AFRICA UNIVERSITY

(A United Methodist-Related Institution)

DISPARITIES IN BIRTH OUTCOMES BETWEEN HIV-POSITIVE WOMEN UNDERGOING ANTIRETROVIRAL THERAPY AND HIV-NEGATIVE WOMEN IN MASVINGO PROVINCE, 2023-2024

BY

VITALIS GUVAVA

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF PUBLIC HEALTH IN THE COLLEGE OF HEALTH, AGRICULTURE AND NATURAL SCIENCES

2025

ABSTRACT

Maternal antiretroviral (ART) use has not been conclusively shown to lead to comparable birth outcomes with HIV negative women. Different studies have shown conflicting results with some studies in sub-Saharan Africa showing that adverse birth outcomes continue to occur more in HIV positive women despite ART use. The main objective of this study was to determine if there are disparities in the occurrence of low-birth-weight infants and stillbirths by HIV status in Masvingo Province and considered deliveries between January 2023 and December 2024. Delivery data for 603 women were collected from delivery registers from 18 randomly selected sites from Masvingo, Mwenezi and Chiredzi districts. Of these 304 were of HIV positive women virally suppressed on tenofovir-lamivudine-dolutegravir and 299 were of HIV negative women. The variables of interest were HIV status, place of residence, maternal age at delivery, gestational age at booking and the outcomes of interest were gestational age at delivery, fetal status at delivery and birth weight. A total of 9% of the deliveries had a low-birth-weight infant. HIV status was not associated with low-birth-weight deliveries (AOR 0.9, 95% CI 0.5-1.6, p=0.715). The stillbirth rate was 16 per 1000 deliveries and this did not differ by HIV status (AOR 0.2, 95% CI 0.1-1.12, p=0.079). Approximately 9% of the deliveries were premature deliveries. HIV status was not associated with preterm deliveries (AOR 0.8, 95% CI 0.4-1.4, p=0.444). Among HIV positive women low birth weight deliveries were associated with preterm delivery (AOR 8, 95% CI 2.5-25.7, p=0.001) and multiparity (AOR 0.2, 95% CI 0.1-0.7, p=0.013) while among HIV negative women they were associated with low level of education (AOR 4.4, 95% CI 1.1-17.1, p=0.032), the presence of a maternal comorbidity (AOR 4.8, 95% CI 1.1-20.9, p=0.035), multiparity (AOR 0.2, 95% CI 0.1-0.7, p=0.008) and preterm delivery (AOR 3.4, 95% CI 1.2-9.4, p=0.021). None of the factors analysed for stillbirth deliveries were statistically significant. ART timing for HIV positive women was not associated with occurrence of adverse outcome. Preterm deliveries were associated with the presence of a maternal comorbidity among HIV negative women (AOR 3.7, 95% CI 1-13.4, p=0.047). Higher odds of preterm delivery in HIV positive women were seen in multiparous women (AOR 4.9, 95% CI 0.9-27, p=0.067) and starting ART after conceiving (AOR 5.2, 95% CI 0.9-29.7, p=0.063) but this did not reach statistical significance. The use of dolutegravir based first line ART with viral suppression may lead to birth outcomes that are comparable with those in HIV negative women and ART timing does not seem to affect this finding. Maternal comorbidities need to be well managed in all women to reduce the occurrence of adverse birth outcomes. The study recommends maintaining HIV positive women of childbearing age on the current first line regimen in the event that guidelines are changed until and unless evidence exists that other regimes have a beneficial effect on birth outcomes.

Keywords: Adverse birth outcome; Viral suppression; HIV status

DECLARATION

I declare that this dissertation is my original work except where sources have been cited and acknowledged. The work has never been submitted, nor will it ever be submitted to another university for the award of a degree.

Vitalis Guvava 21/03/2025

Student's Full Name **Student's Signature** **Date**

Dr Abigail Kapfunde_____ _____ 09/04/2025

Main Supervisor's Full Name Main Supervisor's Signature Date

COPYRIGHT

ACKNOWLEDGEMENTS

I am eternally grateful to my academic supervisor Dr Kapfunde and my field supervisor Dr. Masinire for their unending support and constructive criticism at every turn. I would also like to acknowledge Professor Mugomeri who was an ever-present source of guidance through it all. I am also thankful to my employer, J.F Kapnek Zimbabwe, for allowing me to use organizational resources to be able to do this dissertation.

DEDICATION

To my wife Terry, and our kids Mukudzweishe and Munashe for enduring the periods when daddy was present and absent at the same time. To my mothers for their continued support and encouragement. And to my late fathers who never saw this come to fruition. To the TASQC team, we have another baby.

List of Acronyms and Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Care
APGAR	Appearance, Pulse, Grimace, Activity, Respiration
ART	Antiretroviral therapy
AUREC	Africa University Research and Ethics Committee
DHIS	District Health Information System
HIV	Human Immunodeficiency Virus
MOHCC	Ministry of Health and Child Care
PMTCT	Prevention of mother to child transmission of HIV
TASQC	Target, Accelerate, Sustain, Quality Care
TLD	Tenofovir-Lamivudine-Dolutegravir
UN	United Nations
UNICEF	United Nations Children's Emergency Fund
UNAIDS	Joint United Nations Program on HIV and AIDS
WHO	World Health Organization
ZDHS	Zimbabwe Demographic and Health Survey

Definitions of key terms

Adverse birth outcome: A multifactorial outcome that mainly includes preterm birth, low birth weight, stillbirth, macrosomia, congenital anomaly, and infant/neonatal death.

Preterm birth: a delivery that occurs before 37 completed weeks of a pregnancy.

Low birth weight: weight below 2 500 grams at birth.

Suppressed viral load: HIV viral load below a 1000 copies/ml of the patient's blood

TABLE OF CONTENTS

List of tables

List of figures

List of appendices

CHAPTER 1 INTRODUCTION

1.1 Introduction

Untreated maternal HIV infection is associated with adverse birth outcomes including preterm births, low birth weight, stillbirths, and small for gestational age infants (Murray et al, 2023 and Wedi et al, 2016). The mechanisms by which HIV infection leads to poorer birth outcomes include acute and chronic placental inflammation because of direct placental HIV infection or other genital infections, poor placental development and placental dysfunction (Bruce-Brand, Wright and Schubert, 2022 and Ikumi and Matjila 2021). HIV infected women may also have a higher prevalence of other factors that may lead to adverse birth outcomes such as low socioeconomic status, poor nutrition, and poor access to care.

The Sub- Saharan African region remains disproportionately affected by both HIV and adverse birth outcomes. According to Chasekwa et al (2022) the Zimbabwean preterm birth rate has been observed at almost twice that seen globally. In a study by Chaibva, Olorunju, Nyadundu, and Beke (2019) infants with low birth weight accounted for 14.6% of births in Mutare, Zimbabwe.

Adverse birth outcomes are a leading cause of neonatal mortality and morbidity and children born prematurely and with low birth weight are prone to physical and neurological problems, are likely to be stunted and have poor cognitive development and learning problems and are also likely to be at higher risk of non-communicable diseases in later life (WHO 2024a). Still births are a source of pyschological stress to women, their immediate families and their communities at large and can lead to

financial repercussions for families and the broader economy as well as being a source of stigma and discrimination.

An estimated 1.3 million women living with HIV deliver annually globally and approximately 85% are in 21 top priority countries burdened with HIV, of which Zimbabwe is one (UNAIDS, 2020). It is estimated that in 2019 a total of 64 000 women living with HIV delivered in Zimbabwe. With such a high burden of HIV it remains paramount to try and address birth outcomes among women living with HIV.

This retrospective cohort study sought to assess whether there are differences in birth outcomes between HIV negative women and HIV positive women on tenofovir/lamivudine/dolutegravir. There are varied findings from studies done in Denmark, India, the USA and sub-Saharan Africa in relation to ART and birth outcomes. No such studies have been done in Zimbabwe and this study sought to cover this gap locally in Zimbabwe.

1.2 Background to the Study

Antiretroviral coverage in pregnancy has been improving over the years (UNAIDS, 2020). According to the UNAIDS (2023) Zimbabwe has reached the UNAIDS 95-95-95 targets. With approximately 64 000 HIV positive women delivering and a high ART coverage this means that more and more HIV positive women are delivering while on ART. For women established on ART who deliver the maternal to child transmission rates have been falling as the antiretroviral coverage has been going up.

Evidence for the effects of maternal ART use on adverse birth outcomes is conflicting. Some studies have reported that adverse outcomes remain high in HIV positive women on ART (Slogrove et al, 2024 and Tukei et al, 2023) while other studies report comparable outcomes for women on ART and HIV negative women (Mugo et al, 2022,

Quinn et al, 2022, and Twabi, Manda and Small, 2020). These studies mainly looked at women receiving Tenofovir/Lamivudine/Efavirenz, the recommended first line regimen at the time but no studies to our knowledge have looked at the current ART regimen with Tenofovir/Lamivudine/Dolutegravir.

