encouraged to be tested. These women may have poor engagement with the health care system, may be hard to reach population or those who are reluctant to use antenatal service. This specific group of women is generally associated with adverse pregnancy outcomes, including HIV infection.

The non-participation of male partners in HIV testing remains a great concern for PMTCT services in Nigeria. In this study, none of the study participants reported to the clinic with their male partners. Non-participation of the male partner in HIV testing often leads to violence and physical abuse of the woman. Innovative strategies to encourage male partner participation is urgently required.

The fourth challenge was a lack of accurate record-keeping in the antenatal unit. Record-keeping was generally poor, as the proper record of the previous ANC attendees could not be fully ascertained. The names of some of the booked women were not entered the regular

booking register and there was inconsistency in the data collected from attendees. The old record book showed missing information on women who previously tested for HIV or mutilated results. Information on the positivity rate and referral to PMTCT services or record of follow-up information were all muddled up; either some information missing in the register or the entire register could not be located. Although the facility is trying to upgrade to the computerised system, this has not yet been very successful. The study was unable to establish a temporal trend due to a lack of this record. Additionally, for a country to receive WHO validation for the elimination of MTCT, part of the requirement is the country's ability to provide evidence for accurate record-keeping of ANC activities, which include the following:

i. Minimum of two years data indicating that above 95% of pregnant women attended ANC visit at least once,

ii. And that they had HIV screening and received results.

iii. Infected women were adequately treated.

The training, which was conducted for the midwives, was not sufficiently comprehensive because of the limited time and, as a result, some vital aspects were left out. Besides, some midwives did not pass the assessment. Perhaps, their limited knowledge might have influenced their performance during the booking period regarding the number of women booked.

9.4.4. Limitations

There are certain limitations to this study. First, the study was conducted only in one urban facility and did not involve multiple and diverse facilities, nor did it involve facilities from rural areas. The study facility is also restricted to a defined population of public servants and their families. This attribute inherently limits the generalizability of the findings in this study.

Evaluation of effectiveness of the routine HIV testing in diverse settings would have improved the usability of the findings in the general population.

Second, the astounding results recorded during the routine testing regime of this study could be attributed to apparently well-motivated and enthusiastic midwife counsellors who were involved in this study. Generally, in comparison with other health facilities, the staff of the study facility is regarded as receiving better remuneration including incentives compared to other health facilities in this region. This, on its own, is an encouragement for the staff to be more dedicated to their job roles. Staff is exceptionally vigilant in the provision of high-quality service knowing fully well that they deal with top government officials. Apart from these, the midwife counsellors received a 3-day specialized training on counselling skills from HIV prevention experts even though they have been HIV counsellors in the study site for a long period. The counsellors who are fluent in indigenous dialects provided the counselling both in English and in the various indigenous dialects. These measures may not apply in other settings in Nigeria, especially in busy facilities with under-staffing level. For example, in a similar study in Zimbabwe, community counsellors were trained as the ad-hoc staff who performed counselling and testing tasks due to understaffing challenges in a busy health facility (Chandisarewa et al., 2007). This is because the facility lacked adequate staffing strength to cover the counselling sessions.

Another limitation of this study is that this study was not a randomized controlled trial. In addition, a certain subgroup of ANC attendees was not accounted for either because they were discretely booked (Top government functionaries) or because the women arrived as an emergency and therefore did not follow the formal booking procedure. According to Sica (2006), bias occurs when the selection of the study participants does not accurately reflect the entire population due to the inability of equal and random assignment of participants into

groups. The target population should have an equal chance of being selected (Sica, 2006). As these categories of users are of a vital part of the target population, their inadvertent non-involvement in the research may have introduced some degree of bias. While it is difficult to predict the behaviour of this sub-population in the study, the generalizability of the findings is therefore difficult as this factor might be sources of limitation to the study findings.

Largely, the astounding increase in HIV testing and PMTCT service uptake recorded in this study would have been influenced by these factors and they may not apply in other settings and therefore, may limit the generalizability to the entire population.

The findings of the present study showed that the routine offer of HIV led to many women learning their HIV status in pregnancy, and for those who were diagnosed seropositive, access to antiretroviral treatment.

9.5. Summary of the Study Findings in Relation to the Research Questions.

9.5.1 The Overall Summary of The Research Findings Based on The Research Questions (Refer to chapter 5)

Put together, this study recorded remarkable acceptance rates of HIV testing under routine opt-out HIV testing regime compared with the client-initiated-testing strategy. Specific knowledge about HIV acquisition and benefits of testing was influenced by the mode of offering the test to the woman such that women who received group counselling were the most to have this knowledge as reflected in testing uptake.

During the study period, approximately 700 pregnant women registered for antenatal services, of whom 615(87.6%) eligible women accepted to participate in the study. HIV test acceptance rate remarkably increased from 48.7% under the on-request approach to 94.5% using routine HIV testing strategy. In other words, testing was influenced by the method of

offering the test. In addition, of 149 women tested under client-initiated testing, seven women (2.3%) did not return for post-test counselling, although these women tested negative to HIV antibodies. In contrast, routine testing strategy recorded nearly 100% post-test counselling for the 292 participating women. Thus, presenting specific and relevant information about HIV transmission coupled with a brief group discussion with the midwife counsellor improved women's knowledge of HIV and enabled them to make an informed decision about HIV testing. This, in addition to the all-inclusive nature of routine such that most women did not feel isolated improved test acceptance.

Women's demographic information played an important role in test acceptance. The study found an association between HIV test acceptance and demographic data. Testing increased linearly with age and peaked at ages 25-29. Women with higher education and those who are employed, also have higher test acceptance rate. Religion and tribe would have played a role but there is no significant statistical difference between uptake and type of religion.

The main goal of testing is to identify women who are living with the virus. In this study, of the 441 women who tested for HIV, 59 (13.37%) were newly identified HIV positive. Of whom 15(4.9%) were newly identified under the client-initiated testing strategy while a further 44(9.97%) women were identified using routine opt-out HIV testing approach. Routine testing identified nearly threefold the proportion of infected women compare to client-initiated testing approach.

The hallmark of identifying women living with HIV was to initiate treatment for PMTCT. Treatment for PMTCT rose from 10 (66.7%) during the on-request testing strategy to nearly 100%. Normally, if an HIV infected woman takes HAART, the likelihood of passing the virus to her baby is considerably decreased.

The midwife has a pivotal influence on women's test acceptance. The test acceptance rate among study participants associated with individual midwife ranged from 11.34% to 27%, depending, however, on educational level and years of experience of the midwife. The midwife who had earned over ten years of work experience in addition to a master's degree recorded the highest HIV test acceptance(n=120) in contrast with the one with only primary education and less than five years of work experience (n=50).

The difference in cost per case delivery of the interventions did not differ substantially because the only change is the time taken for the midwife to conduct counselling; however, based on aggregate cost routine testing was higher. Computed based on per unit cost, amounts to £129.40 versus £121.60 for client-initiated and provider-initiated strategies respectively. Regarding the cumulative cost for delivering the separate interventions per quarter of a year, this amounted to £39484.41 for self-referral and £73681.08 for routine testing. From an economic viewpoint, the incremental cost-effectiveness ratio of £3000 per case of HIV averted in children indicates that routine testing is economically dominant over client-initiated VCT.

Women receive important life-changing information during ANC booking; as such, the introduction of any new testing program must not compromise this goal. Aside from this concern, HIV testing has long been a controversial issue degrading the quality of care. Data from this report suggest that this anxiety is only speculative as largely, the introduction of routine HIV testing was overwhelmingly accepted in a population of pregnant women attending ANC indicating its potential influences on the overall PMTCT programs. Equally, in the present study, all the women who were identified HIV positive probably understood the long-term benefits of testing in relation to PMTCT as they all embarked on ART treatment. In the light of this emerging evidence and in recognition of recent demands, which prescribes

normalizing HIV testing like other medical and antenatal screening, I propose the adoption of routine ANC testing of HIV in FCT, Abuja. Similar trials should also be replicated in other parts of the country before the widespread adoption of this policy. Such an approach should involve first, a discussion with the midwife who provides clear and specific information on the benefits of HIV testing and second carrying out the test unless the woman rejects the offer. FCT, Abuja is one of the cities in Nigeria with the highest prevalence of HIV in women of reproductive age and current testing policies are not sufficiently identifying most infected women (NACA, 2017). During the present trial, only fifteen women were identified with HIV using the current testing policy, just about one-third of the alternative. Clearly, there is, therefore, critical need to develop urgent steps to increase test acceptance that could be acceptable and accessible to all women with the potential to identify all those who are living with HIV during the ANC. Data from this study shows that the test offered through provider-initiated (midwife) approach led to a 94.5% uptake rate, which is certainly more effective than the policy of making screening available to women on request. This result is also comparable to the 90% acceptance rate set by WHO (UNAIDS, 2014) and results from Europe (Townsend et al., 2006) and Africa (Chandisarewa et al., 2007). Therefore, it is evident that routine opt-out HIV testing approach in which test offer is provided routinely to women in-group with the offer to decline is an effective technique for achieving high-test uptake as well as case detection rates and should be implemented in ANC facilities in FCT, Abuja. This study also found that routine testing is cost-effective.

Chapter 10: Summary, Recommendations and Conclusion.

10.1. Introduction.

This chapter presents the concluding thoughts of this thesis involving a concise summary of the entire thesis. This is followed by recommendations, which include both the clinical and economic recommendations as well as those for policy and further research recommendations. The thesis wrapped up with a concluding remark, which ended the thesis.