Zimbabwe remains with high neonatal and under 5 mortality rates of 21 and 48 per 1000 live births respectively, and as the world moves to reach the sustainable development goal of ending preventable deaths of newborns and children under 5 years of age, and aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births in all countries (United Nations, 2024) it becomes paramount to understand the role that ART may play in improving birth outcomes and/or whether additional interventions need to be focused to women living with HIV on ART.

JF Kapnek Zimbabwe is a local non- governmental organization operating in different areas within the country. In 6 districts of Masvingo province, Chiredzi, Chivi, Gutu, Masvingo, Mwenezi and Zaka, the organization is implementing the Target, Accelerate, Sustain Quality Care for HIV epidemic control program, known in short as the TASQC program. The program offers support to the Ministry of Health and Child Care (MOHCC) in meeting the 95-95-95 UNAIDS goals that seek to ensure that 95% of all people living with HIV know their status, 95% of those who know their status are on antiretroviral therapy, and 95% of those on antiretroviral therapy have a suppressed viral load.

The province is the 6th most populated within the country out of the 10 provinces and has a predominantly rural population with 87% of the female population residing within rural areas (ZimStat, 2023). Furthermore, according to the 2022 census the

province has a total population of women of childbearing age of 386 013, representing 44% of the female population within the province. HIV prevalence for the province was at 12.9% according to the 2015 Demographic and health survey (ZimStat, 2016).

Approximately 39 798 women booked for antenatal care in the province in 2023 in the 6 districts according to the District Health Information System (DHIS-2), and of these 37 091 (93%) had a documented HIV status. The HIV prevalence stood at 9% with 23% of the HIV positive women being newly identified in the antenatal period. ART Coverage was at 116% representing HIV positive women previously identified who were newly initiated on ART during their ANC period. All public health care facilities in the province offer delivery services. With more women living with HIV started on antiretroviral therapy and mother to child transmission rates dropping it becomes important to understand whether the benefits brought about by ART also translate to better birth outcomes in women delivering within the province.

1.3 Statement of the Problem

Approximately 64 000 women living with HIV deliver annually (UNAIDS, 2020) in Zimbabwe and in the 6 districts that JF Kapnek supports in Masvingo Province this number is close to 3 000 deliveries among women living with HIV annually. With a neonatal mortality rate of 31 per 1000 and a low-birth-weight rate of 15% in the general population these could be higher in the women living with HIV. With no understanding of the effects of maternal ART use on birth outcomes, women living with HIV may continue to experience adverse birth outcomes and not have any interventions earmarked for them. As a result, the country may fail to attain the SDGs of reducing neonatal and infant mortality and neonatal morbidity and mortality may continue to be high. The results of this study can help spark policy discussions on the current ART guidelines and target interventions that seek to improve maternal and child health

among HIV positive women who have traditionally been disproportionately affected by poorer birth outcomes.

1.4 Research Objectives

1.4.1 Broad Objective

The study sought to assess differences in prevalence of low birth weight and still births between HIV positive women on antiretroviral therapy and HIV negative women in Masvingo Province for the period 1 January 2023 to 31 December 2024.

1.4.2 Specific Objectives

i. To determine the prevalence of low birth weight and still births among HIV-positive women on ART and HIV negative women in Masvingo Province from 1 January 2023 to 31 December 2024

ii. To compare the occurrence of low birth weight and still births between HIV positive women on ART and HIV negative women in Masvingo Province from 1 January 2023 to 31 December 2024.

iii. Determine factors associated with high risk of low birth weight and still births among HIV positive women on ART and HIV negative women in Masvingo Province from 1 January 2023 to 31 December 2024.

1.5 Research Questions

1. What is the prevalence of low birth weight and stillbirth deliveries in HIV positive women on ART and HIV negative women Masvingo Province for the period 1 January 2023 to 31 December 2024?
2. Are the proportions of children born with low birth weight and stillbirth deliveries different between HIV positive women and HIV negative women in Masvingo Province from 1 January 2023 to 31 December 2024?

3. What are the factors associated with higher risk of low-birth-weight deliveries and stillbirth deliveries in HIV positive women on ART and HIV negative women in Masvingo Province from 1 January 2023 to 31 December 2024?

1.6 Hypotheses

Hypothesis 1

H0: There is no difference in rates of low-birth-weight deliveries between women living with HIV on ART and HIV negative women in Masvingo Province.

H1: There is a difference in rates of low birth deliveries between women living with HIV on ART and HIV negative women in Masvingo Province.

Hypothesis 2

H0: There is no difference in rates of stillbirth deliveries between women living with HIV on ART and HIV negative women in Masvingo Province.

H1: There is a difference in rates of stillbirth deliveries between women living with HIV on ART and HIV negative women in Masvingo Province.

1.7 Significance of the Study

The use of antiretroviral therapy has resulted in improvements in maternal health and in reducing mother to child transmission of HIV. Understanding the effects of ART use on birth outcomes becomes important in that it allows for the determination of need of any further interventions to improve child health and allows for possible policy changes as the world continues to seek for optimal outcomes for pregnant people living with HIV and their children, in line with global goals.

1.8 Delimitations of the Study

The study was limited to three districts in Masvingo province and hence the results of the findings may not be generalizable to the whole province or whole country. The results are valid only for women on the specified ART regimen. The findings of the study were also limited to the data collection tool utilized and may not apply to use of different tools with different variables. The study used data collected for the period between 1 January 2023 and 31 December 2024 and the findings may only be applicable to this time period. Ideally the study would have enrolled every woman delivering but due to time and financial constraints the study was limited to the sampled 603 women.

1.9 Limitations of the Study

The study used secondary data and as such had no control on potential confounders. A multistage sampling procedure with purposive selection of the province and districts, simple random selection of facilities and systematic random sampling of participants was utilized for both HIV negative and positive women and the random selection helped control by having an almost representative sample of the population delivering at the facilities.

CHAPTER 2 REVIEW OF RELATED LITERATURE

2.1 Introduction

This chapter explores the literature on adverse birth outcomes in the setting of HIV infection. It begins by exploring the current theories on how untreated HIV leads to adverse birth outcomes and then looks at evidence of untreated HIV infection and adverse birth outcomes. Literature on how maternal ART affects the different birth outcomes is then explored.

2.2 Theoretical Framework

According to Bruce-Brand, Wright and Schubert (2021) there is a vast spectrum of placental pathology that occurs because of HIV infection **(Figure 2.1)**.

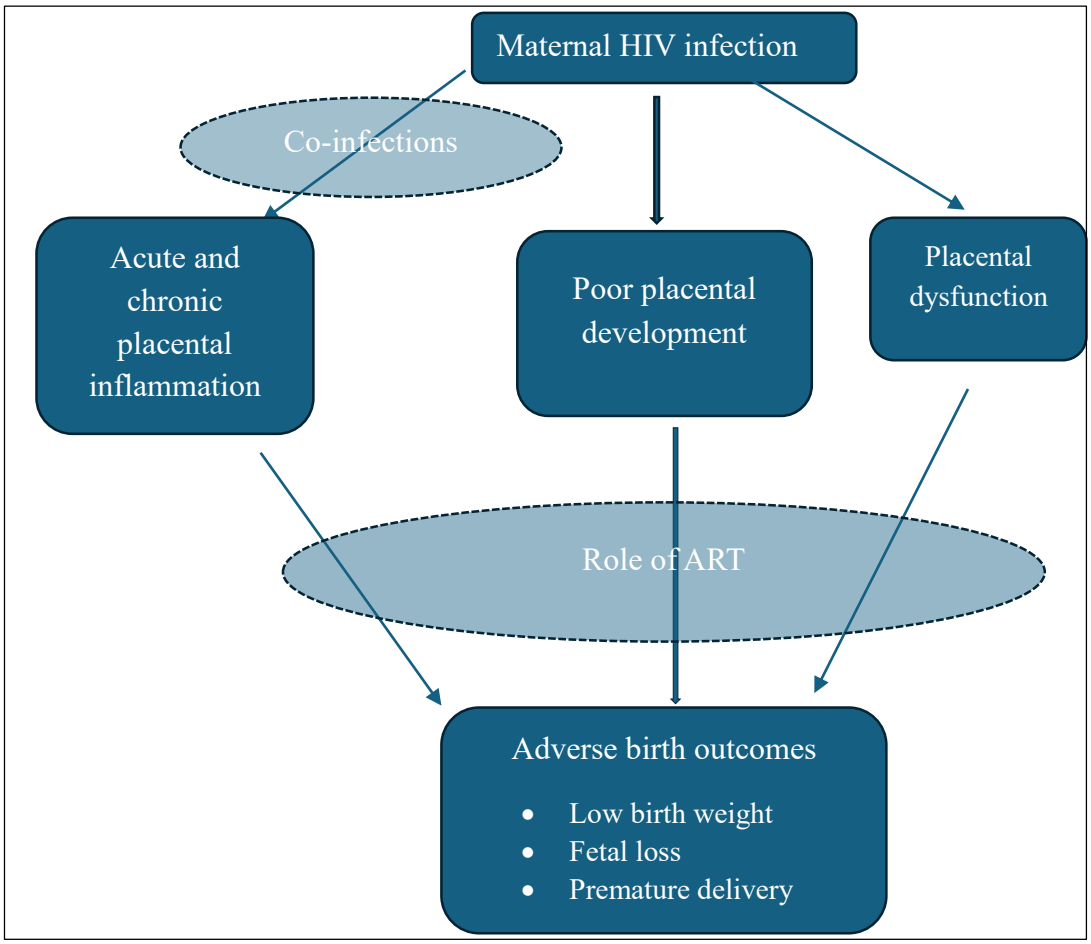

FIGURE 2.1 Maternal HIV infection and adverse birth effects: A theoretical framework (Adopted and adapted from Bruce-Brand, Wright and Schubert 2022 and Ikumi and Matjila 2021)

They postulate that the observed maternal and child mortality and morbidity that occur due to HIV infection may occur because of direct placental tissue HIV infection, placental changes as a response to HIV infection, and downstream consequences of HIV infection.