10.1.1 Contextualizing the study findings to Nigeria.

Currently, Nigeria has the highest burden of prenatal HIV infection in the world, with an estimated 270,000 HIV infected children. Mother to child transmission is the predominant mode of acquisition, usually through their undiagnosed mother. Infection can, however, be reduced from 45% to nearly 1% if appropriate measures are taken during the critical periods when transmission occurs. HIV counselling and testing is the critical entry point to treatment for the prevention of mother to child of HIV. The advent of ART has transformed HIV from being a terminal disease "death sentence", to one, which can be well managed and controlled. Hence, HIV treatment for PMTCT has evolved considerably ever since the emergence of HAART, both in terms of laboratory investigations required before initiation of treatment and pill-burden associated with it.

In chapter 2, I extensively reviewed the literature on the epidemiology of HIV followed by HIV counselling and testing and factors that impact test acceptance in chapter 3. The magnitude and impact of HIV are overwhelming in LMIC, particularly Sub-Saharan Africa. Nigeria is the hardest hit of MTCT in the world. A lack of or low delivery of HIV testing is one of the major public health concerns impeding effective PMTCT programs. Besides, in this chapter, both the global and national epidemiology of MTCT of HIV is succinctly summarized. There is evidence

to suggest that Nigeria is not progressing well in terms of PMTCT program: suboptimal test acceptance among pregnant women continues to retrograde success in this area resulting in a disproportionately high burden of HIV acquisition in children during pregnancy. An offer of HIV counselling and testing in Nigeria is generally provided at the direct request of an individual woman (client-initiated VCT) or to those perceived to be at higher risk, and most women living with HIV remained undiagnosed.

One known reason for low HIV testing uptake among women of childbearing age in sub-Saharan Africa, including Nigeria, is the way the test is offered to the women. The current testing program is grossly associated with stigma and discrimination and this is pivotal to ongoing concern for women who learn their HIV status through client-initiated counselling and testing. Women may decline testing or go underground altogether because of stigma and discrimination associated with this mode of HIV testing and this has a ripple effect on the society. In particular, this condition contributes to the overwhelming HIV epidemic in children as well as concomitant ill health in their mothers. Data show that many developed countries and even some developing countries have used provider-initiated routine HIV testing to overcome this challenge. However, scaling-up HIV testing rate through the adoption of a new testing strategy such as routine opt-out testing approach would require further research for a setting-specific clinical and economic understanding of the strategy.

Two published systematic literature reviews in clinical and economic studies of ANC routine HIV testing were performed, as both were inevitably relevant to this study. Hence, in chapters 4 and 5 comprehensive logical appraisals of existing literature in these fields were undertaken and represented as published articles. These reviews provided pertinent resources to support

evidence-based practice while perving the way for the foundation of this study. The review also brought the well-deserved credence to this thesis work.

The methodological approaches for the clinical and economic studies were also presented in chapters 6 and 7 respectively. These chapters provided the theoretical framework underpinning this study. An explanation of the intervention types, the study population as well as the ethical dimensions of the research were all discussed in chapter 6. In addition, the statistical tools employed in the analysis of the data of this study including measures undertaken to improve and ensure quality data collection were all discussed. Chapter 7 focused on the economic principles and the theoretical framework of the study.

Chapter 8 focused attention on the presentation of the study findings. Data from this study were analysed using appropriate statistical tools. In chapter 9, is the discussion chapter, which highlighted the implication of the study findings.

10.2 Recommendations

10.2.1 Clinical Recommendations

Routine HIV testing should be introduced in State House Medical Centre where this study was conducted and in other ANC facilities in FCT Abuja including settings in the suburbs of FCT where women seek ANC services.

Pregnant women should receive offers for routine HIV testing at the early stages of pregnancy or as early as possible for those who present late for antenatal care. Women who refuse testing should be given personalized counselling to dispel their concerns and should never be discriminated against in other clinical care based on their refusal of testing.

Women who acquire HIV in pregnancy or those who seroconvert are at greater risk of transmitting the virus to their unborn children. Because of this high risk of transmission, women who previously tested negative early in pregnancy should receive another testing during the trimester stages. Alternatively, male partner testing is strongly recommended to ameliorate this circumstance.

Unbooked women who arrive in labour should receive bedside rapid HIV testing after counselling, and with a reactive test result, the woman and the infant should be given ARV according to the local guidelines. The test results of all the booked women should be in the labour ward with a clear protocol for checking the result of a woman who arrives in labour. In all circumstances, the results must be kept confidential.

Exposed infants born to HIV positive mothers are required to have their blood samples taken for HIV test (not cord blood as this is contaminated with maternal blood) tested. The sample should be tested alongside the mother's blood. The infant should receive within four hours of birth ARV prophylaxis, and Zidovudine should be given orally 4mg/kg twice daily for four weeks. This in addition to the mother's antiretroviral treatment significantly reduces the risk of transmission to the baby.

Provider-initiated routine testing costs less and is also cost-effective, however, additional specific information regarding the benefits of testing should be highlighted and women must be informed that they have the right of refusal. Data from this study suggest that these measures will improve women's knowledge about HIV testing.

Some women did not quite understand the magnitude of the psychosocial impact of having an HIV-positive test result since the midwives trivialized the HIV test as 'mere routine', challenges were therefore not foreseen. Although the test offer is routine, midwives should

highlight the likelihood that a woman may receive a positive test result, particularly in a place like Nigeria where infection with HIV has many connotations. Such an explanation will also go a long way in a woman's informed decision process.

An important tool for improving the test acceptance rate is to develop a standard and uniform protocol containing information to remember during the discussion session. This method is particularly ideal for increasing the ability of the counsellor to convey the information properly and in a structured manner, enabling the women to understand the key points accurately. This protocol should be printed in bold and simple grammar and should be accessible in each consulting room.

 Patients' preferences are a hallmark of patient-centred care in any given clinical setting, and an understanding of how the wording of 'offer of testing' can influence perceived preferences (self-referral versus provider-initiated) is important in preserving patients' right and autonomy. Clearly, the client-initiated testing approach is unique, with a test acceptance pattern that may approximately reflect accurate patients' preferences. However, it is important to strike a balance between a woman's autonomy and steering the woman towards an intervention that optimizes health outcomes. This is especially essential when patients may erroneously perceive themselves as low risk and therefore reluctant to seek testing on their own. Encouraging all women to undergo an HIV test through provider-initiated testing approach would definitely yield health benefits to both the woman and their babies. In this study, I found that routine opt-out testing increased testing uptake irrespective of woman's demographic characteristics. This approach should, therefore, be the mainstay of HIV testing during pregnancy. However, the client-initiated approach should still be available for the few women who may want to access this option.

All ANC facilities should maintain a uniform and accurate record of ANC attendees, showing the number of women who receive offers for HIV testing, and the proportion declining or accepting the offer and being tested. A sound system for monitoring test acceptance should be established. This may require an introduction of a simple, unified and robust system of recording the statistics of women booking for antenatal care, being offered an HIV test and those accepting or declining to test, in every health facility. I strongly propose that test acceptance should be the sole prerogative of the woman and the nurse should receive training on how to respect the decision of the woman without reproach. For the women who decline the offer, explanations for refusing should be ascertained and another offer made at 28weeks gestation. All information obtained during this dialogue should be properly recorded into the relevant login book. As noted in this study, some women were discretely booked for ANC, and there was no record of their data lodged in the ANC login book. This practice negates an ideal clinical health care service. This task is required for accurate data enumeration, which is required for statistical computation for policy planning.

Couple or partner HIV testing is an important strategy to encourage uptake of testing and improve timely linkage into PMTCT services. It can also improve mutual disclosure and improve adherence to treatment if one or both partners are receiving treatment. Couples' testing aids in early identification and enrolment into care among men who normally test late and subsequently initiate treatment at the late stages of the infection. Broadly, couples' HIV testing allows partners to learn their HIV status together and at the same time, respond appropriately to avoid transmission. Couple testing in this study was completely elusive as none of the women was tested with their husband or partner. Women should be encouraged to bring their partners to the ANC so that they can learn their HIV status together. This situation can be enhanced by creating a male-friendly environment such as couple and male-

focused sessions. Studies show that the PMTCT program succeeds better when the male partner is involved in the testing exercise as this facilitates disclosure of test result, initiation and adherence to ARV treatment (Becker et al., 2010; Peltzer et al., 2011).

All the women who received testing reported alone for post-test counselling without being accompanied by someone they could confide in such as a friend, relative or their spouse. HIV test results come with many challenges such as anxiety; fear of rejection and of course, depending on the outcome self-harm or even suicidal tendencies. These women should be advised to come for post-test counselling with a confidant or anyone who could support them. For the women who may wish to receive their result with an unknown person, a peer support staff could stand-in. studies suggest that many people that receive HIV-positive test results contemplate self-harm and suicidal ideation (Carrico et al., 2007). In circumstances where the woman refuses support from someone else, her individual needs should be evaluated, and support given to her. In addition, counsellors or any identified confidant should be involved during the disclosure process to present a culturally sensitive atmosphere to support the woman.

10.2.2 Training of Midwife.

Midwives should receive regular appropriate and updated training and certifications to support women who are undergoing an HIV test. This should involve clear communication of test results, giving personalized support, maintaining the confidentiality and giving accurate information regarding the impact of an HIV positive test result. Furthermore, midwives' training should involve ways to increase their positive attitudes towards HIV testing and responses in the event of a positive test result. This might be an essential element, which outweighs their knowledge about HIV. For instance, it is not clear why some women refused

at the onset, only to accept to test during follow-up contact. It could probably be that these women experienced some level of stigma or perhaps did not understand the benefits of treatment. Stigma obviously erodes one's self-worth, especially as HIV acquisition in the African community is often perceived as a self-inflicted condition undeserving of any form of sympathy or empathic understanding. The way and manner in which the midwife conveys knowledge about HIV are critical for the woman's informed decision-making process on whether to test or not to test. Therefore, communication skills rather than information giving should be emphasised during the training exercise. A strategy to improve this skill may involve role-playing among the midwives plus feedback discussion when the midwife has had real-life experience performing counselling. It may also be helpful for the midwives to form an ongoing support network to share and address common problems that arise in practice such as having to deal with a hostile client. Additionally, the junior midwives should have easy access to experienced counsellors so that they could seek assistance and support when they encounter some difficulties.