An increased risk of acute chorioamnionitis has been noted in the setting of HIV infection. This may be because of depressed immunity noted due to HIV, concomitant sexually transmitted infections and other HIV associated factors such as vaginitis (Bruce-Brand et al, 2021). In addition, women living with HIV have a higher prevalence of non-pregnancy related infections such as syphilis which can also induce

placental changes. As Ikumi, Matjila, Gray, Anumba and Pillay (2021) note the severity of acute chorioamnionitis is linked to preterm deliveries, low birth weight and small for gestational age infants.

Chronic inflammation noted with villitis of unknown aetiology, chronic chorioamnionitis and chronic deciduitis have been noted to be associated with adverse birth outcomes like preterm labour, premature rupture of membranes, small for gestational age foetuses and spontaneous pregnancy loss (Ikumi et al, 2021). The relationship between these chronic inflammatory conditions and HIV is still under scrutiny with some studies showing increased risk in women living with HIV and others showing no relationship between HIV and these conditions (Ikumi and Matjila, 2022). The role of maternal ART on the occurrence of chorioamnionitis and other co-infections needs investigation (Bruce-Brand et al, 2021).

Placental dysfunction has been defined by Ikumi and Matjila (2022) to include poor perfusion and placental insufficiency. The same phenomenon is termed maternal vascular malperfusion by Bruce-Brand et al (2021) and is linked to low placental weight, thin umbilical cords, and infarction in preterm placentae, accelerated placental villous maturation, and retro placental haemorrhage among other placental changes and has been linked to fetal death, spontaneous preterm birth and fetal growth restriction. Ikumi et al (2021) note that some studies have reported higher rates of maternal vascular malperfusion among women living with HIV and there is an increase in women that started ART pre-conception compared to those starting ART during pregnancy. Bruce Brand et al note conflicting results from different studies with some showing no relationship between maternal vascular malperfusion and HIV status and others showing an increased risk in HIV positive women.

Antiretroviral therapy has also been linked with adverse birth outcomes, especially preterm labour. As Ikumi and Matjila (2022) note protease inhibitor-based ART is associated with an increased risk of preterm births. Lockman et al (2021) also reported a higher risk of preterm delivery in women receiving tenofovir disoproxil fumarate/emtricitabine/dolutegravir or efavirenz regimes when compared with women receiving tenofovir alafenamide/emtricitabine/dolutegravir.

2.3 Relevance of the Theoretical Frame to the Study

The role of antiretroviral therapy in reducing the risk of mother to child transmission of HIV and in reducing morbidity and mortality among people living with HIV has been well described. ART is also associated with a reduction in opportunistic infections among people living with HIV as a result of improvements in immune status as evidenced by improving CD4 cell counts and viral suppression.

Untreated HIV infection has been seen to be associated with adverse birth outcomes as outlined in the previous section and certain ART regimens have also been seen to result in adverse birth outcomes. This study sought to explore whether treatment particularly with tenofovir disoproxil fumarate/lamivudine/dolutegravir (TLD) results in improvement in birth outcomes in women living with HIV in Masvingo. It also sought to explore whether ART timing (pre-conception vs post conception) would show any differences in birth outcomes in women living with HIV.

The role of co-infections like syphilis in contributing towards adverse birth outcomes was also explored.

2.4 Adverse Birth outcomes

The term adverse birth outcome refers to a multifactorial outcome that mainly includes preterm birth, low birth weight, stillbirth, macrosomia, congenital anomalies and

infant or neonatal death (Abadiga et al, 2022). Globally, Yahaya, Adeyemo and Kumah (2024) note that approximately 30 million infants are delivered with a low birth weight annually with 50% of these occurring in sub-Saharan Africa. There are an estimated 15 million preterm deliveries annually globally with approximately 81% of these occurring in South Asia and sub-Saharan Africa. There are 2.6 million third trimester stillbirths annually and 41% of these occur in sub-Saharan Africa

Abadiga et al (2022), Tamirat et al (2021) and Yahaya et al (2024) all note that the aetiology of adverse birth outcomes is multifactorial with maternal, nutritional, environmental, and health care system factors contributing to their development. Socio-demographic factors such as maternal age, educational level, income level and place of residence have all been shown to have an association with adverse birth outcomes. In addition, obstetric factors such as previous history of adverse birth outcomes, antepartum haemorrhage, gestational age, pregnancy interval, usage of antenatal care services, hypertensive disorders of pregnancy, and parity have also been associated with adverse birth outcomes.

In Zimbabwe according to Chibura, Twabi, Maluleke, and Musekiwa (2024) and Chaibva et al (2019) an estimated 15.6-16.3% of pregnancies are complicated by adverse birth outcomes. Chaibva et al noted that preterm deliveries accounted for 18.2% of all deliveries, low birth weight deliveries accounted for 9.8% and stillbirths accounted for 2.3% of all deliveries. The risk factors observed for adverse birth outcomes in Zimbabwe include maternal comorbidities like anaemia, HIV infection, lack of antenatal care, non-institutional delivery, high maternal age, residence in rural provinces and parity. These are similar to those noted on a global scale.

Untreated HIV infection has been noted to increase the rate of adverse birth outcomes. Wedi et al (2016) note that women living with HIV have a higher risk of preterm delivery, low birth weight, small for gestational age infants and stillbirths. In Sub-Saharan Africa, where the largest burden of both HIV and adverse birth outcomes exists, Murray et al (2023) noted that between 1990 and 2020 the proportion of preterm births, low birthweight and small for gestational age infants attributable to untreated maternal HIV were 78%, 80% and 80% respectively. Evidence from Zimbabwe also shows that untreated maternal HIV was associated with increased risk of low birth weight, very low birth weight, a low APGAR score and fetal growth restriction (Ticconi et al, 2003) with Friis et al (2004) also noting that birth weight declined in babies born to HIV positive women as HIV viral load increased.

2.5 Adverse outcomes in the era of HAART

The use of antiretroviral therapy in HIV infection in pregnant women living with HIV has evolved from a time when single dose nevirapine and zidovudine monotherapy were used to reduce the risk of mother to child transmission of HIV to a time when combination ART is now being used for all people living with HIV irrespective of their immunological status. ART regimens have evolved from use of tenofovir-lamivudine-efavirenz to the current first line regimen which has tenofovir-lamivudine-dolutegravir.

The role of ART in reducing mother to child transmission of HIV is indisputable. **Figure 2.2** below shows how mother to child transmission rates have been falling as ART coverage has been rising (UNAIDS 2020).

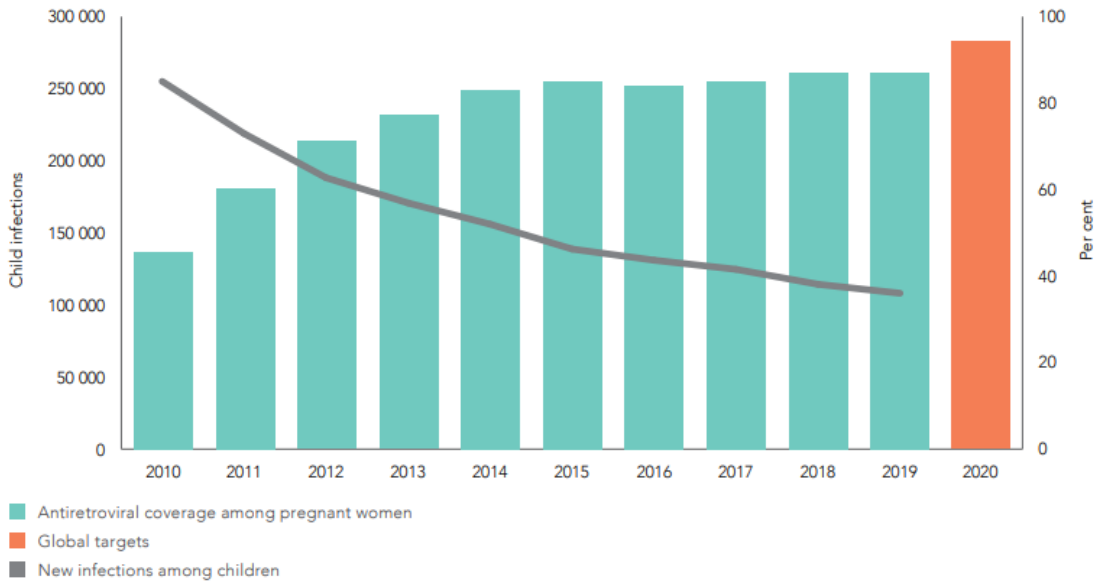

Figure 2.2: ART coverage among pregnant women compared with new HIV infections in children.