10.2.3. Programmatic Recommendations.

There is a need to incorporate family planning and HIV testing and counselling into ANC. Because women who seek these services often have common needs and concerns, integrating them into ANC service will enable the health care provider a greater opportunity to serve their clients more comprehensively and efficiently. For instance, merging HIV testing and counselling with family planning means that the population who typically use family planning such as couples (intimate partners), sexually active young women, and those who are at higher risk of contracting HIV, such as sex workers can easily access HIV testing. Additionally, incorporating these services into ANC/PMTCT enables women who are already

infected with HIV and who desire to become pregnant to initiate ARV treatment to reduce the risk of MTCT. For those women living with the virus but do not wish to become pregnant, an opportunity to consistently use a contraceptive to prevent unintended pregnancy.

While it is important to introduce routine HIV testing in ANC to encourage screening and treatment of infected women and reduce the risk of MTCT, the preference not to accept to test or perhaps the ambivalence that follows test acceptance is a major setback that needs tackling. Women seeking an HIV test who feel this way, particularly those who view themselves at risk of infection do so because of perceived stigma and discrimination toward HIV infected individuals that normally abound in the community. Community mobilization and continuous health education should be introduced in the various community to raise awareness and mitigate the impact of stigma. Social mobilization is a way of engaging the community and dispelling the myths about HIV. By involving the community, HIV counselling and testing are normalized with the resultant reduction in stigma and discrimination (Lippman et al., 2017).

Cross-training of all health professionals, particularly the midwife counsellors who are directly involved, on the dynamics of the virus. This will help in the provision of evidence-based current information to the clients. For instance, management of HIV in pregnancy has transited from treatment to reduce the risk of MTCT (option B) to treatment to improving the woman's health and reducing the risk of MTCT (option B+). The counselling and communication skills of the midwives should be strengthened through refresher courses.

Communication between women and their male partners whereby both parties can openly discuss issues about their sexuality. For instance, organising training programs that tend to strategically, empower women to take full control of their sexual and emotional relationship through challenging gender norms.

10.2.4 Recommendations for Further Research

Further studies should focus on evaluating the impact of routine HIV testing in other parts of Nigeria. The evaluation should be conducted before a wide-spread adoption of the program. Midwife counsellors play an important role in the whole process of HCT services, including test acceptance. Their attitudes during counselling and testing seem to be instrumental in testing uptake and therefore qualitative research should focus on how to modify midwife's attitude to improve test acceptance.

Intimate partner violence has been deeply implicated as a barrier to women seeking HIV testing. Research suggests that women refrain from testing due to fear of an intimate partner violence. Women are also meted with violence when they disclose their HIV status to an intimate partner. Disclosure of HIV status is an important measure towards prevention effort and for ensuring that women who are infected with the virus can receive psychological support from their loved ones, and for the pregnant women access and adherence to ART treatment for PMTCT. Since routine testing provided HIV testing as a battery of ANC screening, further studies should focus on understanding the role of intimate partner in a discordant HIV result regarding adherence to treatment.

Since this intervention is relatively a new program, at least in this domain, research should focus on not only uptake of the intervention but primarily on retention of women who tested positive and accessing HIV treatment. Also recommended for further study is a meta-analysis of test acceptance to understand the effect size of the program.

10.3. Study Conclusion.

Overall, antenatal care is an important event in pregnancy during which sensitive health information is gathered and exchanged between the woman and the health care provider, to improve the outcomes of the pregnancy. Part of this care is screening for diseases and taking

steps to minimize the risks involved. The current WHO guidelines endorse routine screening in antenatal settings, a complete policy departure from the client-initiated testing approach. Data from this study suggests that the adoption of routine HIV testing compared with the client-led VCT, gave many women the opportunity to learn their HIV status and for the infected women to take concrete measures to reduce the risk of MTCT. Unlike the previous VCT, method of testing that resulted in low testing rates (Nigeria Federal Ministry of Health (FMoH), 2013), routine testing approach resulted in the reduction of the high rate of undiagnosed cases of HIV in pregnant women who visit an antenatal clinic. This method of HV counselling is also more time-efficient. Indeed, this seems most appropriate in high prevalence dense population such as Nigeria. HIV testing is the critical gateway to PMTCT services and should be integrated into ANC so that the service providers can better serve the service users. Studies have shown that short messages about the benefits of HIV testing encouraged more women to accept testing and adhere to treatment plans than prolonged comprehensive counselling (Simpson et al., 1998b; Dewing et al., 2012). Besides, in the past, undiagnosed and late diagnosis of infections, which are the primary drawbacks of VCT opt-in, have led to disproportionate MTCT in the Nigerian society.

In the light of this evidence and in furtherance of recent demands that HIV test should be normalized like any other medical test, I propose that the offer of routine opt-out approach to HIV testing should be adopted in the study site and across ANC health facilities in FCT, Abuja. Such an approach would require giving concise but, clear and specific information, discussion and then conduction of the test unless the woman declines to be tested. Moreover, the test must be conducted in a manner that minimizes any form of coercion and should highlight volunteerism. Women who are diagnosed with the virus must be adequately linked to PMTCT services.

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REVIEW

Clinical outcomes of routine opt-out antenatal human immunodeficiency virus screening: a systematic review

Everistus Ibekwe, Carol Haigh, Fiona Duncan and Francis Fatoye

Aims and objectives. To evaluate the clinical outcome of routine screening of human immunodeficiency virus in antenatal clinic settings.

Background. Despite the growing advances in human immunodeficiency virus management, nearly 30% of the estimated 1·5 million seropositive pregnant women are undiagnosed. Routine opt-out testing is a strategy endorsed by the World Health Organization in 2007 to increase testing rates in clinical settings.

Design. A systematic review of relevant published literature.

Methods. A comprehensive electronic search for relevant studies in Science Direct, MEDLINE, SCOPUS, CINAHL and PubMed was conducted with search terms (Box 2). Hand searches were also conducted for additional resources. There were no geographical restrictions. Searches were restricted to English language and studies conducted between 1998–2015; totaling 1097 were retrieved and carefully appraised for review. Eighteen studies were eligible for review: eight from Africa, five from the United States, three from Europe, one from Australia and one from Asia.

Results. Fourteen studies reported increases in human immunodeficiency virus testing rate. Following the introduction of routine testing, human immunodeficiency virus testing rates increased from values ranging from 68–99·9% with median value of 88%. The comparison studies reported testing uptake of 22–93·5% with median value of 59%. Maternal human immunodeficiency virus case detection rates nearly doubled following adoption of routine testing at values of 99 and 45% during opt-in. Linkage to treatment and care for prevention of vertical transmission was reported on six studies, and results ranged between 12·9–77·2%.

Conclusion. The findings show that irrespective of human immunodeficiency virus epidemiological scenarios, routine testing gave more women opportunity to learn their human immunodeficiency virus status and take measures for prevention of mother-to-child transmission of human immunodeficiency virus. Future studies should focus on identifying strategies to improving linkages to treatment and care for prevention of vertical transmission.

What does this paper contribute to the wider global clinical community?

- Understanding the contributions of routine opt-out HIV testing in ANC would encourage health care practitioners and policymakers adopt the novel testing model for more women to learn their HIV status and take measure for PMTCT.

Authors: *Everistus Ibekwe*, AIMLT, BSc, MPH, PhD Candidate, Nursing Department, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester; *Carol Haigh*, PhD, Professor of Nursing, Nursing Department, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester; *Fiona Duncan*, PhD, RN, Members of supervisory team, Department of Research Institute for Health & Social Change, Faculty of Health, Rehabilitation and Psychology, Manchester Metropolitan University, Manchester; *Francis Fatoye*, PhD, MSc, BSc, Members of supervisory team, Department of Health Professions, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester, UK

Correspondence: Everistus Ibekwe, PhD Candidate, Nursing Department, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Birley Building, Birley Fields Campus, 53 Bonsall Street, Manchester M15 6GX, UK. Telephone: +44 1612472606.
E-mail: everistus.ibekwe2@stu.mmu.ac.uk

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Appendix A

REVIEW

Economic impact of routine opt-out antenatal human immune deficiency virus screening: A systematic review

Everistus Ibekwe PhD Candidate[1] | Carol Haigh PhD, Professor of Nursing[1] | Fiona Duncan PhD, RN, Proof reading, Mentoring[2] | Francis Fatoye BSc, MSc, PhD, Proof reading, Mentoring[3]

[1]Nursing Department, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester, UK

[2]Department of Research Institute for Health & Social Change, Faculty of Health, Rehabilitation and Psychology, Manchester Metropolitan University, Manchester, UK

[3]Department of Health Professions, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester, UK

Correspondence
Everistus Ibekwe, Nursing Department, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, Manchester, UK
Email: everistus.ibekwe2@stu.mmu.ac.uk

Aims and objectives: To evaluate the economic impact of routine testing of human immune deficiency virus in antenatal settings.