However, the evidence in terms of adverse birth outcomes remains conflicted. Studies in Sub-Saharan Africa and abroad have shown different results. Slogrove et al (2024), Tukei et al (2021), Fentie, Yeshita and Bokie (2022), Zash et al (2017), Worku, Azale, Ayele and Mekonnen (2022), and Yingjuan et al (2023) noted worse birth outcomes in HIV positive women on ART compared with HIV negative women while Mugo et al (2022), Twabi, Manda and Small (2020) and Quinn et al (2022) showed no differences in adverse birth outcomes between HIV negative women and HIV positive women. The later findings are consistent with findings from Denmark (Moseholm, 2021) and the USA (Thompson et al, 2022).

Comparing ART regimens Lookman et al (2021) in a randomized controlled trial found no differences in rates of composite adverse pregnancy outcome between clients receiving Tenofovir disoproxil fumarate/emtricitabine/dolutegravir compared to Tenofovir disoproxil fumarate/emtricitabine/Efavirenz (TLE). This is also similar to findings from Zash et al (2017) from Botswana. There are no studies to our knowledge

that compare women on TLD and HIV negative women in the real-world. This becomes key because most of the studies looking at ART and adverse birth outcomes have looked at other regimens.

2.6 Low birth weight in women living with HIV on ART

Fentie et al (2022), Slogrove et al (2024), Tukei et al (2021), Worku et al (2022) all reported a higher risk of low birth weight in children born to HIV positive women compared to HIV negative women. A notable feature in Slogrove et al is the very low availability of viral load results with only 24% of the cohort of women having a viral load result and no attempt was made to stratify by viral load suppression. Further to this, a higher CD4 cell count in women living with HIV was associated with better outcomes compared to women not on antiretroviral therapy (Slogrove et al, 2024). This stratification by CD4 cell count is missing in the study by Fentie et al (2022).

Yingjuan et al (2023) in a retrospective cohort study in China noted that HIV positive women had more than twice higher odds of delivering low birth weight infants compared to their HIV negative counterparts. In their study however there is no mention of the ART regimens and virological or immunological status of the HIV positive women that were enrolled and no stratification of results by these characteristics which Slogrove et al (2024) did. In this retrospective cohort study a key difference was that only women on the current first line regimen who are confirmed to be virologically suppressed were enrolled to try and see whether HIV infection continued to be a recognized risk factor for low-birth-weight deliveries and other outcomes in women who were clinically stable.

This methodology used by Slogrove et al (2024), Fentie et al (2021) and Yingjuan (2023) is in direct contrast to the approaches utilized by Dadhwal et al (2017) and

Dadabhai et al (2019) who enrolled healthier women with better immune systems either in stage 1 HIV disease or with CD4 cell count results which were above 350 and had a relatively higher viral load coverage and which observed that there were no differences in low birth weight rates between HIV positive women on ART and HIV negative women. This would seem to suggest that relatively healthier HIV positive women on ART will have comparable outcomes with HIV negative women. This study enrolled HIV positive women well established on ART with undetectable viral loads to try and reduce the potential confounding effect of raised viral loads and a generally unhealthy pregnant mother.

2.7 Preterm birth in women on ART

Mugo et al (2022) noted no differences in rates of preterm delivery between HIV positive women on ART and HIV negative women. While the ART regimen and virologic or immunological status of the women was not mentioned the study had a relatively high ART coverage of 91% and another strength was that of a large sample size. Quinn et al (2022) also noted no differences in preterm births between HIV positive women and HIV negative women. Despite the study being a secondary data analysis and having no prior sample size calculation for birth outcomes the study had a large sample size. Of note as well was that in this study there were no differences in outcomes despite the study having a relatively low proportion (41%) of women on ART starting the medicines pre-conception. Dadhwal et al (2017) and Dadabhai et al (2019) also reported no differences in preterm births between HIV positive women on ART and HIV negative women.

Stratifying women who were on ART by viral load results, Moseholm et al (2022) noted that preterm deliveries were higher in HIV positive women who had viral load results with 50 or more copies/ml of the patient's blood. This retrospective cohort

study also stratified patients by their ART regimen but notably very few patients were on integrase stand transfer inhibitors.

Tukei et al (2021) and Worku et al (2022) reported rates of preterm deliveries that were higher in HIV positive women than in HIV negative women. These studies had a priori sample size calculation (Worku et al) or a large sample size (Tukei et al), high ART coverage and high viral load suppression rates which is in direct contrast with the works of Mugo et al (2022) and Quinn et al (2022). While Worku et al (2022) and Mugo et al (2022) do not specify the ART regimens that the women were on, in Tukei et al (2021) and Quinn et al (2022) Tenofovir/Lamivudine/Efavirenz was the first line regimen being used by the vast majority of clients and the studies still had different outcomes. The reasons for these differences remain unknown.

In their study Yingjuan et al (2023) noted preterm deliveries that were almost twice those among HIV negative women. As noted previously one weakness of their study is that there is no mention of the ART regimen, the virological or immune classification of the patients and there is no stratification of women by these characteristics.

This current study enrolled women who were taking Dolutegravir based first line therapy which is the currently recommended ART regimen in the Zimbabwean guidelines. This was to ensure that no cofounding of results by ART regimen would occur.

2.8 Stillbirths in women on ART

There remains ambiguity on the effects of ART on stillbirth rates. While fewer studies have looked at stillbirths compared to preterm deliveries and low birth weight infant deliveries it is interesting to note that in studies like those of Slogrove et al (2024) which noted higher low birth weight rates in HIV positive women no such significant

associations were noted with stillbirths. This is also a similar finding with Worku et al (2022) and Mugo et al (2022) who noted no significant differences in low birth weight and preterm deliveries and also noted no differences with stillbirths between HIV positive women on ART and HIV negative women.

This contrasts with Tukei et al (2021) who had adverse birth outcomes higher in HIV positive women on ART encompassing low birth weights, preterm deliveries and stillbirths. In an observational study in Botswana mainly focusing on adverse birth effects by ART regimen Zash et al (2017) noted higher rates of stillbirths among HIV positive women on ART compared to HIV negative women. This study had a strength of a large sample size but mainly focused on protease inhibitor and non-nucleoside reverse transcriptase inhibitor-based ART and did not include Dolutegravir based ART, which distinguishes it from this retrospective cohort study.

Yang et al (2022) noted that still birth rates were higher among HIV positive women in Brazil compared to HIV negative women. In this study a key strength is that they used a large sample size. A key difference however is that this study was conducted at a tertiary level facility which likely sees clients with more complicated cases which as a result may not match the disease occurrence in the general population. Another weakness of the study is that there is no mention of whether the enrolled HIV positive women were on ART and there is no stratification by virologic suppression and/or CD4# as a marker of being clinically stable.

Thompson et al (2022) examined still births in a cohort of women delivering in the United States who were in the Medicaid program. In this study when adjusting for all variables they didn't see any differences in the rates of stillbirths by HIV status. A

weakness of this review is that it did not have maternal ART status or clinical condition as a variable and hence it is not clear what ART regimens if any the patients were on.

Fewer authors have looked at stillbirths compared to other adverse birth outcomes and this study sought to enlarge the body of evidence on the effects of maternal ART intake on this adverse outcome.

2.9 ART timing and adverse birth outcomes

In their review on ART and birth outcomes in Sub-Saharan Africa Murray et al (2023) note that since the use of combination ART regimens the rate of adverse birth outcomes started going up compared to the time when zidovudine monotherapy or dual therapy with zidovudine/lamivudine was the standard of care. This would seem to suggest that ART use preconception is associated with adverse birth outcomes. From a theoretical perspective one would assume that with improved maternal immunity and viral suppression due to combination ART the placental pathology described earlier would improve as Quinn et al (2022) also note. These findings would then perhaps suggest the drugs themselves being used as ART are responsible for adverse birth outcomes but as the discourse on low birth weight, preterm deliveries and stillbirth shows the evidence remains ambiguous on this.

In their study Dadabhai et al (2019) stratified HIV positive women to those starting ART pre-conception and those starting ART after conception. They however did not identify any differences in birth outcomes by ART timing. This is similar to the findings of Tukei et al (2021). Twabi et al (2020), in an analysis of findings between Demographic Health Surveys done between 2010 and 2015 noted improvements in birth outcomes between the two time periods. Of note is that in 2010 and before the country was using single dose nevirapine and/or zidovudine monotherapy while by

2015 the country had adopted WHO Option B+ recommendations which meant all women would be on combination ART for their health. Slogrove (2024) noted that women who received 20 weeks or less of ART had the highest prevalence of adverse birth outcomes compared to women on ART for 40 weeks or more.

In a high resource setting Moseholm et al (2022) noted no differences in birth outcomes by ART regimen or ART timing. In this analysis it is notable that clients were stratified by ART regimen with the common regimens being protease inhibitor based, and nucleoside reverse transcriptase based with a very low population being on integrase strand transfer inhibitors. Another notable feature is that a very high proportion of clients were noted to be virally suppressed.

While Quinn et al (2022) noted no significant differences in birth outcomes between HIV positive women on ART and HIV negative women they did note a higher rate of preterm deliveries in women who had started ART after conception but before 20 weeks gestation when compared to women starting ART after 20 weeks gestation. They however noted no differences between ART started preconception and ART started after conception but before 20 weeks gestation in terms of birth outcomes. In all these studies the women were receiving TLE, a regimen that has since been phased out in favour of the more efficacious Tenofovir/Lamivudine/Dolutegravir. This current study specifically focused on women on Dolutegravir based first line therapy and sought to add to the body of knowledge on this specific ART regimen.

Msukwa et al (2019) in a cohort study looked at the association between stillbirths and ART timing. Their study involved multiple ART regimens but noted no association between ART timing and increased odds of stillbirth.

In a systematic review Shinar et al (2022) also noted a higher risk of preterm deliveries with preconception ART compared with antenatal ART initiation. There were no associations between low birth weight and timing of ART initiation. There is no specification of the ART regimens which were used in the various articles they reviewed. This retrospective cohort study was focused on HIV positive women on a dolutegravir based regimen, which is the current recommended first line regimen for pregnant women living with HIV in Zimbabwe.

2.10 ART regimens and birth outcomes

Antiretroviral therapy usage in pregnancy has evolved from use of single dose nevirapine and/or zidovudine monotherapy to a time when pregnant women were using combination antiretroviral therapy to reduce maternal to child transmission to using combination ART for their own health and reducing mother to child transmission.

Integrase strand transfer inhibitors, of which dolutegravir is one are a relatively new class of antiretroviral therapy compared to other regimens and very few studies have looked at this regimen. Zash et al (2018) compared birth outcomes between women receiving dolutegravir based therapy and efavirenz based therapy in Botswana. In this study they noted that dolutegravir based ART had comparable outcomes to efavirenz based ART. This study however did not enrol HIV negative women to assess whether outcomes were different by HIV status. While they analysed maternal clinical status by CD4 count measurements notably fewer women on dolutegravir had a CD4 count, and they did not report on viral load results for the cohort of women they had.

No studies in the literature compare outcomes for women living with HIV on dolutegravir based antiretroviral therapy and HIV negative women and the literature

search did not show any studies that looked at only women well established on ART. This retrospective cohort covers this gap as it looked at women on DTG based ART who are virally suppressed and clinically stable.

2.11 Summary

This chapter reviewed the literature on adverse birth outcomes in women living with HIV. While the evidence on untreated maternal HIV infection is quite clear there is still no consensus on how maternal ART intake affects birth outcomes. Furthermore, the evidence on ART timing and adverse birth effects also remains ambiguous. This study sought to understand the effects of TLD on birth outcomes in stable women and add to the body of literature with evidence from Zimbabwe and on this ART regimen.

CHAPTER 3 METHODOLOGY

3.1 Introduction

This chapter explains the methodology that was used in the research. The study design that was used, the variables of interest, the study setting, and participant's selection are outlined. In addition, the data collection instrument that was used, sample size calculation and ethical considerations for the study are also explained.

3.2 The Research Design

A retrospective cohort study design was conducted using secondary data already in facility delivery registers. These contain demographic information on all delivering women, have HIV status and for HIV positive women have data on the ART regimen of the client and viral load result during the antenatal period. Data on the duration on ART and the viral load result was missing from the delivery register for some deliveries and triangulation was done with the facility held patient OI ART booklets, also known as the greenbook.

The exposure of interest was the HIV status of the patient. The current Zimbabwean ART guidelines have Tenofovir/Lamivudine/Dolutegravir (TLD) as the first line regimen and women on this regimen who were virally suppressed were eligible for enrolment. No studies to the knowledge of the investigator have looked at this regimen and birth outcomes in Zimbabwe or other similar settings. ART timing was also collected (preconception vs during the pregnancy) and duration on ART at the time of delivery was collected. A suppressed viral load was part of the inclusion criteria, and this follows on the work of Dadabhai et al (2019) who enrolled a cohort of women stable on ART for their study. Since the effects of untreated HIV on birth outcomes are quite clear this study sought to see outcomes in women well established on ART.

The outcomes of interest were estimated gestational age at delivery, birth weight at delivery, and fetal status at delivery (live birth or stillbirth). Other variables of interest were maternal age at delivery, parity of the woman, any co-morbidities, area of residence (rural vs peri-urban vs urban), and level of education. These helped in determining the factors associated with low birth weight and stillbirths in the two groups being studied.

Data was collected for deliveries between 1 January 2023 and 31 December 2024. The study focused on pregnancy outcomes after 28 weeks of gestational age. Women delivering after 28 completed weeks were eligible for enrolment within the study. For women with more than one delivery within the specified period the first instance was considered.

3.3 Study setting

The study was conducted in Masvingo Province. The province was purposively sampled because JF Kapnek Zimbabwe is implementing an HIV care and treatment program in 6 districts in Masvingo Province namely Chiredzi, Chivi, Gutu, Masvingo, Mwenezi and Zaka.

The province is the 6th most populated within the country out of the 10 provinces and has a predominantly rural population with 87% of the female population residing within rural areas (ZimStat, 2023). Furthermore, according to the 2022 census the province has a total population of women of childbearing age of 386 013, representing 44% of the female population within the province. HIV prevalence for the province was at 12.9% according to the 2015 Demographic and health survey (ZimStat, 2016).

Approximately 39 798 women booked for antenatal care in the province in 2023 in the 6 districts according to the District Health Information System (DHIS-2), and of these

37 091 (93%) had a documented HIV status. The HIV prevalence stood at 9% with 23% of the HIV positive women being newly identified in the antenatal period. ART Coverage was at 116% representing HIV positive women previously identified who were newly initiated on ART during their ANC period.

All public health care facilities in the province offer delivery services. Three districts out of the 6 supported districts, Chiredzi, Masvingo and Mwenezi were selected for the study as they had the largest cohort of HIV positive women accessing delivery services in the study period.

3.4 Study population and Inclusion/Exclusion criteria

The study focused on records of women delivering between the period from 1 January 2023 to 31 December 2024. For women who had more than one delivery within that period the first delivery was considered. The inclusion and exclusion criteria are summarized in **Table 3.1** below:

Table 3.1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Deliveries after 28 weeks of gestation • Documented confirmed HIV status • HIV positive women on Tenofovir/Lamivudine/Dolutegravir regimen • HIV positive women with a documented suppressed viral load	• Deliveries before 28 weeks of gestation • HIV positive women on other ART regimens besides the specified regimen • HIV positive women with an unknown or unsuppressed viral load • Twin deliveries

3.5 Sample size and sampling procedure

Sample size was calculated using the Fleiss formula with continuity correction. The Fleiss formula is:

$$n' = \frac{[Z_{1-\alpha/2}\sqrt{((r+1)\bar{p}\,\bar{q}}) + Z_{1-\beta}\sqrt{(r p_1 q_1 + p_2 q_2)}]^2}{r(p_1 - p_2)^2}$$

where: n_1 = number of exposed (HIV positive women)

n_2= number of unexposed (HIV negative women)

$z_{\alpha/2}$= z score for a two tailed test based on α level

$z_{1-\beta}$= z score for a one tailed test based on β level

r= ratio of unexposed: exposed

p_1= proportion of exposed with disease

q_1= 1-p_1

p_2= proportion of unexposed with disease

q_2= 1-p_2

$\bar{p} = \frac{p_1 + rp_2}{r+1}$

$\bar{q}$ = 1- $\bar{p}$

The continuity formula is:

$$n_1 = \frac{n'}{4}[1 + \{\frac{2(r+1)}{n' r|p_1 - p_2|}\}^{1/2}]^2$$

Following on from the approach of Worku, Azale, Ayele and Mekonnen (2022) incidences of composite (overall) adverse birth outcomes were used to calculate the sample size where:

p_1 = 35.2%

p_2 = 24.3%

α= 0.05

β= 0.2

r = 1

$\bar{p}$ = 0.3

$\bar{q}$ = 0.7

n_1 was equal to 294 and since r=1 n_2 was also equal to 294 giving a total sample size of 588. From the pretest of the data collection tool approximately 10% of records had missing viral load results or gestational age at delivery and using this the sample size for data collection was calculated at 650 records (588 plus 59 records to cover for missing data rounded up to 650).