Background: Many children are being infected with human immune deficiency virus through mother-to-child transmission of the virus. Most of these infections are preventable if the mothers' human immune deficiency virus status is identified in a timely manner and appropriate interventions put in place. Routine human immune deficiency virus testing is widely acclaimed as a strategy for universal access to human immune deficiency virus testing and is being adopted by developed and developing poor income countries without recourse to the economic impact.

Design: A systematic review of published articles.

Methods: Extensive electronic searches for relevant journal articles published from 1998–2015 when countries began to implement routine antenatal HIV testing on their own were conducted in the following databases: Science Direct, MEDLINE, SCOPUS, JSTOR, CINAHL and PubMed with search terms as listed in Box 2. Manual searches were also performed to complement the electronic identification of high-quality materials. There were no geographical restrictions, but language was limited to English.

Results: Fifty-five articles were retrieved; however, ten were eligible and included in the review. The findings showed that many programmes involving routine human immune deficiency virus testing for pregnant women compared to the alternatives were cost-effective and cost saving. Data from the reviewed studies showed cost savings between $5,761.20–$3.69 million per case of previously undiagnosed maternal human immune deficiency virus-positive infection prevented. Overall, cost-effectiveness was strongly associated with the prevalence rate of human immune deficiency virus in the various settings.

Conclusions: Routine human immune deficiency virus testing is both cost-effective and cost saving compared to the alternatives. However, there are wide variations in the methodological approaches to the studies. Adopting standard reporting format would facilitate comparison between studies and generalisability of economic evaluations.

Relevance to clinical practice: (i) Healthcare decision-makers should understand that routine antenatal screening for human immune deficiency virus is both cost-

Appendix B

Appendix C

Appendix D

CONSENT FORM

Study Number: 13162768.

Centre Number (SHMC023): Patient Identification Number for this trial:

Title of Project Opt-Out Model of Antenatal HIV Screening- A study in Federal

Capital Territory Abuja, Nigeria.

Name of Researcher:

Please initial box

1. I confirm that I have read and understand the information sheet dated.................... for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the sponsor or regulatory or from regulatory where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I agree to take part in the above study.

_____   _____   _____
Name of Patient   Date   Signature

_____   _____   _____
Name of Person   Date   Signature
taking consent

Appendix E

Participants' information Sheet.

Date: 9th March 2015

Principal investigator: Mr. Everistus Ibekwe.   Participant's unique number:

1. **Study Title:**

   Opt-Out Model of Antenatal HIV Screening- A study in Federal Capital Territory Abuja, Nigeria

2. **Invitation paragraph**

   I am inviting you to take part in a research study. In order for you to volunteer to participate, it is important that you understand why the research is being conducted and what it will involve. Please, carefully read the information provided here and discuss it with whomever you are comfortable. Ask for more clarification about any issue you are not comfortable with or you want more information. Decide on your own if you would want to participate. The exercise is voluntary and you are free to decline at any stage of the research. Thank you for taking time to go through this information sheet.

3. **What is the purpose of this study?**

   The aim of this study is to evaluate the effectiveness of opt-out model of HIV screening and to assess how much this would cost.

   The study will look at:

   - Antenatal HIV Testing rate
   - Case finding, that is number of people tested and how many are HIV positive
   - HIV status of babies born to HIV positive mother
   - Rate of acceptance of HIV prophylaxis that is the number of HIV positive mothers who agreed to take drug to prevent HIV infection to their babies.
   - The cost of resources used in testing and managing the disease.

   There is urgent need to develop a testing approach that will encourage more women that are pregnant to test for HIV given the rising number of children in Nigeria who born with HIV or were infected from their mother during breastfeeding.

4. **Who can take part?**
   - You must be pregnant

Appendix F

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/ COUNSELLING AND TESTING REGISTER

LGA _____

_____ Within facility (e.g. CT, TB, Blood bank, FP, Ward or others): _____

If mobile service give target group)

If mobile service give location of service delivery)

HIV TEST RESULT NEGATIVE (Mark "X" in the box)				HIV TEST RESULT POSITIVE (Mark "X" in the box)				POST TEST COUNSELLED AND RECEIVED RESULT (Mark "X" in the box)				Mark "X" in the boxes							
Male		Female		Male		Female		Male		Female		STI		Confirmed TB Patient		Clinical TB Screening			
Age Group (years)		Age Group (years)		Age Group (years)		Age Group (years)		Age Group (years)		Age Group (years)						Score 0		Score 1+	
15-19 / 20-24 / 25-49 / 50+		<2 / 2-14 / 15-19 / 20-24 / 25-49 / 60+		<2 / 2-14 / 15-19 / 20-24 / 25-49 / 50+		<2 / 2-14 / 15-19 / 20-24 / 25-49 / 50+		<2 / 2-14 / 15-19 / 20-24 / 25-49 / 50+		<2 / 2-14 / 15-19 / 20-24 / 25-49 / 50+		HIV neg / HIV pos		HIV Neg / HIV pos		HIV Neg / HIV pos		HIV Neg / HIV pos	

Appendix G

Handout for midwife training for HIV counselling and testing

Introduction

- The doctor suggests the HIV test and a counsellor provides one-to-one counselling, or group pre-test information and post-test counselling.