Sampling procedure

The sampling procedure that was utilized is shown in **Figure 3.1** below:

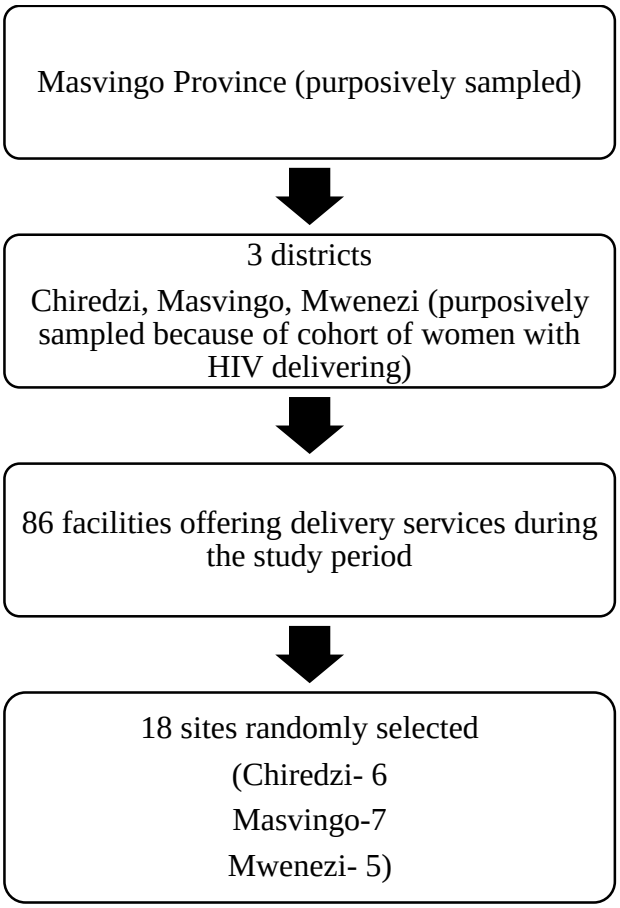

Figure 3.1 Sampling procedure for facilities utilized for the study

The selected districts have a total of 91 sites. Of these, from data in the District Health Information System between 1 January 2023 and 31 December 2024, 86 had deliveries among HIV positive women. The 3 districts had a total of 3 326 deliveries among HIV positive women in the period with Chiredzi District contributing 32%, Masvingo District contributing 39% and Mwenezi District contributing 29% respectively.

Using proportional apportionment for the sample size of 588 according to the proportion of deliveries Chiredzi District contributed 187 women, Masvingo District contributed 231 and Mwenezi contributed 178 women respectively. Simple random selection of sites was done until the total HIV positive women delivering was reached and accounting for a possible 10% loss due to ineligibility the sites chosen per district

were 6 for Chiredzi District: Chilonga, Tshovani, Chambuta, Chipiwa, and Chizvirizvi clinics and Chiredzi Hospital. A total of 7 sites were randomly selected for Masvingo district and these are Bondolfi, Gokomere, Mucheke, and Nemamwa clinics and Morgenster, Masvingo provincial and Nyikavanhu hospitals. For Mwenezi district Chingwizi, Lundi, and Rutenga clinics and Matibi and Neshuro Hospitals were randomly selected.

From the total deliveries at these facilities which amounted to 555 for Chiredzi District, 931 for Masvingo District and 608 for Mwenezi district systematic random sampling was done and the k-value for each district was 3 for Chiredzi District and 4 for both Masvingo and Mwenezi Districts. The number of HIV negative women delivering in the selected sites was 9610 and using systematic random sampling for the HIV negative cohort the k-value was 15. The "RANDBETWEEN" function in excel was used to determine the first patient whose details would be recorded, and every eligible 15^{th} patient would then be recorded until the sample for each site was reached. This approach differs from that of Slogrove et al (2024) who used the whole cohort available to them from the Western Cape and this difference was because of time and resource constraints.

3.6 Data Collection Instruments

A standard data collection form was utilized (see appendix 1). The form had a unique identifier code, age, residential place, HIV status, and duration on ART at time of delivery, viral load result, and estimated gestational age at delivery, infant status at birth (live birth or stillbirth), birth weight, Apgar score and any maternal or neonatal complication. These are the standard data points used by other researchers on the same topic (Dadabhai et al, 2019 and Slogrove et al, 2024). The data was collected electronically using an Excel spread sheet. Each patient was entered on a new row in

the spread sheet. All data collectors had laptops to use for data collection and data was saved on the cloud to ensure its security and availability in case of hardware malfunctions.

The delivery register was the primary source of data but the ANC register and the patient greenbooks were used for data triangulation for any data that was missing from the delivery register.

3.7 Pretesting of the research instrument

A pretest of the data collection tool was done in study districts, Chiredzi, Masvingo and Mwenezi districts at three sites that were conveniently selected. A sample size of 60 records was used for the pre-test which is approximately 10% of the required sample size. This was higher than the minimum of 30 participants as suggested by Perneger, Courvoisier, Hudelson and Gayet-Ageron (2015).

This pretest helped the data collectors familiarize with the data collection instrument. From the pretest it was noted that the registers did not contain information on the educational status of the patients and the knowledge of the health workers, both facility and community based was utilized to complete this section. The delivery register was also noted to have missing viral load results, missing estimated gestational ages at delivery and missing ART regimens for the HIV positive cohort with approximately 10% of the records missing these valuable data points. This 10% was then factored into the final sample size with 650 records being collected across the three districts.

3.8 Data Collection Procedure

Data was collected from delivery registers, antenatal registers and patient greenbooks. The main variables like age, place of residence, estimated gestational age at booking, estimated gestational age at delivery, birth weight, and fetal status were gathered from

the delivery register. Where incomplete data on the demographics and booking history were noted the data collectors would triangulate with the antenatal care register and for viral load information, they utilized the patient greenbook which is an ART record that is kept at the facility. These are all paper based registers. A total of 9 trained data collectors, 3 per district, visited the facilities between the 4th and the 28th of February 2025 for data collection. These were strategic information evaluation officers and data entry clerks who are experienced in data collection and data entry. They were re-imbursed for their time and effort.

Data was entered into excel spreadsheets on laptops. These are password protected laptops which are allocated to and used by specific individuals. They are organizational laptops which were used and once collected the data was uploaded on SharePoint, a cloud-based option that JF Kapnek Zimbabwe utilizes. This ensured that even if any hardware malfunction occurred the data would be secure. The SharePoint facility is also password protected, and access is limited only to people to whom access has been granted. No patient names were utilized and only unique identifier codes, in this case the ANC number, was utilized. This ensured patients could not be identified by outsiders.

3.9 Analysis and Organization of Data

The data was cleaned and coded after collection. Age (<20, 20-34, 35+), place of residence (rural, urban, peri-urban), level of education (none, primary, secondary+), the presence of a maternal comorbidity (yes, no), and booking timing (< 20 weeks gestation, 20+ weeks gestation) were stratified used commonly identified risk groups while birth weight, premature delivery and fetal status at delivery were assigned a binary code with 0 meaning no adverse outcome and 1 meaning the presence of an adverse outcome.

Summary statistics were then calculated and compared according to HIV/ART status and described as frequencies with percentage for categorical variables or median with interquartile range (IQR) for continuous variables. Differences in the independent variables were compared by HIV status with the chi-square test at 95% confidence level used to determine if there were differences.

Adjustment for maternal factors was done and included age at delivery, multiparity, level of education, time of booking the pregnancy, and place of residence with multivariate analysis being done using logistic regression. Odds ratios were used for this analysis. Analysis was also restricted to the two different cohorts using the same variables and for women living with HIV comparison of birth outcomes was also done by pregnancy ART timing. The data was presented mainly in the form of tables.

A 95% confidence interval was utilized to determine statistical significance in all the analyses. Analysis was done using the latest version of Stata (Stata Corp, College Station, Texas, USA). A two tailed p value of < 0.05 was used for statistical significance.

3.10 Ethical Consideration

Study approval was sought and granted from the Africa University IRB (AUREC 3577/25) and from the Provincial Medical Officer (PMD) for Masvingo province (Appendix 2 and 3 respectively). This study did not need informed consent from the patients because all the information needed for the study would be obtained from the records of the women. The data was de-identified before transfer to the investigator. All clients registering for antenatal care are assigned a unique 16-digit code which identifies the province, district, facility and a sequential number of the client starting from 00001 at the beginning of each year. These ANC numbers were utilized as unique

identifiers. No patient names were used and without access to each facility it is difficult to identify these clients.

Data collectors for the research also have non-disclosure agreements with JF Kapnek Zimbabwe which also has a memorandum with the Ministry of Health and Child Care.

3.11 Dissemination of study results

The findings of the study will be shared with the provincial health executive and district health executives of the different districts. This will be done in the form of physical presentations during routine provincial and district health executive meetings. Virtual meetings will be used as an alternative to physical presentations. The investigator will also seek to present the findings at various national and international meetings and conferences. Publication with reputable journals will also be sought.

3.12 Summary

This chapter explained the research the research design. It introduced the study setting and why this specific setting was chosen. Sample size calculation was explained and the need for a pilot study outlined. The chapter also introduced the data collection form, how the data will be collected and kept confidentially and the ethical considerations of the study. The data analysis plan and the dissemination were also explained in detail.

CHAPTER 4 DATA PRESENTATION, ANALYSIS AND INTERPRETATION

4.1 Introduction

This chapter presents the results of the retrospective cohort study. The chapter begings by outlining how the final study sample was selected then looks at the demographic characteristics of the study participants, followed by differences in the characteristics by HIV status. This is then followed by presentation of the adverse birth outcomes noted in the study as well as the analysis by HIV status. Lastly the chapter looks at the factors leading to adverse birth outcomes for the combined population and the 2 cohorts.

4.2 Study Population

From the 18 sites selected for the study a total of 12 302 deliveries were recorded between 1 January 2023 and 31 December 2024. Figure 4.1 below shows how the final study sample was selected.

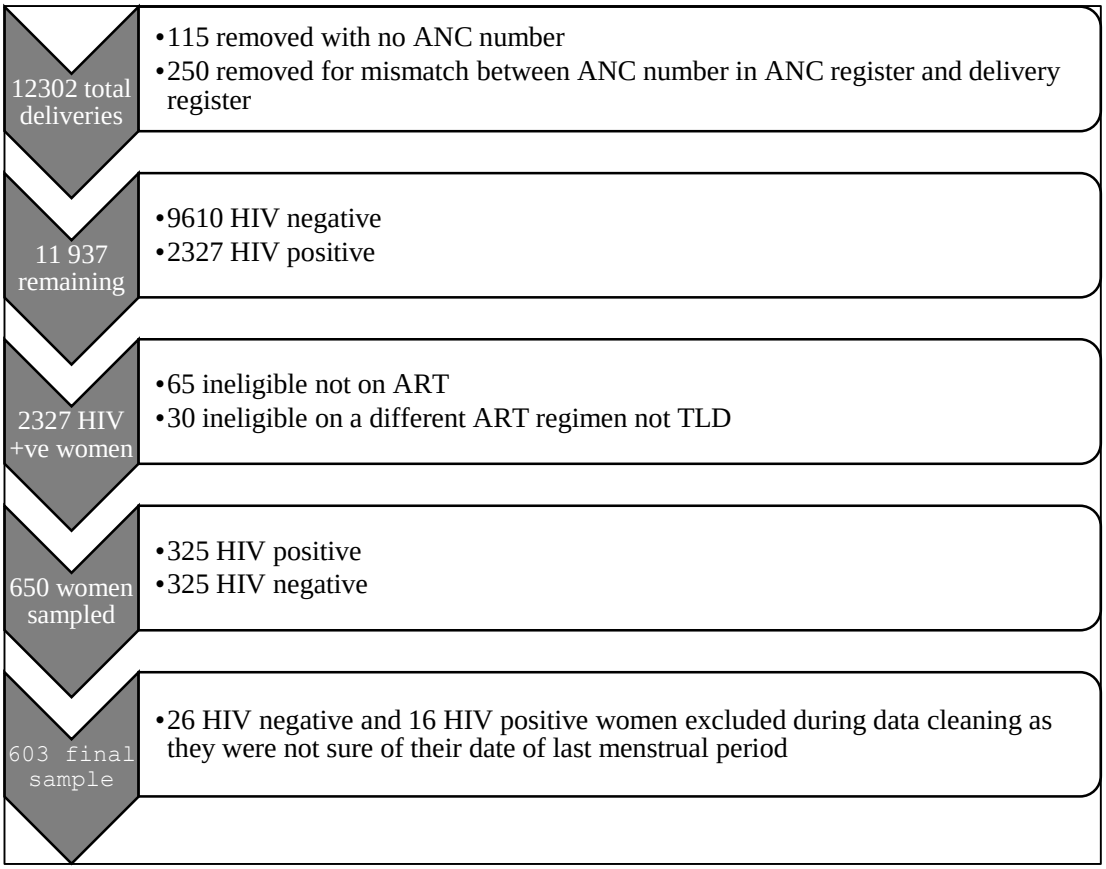

Figure 4.1 Final study sample determination

4.2 Demographic characteristics of participants

603 records were included in the final analysis and of these 299 were of HIV negative women and 304 were HIV positive women.

The demographic characteristics of the study participants are shown in **Table 4.1** below.

Table 4.1 Demographic characteristics of participants

Characteristic	Category	Total	(%)
N		603	
Age	<19	116	19
	20-34	363	60
	35+	124	21
Residence	Rural	436	72
	Peri-Urban	51	8
	Urban	116	19
Level of Education	None	56	9
	Primary	250	41
	Secondary +	297	49
Parity	Nulliparity	207	34
	Multi	396	66
Maternal Comorbidity	Yes	21	3
	None	582	97
Gestational Age at booking	<20 weeks	248	41
	>=20 weeks	355	59

The median age of participants was 25 years with an interquartile range of 20-33 years of age. The majority of participants resided in the rural areas. The proportion of participants living in urban areas (19%) was slightly higher than the provincial average which is 15%. This is because three of the facilities randomly selected, Chiredzi General Hospital, Masvingo Provincial Hospital and Mucheke clinic are all in urban areas and have huge cohorts of women living with HIV.

Most of the participants had at least primary school education with only 9% having no education at all. This was as expected for the province from census and surveys conducted before. For a third of participants this was their first pregnancy with the highest parity recorded being a woman who was on her 8th pregnancy (para 7).

For 21 of the participants there was a maternal comorbidity. 13 of the women had pregnancy induced hypertension and 6 had syphilis infection while one each had anaemia and a bad obstetric history. This is likely underrepresented especially for non-

communicable diseases because of poor access to blood pressure machines and blood glucose monitoring machines and for syphilis this may be because in 2024 some districts and facilities in the province did not have dual syphilis/HIV testing kits which are the main method used to diagnose syphilis infection in pregnant women.

The median gestational age at booking was 22 weeks with an interquartile range of 16 to 28 weeks. Most of the pregnancies were booked late with 59% of women booking after 20 weeks gestation according to their last menstrual period.

Differences existed in the age and parity of the women as shown in **table 4.2** below.

Table 4.2 Differences in demographic characteristics by HIV status

Variable	Category	HIV+	(%)	HIV-	(%)	x^2	p value
N		304		299			
Age	<20	34	11	82	27	32.1	0.001
	20-34	189	62	174	58		
	35+	81	27	43	14		
Residence	Rural	210	69	226	76	3.5	0.172
	Peri-Urban	27	9	24	8		
	Urban	67	22	49	16		
Level of Education	None	30	10	26	9	0.25	0.884
	Primary	125	41	125	42		
	Secondary +	149	49	148	49		
Parity	Nulliparity	80	26	127	42	17.46	<0.001
	Multi	224	74	172	58		
Maternal Comorbidity	Yes	9	3	13	4	1.32	0.25
	No	296	97	286	96		
Gestational Age at booking	<20 weeks	123	40	125	42	0.11	0.737
	>= 20 weeks	181	60	174	58		
ART Timing	Post -conception	35	12				
	Pre-conception	269	88				

HIV positive women were more likely to be older than their HIV negative counterparts. The median age at delivery for HIV positive women was 29 years with an interquartile range of 23 to 35 years while for HIV negative women the median age was 23 years with an interquartile range of 19 to 29 years. This is as noted in the HIV care and treatment program where the bulk of people receiving ART are older individuals above the age of 30 years and numbers of younger individuals are lower. These differences were significant using the Chi-square test at $p<0.05$.

Parity was also different for the two populations. The proportion of women living with HIV who had at least one prior pregnancy was significantly higher than among those who were HIV negative. Considering that these were also older women it is likely that they had previous pregnancy or child losses, perhaps due to HIV, and continue to seek to have a child.

There were no statistical differences in terms of place of residence, level of education, the presence of a maternal comorbidity, and gestational age at booking. While this is true for maternal comorbidities it is notable that the majority of pregnancy induced hypertension cases where in HIV negative women and perhaps this stems from a practice where HIV positive individuals hardly get tested for non-communicable diseases in OI clinics and also from the fact that most primary care facilities, especially those in the rural areas, have limited capacity to test for these condition due to machine breakdown and or general unavailability.

For the HIV positive women, 35, representing 12%, had started their antiretroviral therapy during the current pregnancy while the majority had started ART prior to booking. This was lower than the noted 23% of women starting ART during pregnancy from program data.

4.3 Adverse birth outcomes

A total of 98 pregnancies had an adverse outcome, representing 16% of all the pregnancies. The main adverse outcomes were low birth weight and premature deliveries at 9% each while still birth deliveries accounted for approximately 2% of the pregnancies.