- The doctor suggests the HIV test, provides brief information and also gives the result.

- The doctor suggests the HIV test and provides brief information, but a counsellor gives the results.

HIV testing and counselling: This guidance document is designed for use in PWID settings, in situations with a concentrated HIV epidemic, appropriate for the initiation of PITC. In this document, HIV testing and counselling is recommended in these settings for "diagnostic" purposes (that is, for people with HIV-related symptoms) and to all persons on a regular basis who may, because of their risk behaviours, have HIV but who are not symptomatic. The order of the terms "testing" and "counselling" should not be seen to provide any guidance as to the relative importance of the pre- or post-test components of counselling. HIV testing and counselling should neither be mandatory nor compulsory.

Pre-test information provision is the process by which individuals referred for HIV testing are *provided with sufficient information to ensure informed consent*, perhaps without a full education and counselling session. The minimum amount of information that individuals require in order to be able to provide *informed consent* includes:

- the clinical benefit of undergoing the test, including access to ART and to HIV prevention, care and support services;

- the clear right to refuse the test;

- the follow-up services that will be offered including counselling and referrals; and

- the importance of anticipating the need to inform any persons at ongoing risk who would otherwise not suspect they were being exposed to HIV infection in the event of a positive test result (sexual and drug-using partners).

Post-test counselling is an integral component of the HIV testing process. All individuals undergoing HIV testing must be counselled when their test results are given, with care taken to discuss results and follow-up care in a confidential manner.

Counselling for individuals with HIV-negative test results should include an explanation of the test result, including information about the window period for the appearance of HIV antibodies, basic advice on methods to prevent future HIV transmission and an appropriate time for repeat HIV testing.

The focus of post-test counselling for people with HIV-positive test results is to provide psychosocial support to cope with the emotional impact of the test result; facilitate access to treatment, care and prevention services; prevent HIV transmission; and disclose the result appropriately to sexual and injecting partners.

Confidentiality is the process of ensuring that information provided by the client (including the test result) is accessible only to those authorized to access it and is one of the cornerstones of HIV testing. Confidentiality also refers to an ethical principle associated with health care in which

Appendix H

MANCHESTER METROPOLITAN UNIVERSITY
FACULTY OF HEALTH, PSYCHOLOGY AND SOCIAL CARE

M E M O R A N D U M

FACULTY ACADEMIC ETHICS COMMITTEE

To: Everistus Ibekwe

From: Prof Jois Stansfield

Date: 03/12/2015

Subject: Ethics Application 1296

Title: Opt-Out Model of Antenatal HIV Screening- A study in FCT, Abuja Nigeria.

Thank you for your application for ethical approval.

The Faculty Academic Ethics Committee review process has recommended approval of your ethics application. This approval is granted for 42 months for full-time students or staff and 60 months for part-time students. Extensions to the approval period can be requested.

If your research changes you might need to seek ethical approval for the amendments. Please request an amendment form.

We wish you every success with your project.

Prof Jois Stansfield
Deputy Chair
Faculty Academic Ethics Committee

Appendix I

Reference:

22 October, 2015

SHMC/REC/0008/2015

Dear Everistus Ibekwe,
Department of Laboratory Medicine
State House Medical Centre, Abuja, Nigeria.

SHMC Ethics Reference No: Please quote this ref on all correspondence	SHMC/REC/0008/20015
Project Title:	Opt-out Model of HIV Screening- A Study in Federal Capital Territory Abuja, Nigeria
Researchers Name(s):	Everistus Ibekwe

Thank you for submitting your application and request for ethical clearance for the above-named study which was considered at the SHMC Research and Ethics Committee meeting on 24th September, 2015. The following documents were reviewed:

1. Request for ethical clearance
2. Research Plan
3. Informed Consent Form
4. Participant Information Sheet (PIS)

The State House Medical Centre Research and Ethics Committee (SHMC REC) hereby approves this study from an ethical point of view.

Approval is hereby given till 21st October, 2017. However, if the research has not commenced before the expiration date, a request for an extension must be re-submitted to SHMC REC.

You must also inform the SHMC REC when the research has been completed. If you are unable to complete your research within the stipulated validation period, you will be required to write to SHMC REC.

Any serious adverse events or significant change which occurs in connection with this study and/or which may alter its ethical consideration must be reported immediately to the SHMC REC, for an appropriate Ethical Amendment.

Approval is given on the understanding that the **'NATIONAL CODE OF HEALTH RESEARCH ETHICS'** are adhered to.

Yours sincerely,

Dr. Abraham M. Apilogu
B.Pharm; Pharm.D; MPA; MPhil(UK);AfHEA(UK); FPCPharm; PhD(UK); FRSPH
Secretary, SHMC Research and Ethics Committee

Appendix J