4.3.1 Low birth weight

The mean birth weight was 3062.7 grams with a standard deviation of 502.1 grams. For the HIV negative cohort, the mean birth weight was 3087.4 grams with a standard deviation of 535.9 grams. The mean birth weight for HIV positive women was 3038.4 grams with a standard deviation of 466.1 grams. The differences in average birth weight for the two populations were not significant (p=0.23) using the Z-test for the difference in 2 means.

A total of 55 infants were delivered with a low birth weight. Of these 14 were preterm deliveries while the rest were term low birth weight deliveries.

The low-birth-weight deliveries by HIV status are shown in **table 4.3** below:

Table 4.3 Low birth weight deliveries by HIV Status.

	HIV Positive	**HIV Negative**	**Total**
Low birth weight	25	30	55
Normal birth weight	279	269	548
Total	304	299	603

The risk of delivering a low-birth-weight infant was 8.2% for the HIV positive women and 10% for the HIV negative women. The relative risk for HIV positive women was 0.82 ranging from 0.49-1.36. The relative risk confidence interval includes 1, which

implies that there were no differences in the low-birth-weight rates by HIV status in the bivariate analysis (p=0.44).

4.3.2 Still births

A total of 10 infants were delivered as still births giving a still birth rate of 16.58 per 1000 deliveries. HIV negative women had more still births compared to HIV positive women as shown in **table 4.4** below:

Table 4.4 Still births by HIV Status

	HIV positive	**HIV negative**	**Total**
Still birth	2	8	10
Live birth	302	291	593
Total	304	299	603

The risk of delivering a still birth was 0.66% among HIV positive women and 2.68% among HIV negative women. The relative risk for HIV positive women was 0.25 ranging from 0.05 to 1.15. The relative risk also includes 1 which means that the differences were not statistically significant. The p value was also 0.0524 which is not significant.

4.3.3 Preterm deliveries

The median gestation at delivery was 39 completed weeks with an interquartile range of 38 to 40 weeks. This did not differ by HIV status. Fifty-four infants were delivered before 37 completed weeks and of these 23 were among HIV positive women and 31 among HIV negative women. **Table 4.5** below shows the comparison in preterm deliveries by HIV status.

Table 4.5 Preterm deliveries by HIV Status

	HIV positive	HIV negative	Total
Preterm birth	23	31	54
Term birth	281	268	549
Total	304	299	603

The risk of delivering prematurely was 7.6% for HIV positive women and 10.4% for HIV negative women. The relative risk for HIV positive women was 0.7 with a 95% Confidence Interval of 0.4-1.2. This was statistically insignificant since the confidence interval includes a relative risk of 1 and the p-value was 0.23 which shows that there was no difference in preterm deliveries between HIV positive women and HIV negative women.

4.4 Factors associated with adverse outcomes.

As noted in the previous sections in the bivariate analysis HIV status was not significantly associated with either low birth weight deliveries, still birth deliveries or preterm deliveries. Univariate and multivariate logistic regression was also done using age at delivery (<20, 20-34, 35+), place of residence (rural vs peri-urban vs urban), level of education (no vs primary vs secondary +), the existence of a maternal comorbidity, parity (nulli vs multi), and timing of booking (<20 weeks vs after 20 weeks). For low-birth-weight deliveries and still births, preterm delivery was also used as a predictor variable.

4.4.1 Low birth weight deliveries

Table 4.6 and 4.7 below show the unadjusted and adjusted odds ratios for the various factors associated with low-birth-weight deliveries.

Table 4.6a Unadjusted odds ratios for factors associated with low-birth-weight deliveries

Variable	Category	All populations			HIV Positive			HIV Negative		
		OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Number with Outcome			55			25			30	
N			603			279			269	
Age										
	<20		reference			reference			reference	
	20-34	0.7	0.3-1.4	0.288	2.8	0.4-22.3	0.319	0.5	0.2-1.2	0.108
	35+	0.9	0.4-2.1	0.857	4.1	0.5-33.9	0.187	0.6	0.2-2	0.4
Residence										
	Rural	1.2	0.6-2.6	0.584	0.6	0.3-1.5	0.278	6	0.8-45.2	0.083
	Peri-Urban	1.3	0.4-4.1	0.661	0.3	0.03-2.4	0.246	9.6	1.04-91.3	0.049
	Urban		reference			reference			reference	
Level of Education										
	No	3.6	1.5-8.3	0.003	2.8	0.9-8.8	0.083	4.8	1.4-16.5	0.013
	Primary	2.1	1.1-3.9	0.022	1.2	0.5-3	0.683	3.4	1.4-8.4	0.008
	Secondary +		reference			reference			reference	
Maternal Comorbidity										
	No		reference			reference			reference	
	Yes	3.3	1.2-9.5	**0.024**	1.6	0.2-13.7	0.658	4.4	1.3-15.4	**0.019**
Parity										
	Nulli		reference			reference			reference	
	Multi	0.5	0.3-0.8	**0.008**	0.7	0.3-1.8	0.502	0.3	0.2-0.7	**0.006**
Gestational Age at Booking										
	<20 weeks		reference			reference			reference	
	20+ weeks	1.3	0.7-2.2	0.452	1	0.4-2.4	0.961	1.5	0.7-3.3	0.324

Table 4.6b Unadjusted odds ratios for factors associated with low-birth-weight deliveries

Variable	Category	All populations			HIV Positive			HIV Negative		
		OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Prematurity		4.3	2.2-8.6	0.000	4.9	1.7-13.8	0.003	3.9	1.6-9.7	0.004
HIV Status										
	Neg		reference							
	Pos	0.8	0.5-1.4	0.441						
ART Timing										
	Pre-conception					reference				
	Post-conception				0.7	0.2-2.9	0.568			

For all the women combined level of education, the presence of a maternal comorbidity, parity and prematurity were all significantly associated with a low birth weight in the univariate model. For HIV positive women only, prematurity was significantly associated with low-birth-weight deliveries and for HIV negative women place of residence, level of education, maternal comorbidities, prematurity and parity were significantly associated with low-birth-weight deliveries.

Compared with women with at least secondary level education HIV negative women with no education or primary education only had at least 4 times and 3 times higher odds of delivering low birth weight infants respectively. This ranged from 39% and 37% higher odds to 8- and 16-fold higher odds respectively. This was statistically significant with p values of 0.013 and 0.008 respectively.

Staying in peri-urban locations was associated with at least 9 times higher odds of delivering a low-birth-weight infant when compared with staying in an urban location (p=0.049). Rural residence had no differences with urban residence.

The presence of a maternal comorbidity was associated with at least 3 times higher odds of delivering a low-birth-weight infant and this was significant for the HIV negative cohort where the odds ranged from 20% higher odds to 15-fold higher odds and was statistically significant with a p value of 0.019.

When compared with nulliparous women, HIV negative multiparous women had 67% lower odds of delivering low birth weight infants. This ranged from a 27% to an 85% protective effect and was statistically significant.

For both HIV positive and HIV negative women prematurity was significantly associated with higher odds of delivering a low-birth-weight infant. This was at least

3 times higher odds for HIV negative women and at least 4 times higher odds for HIV positive women.

HIV status and timing of ART initiation were both not significantly associated with low-birth-weight deliveries in the unadjusted model.

In the univariate analysis for HIV positive women higher maternal age had higher odds of delivering low birth weight infants. Women who were between 20 and 24 years of age and those above 35 years of age had at least 2 times and 4 times higher odds of delivering a low-birth-weight infant when compared to women who were less than 20 years of age. This was however statistically insignificant but shows a departure from the recognized pattern when adolescent pregnancies are associated with lower birth weights compared to pregnancies in older women.

Table 4.7a Adjusted odds ratios for factors associated with low-birth-weight deliveries

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Number with outcome			55			25			30	
N			603			279			269	
Age										
	<20		reference			reference			reference	
	20-34	1.4	0.6-3	0.444	3.8	0.4-34.1	0.234	1.3	0.5-3.6	0.566
	35+	2.4	0.9-7	0.099	7	0.7-74.2	0.107	2.2	0.5-10.1	0.328
Residence										
	Rural	1.2	0.5-2.7	0.659	0.4	0.2-1.3	0.12	5.1	0.6-41.4	0.125
	Peri-Urban	1.5	0.5-4.9	0.516	0.3	0.03-3	0.322	9.9	0.99-101.9	0.054
	Urban		reference			reference			reference	
Level of Education										
	None	3.4	1.4-8.1	0.006	2.6	0.8-9	0.127	4.4	1.1-17.1	0.032
	Primary	1.9	1.02-3.7	0.042	1.2	0.4-3.1	0.758	3	1.2-8	0.025
	Secondary +		reference			reference			reference	
Maternal Comorbidity										
	No		reference			reference			reference	
	Yes	4.5	1.5-13.6	**0.008**	1.9	0.2-19.5	0.581	4.8	1.1-20.9	**0.035**
Parity										
	Nulli		reference			reference			reference	
	Multi	0.3	0.2-0.7	**0.002**	0.2	0.1-0.7	**0.013**	0.2	0.1-0.7	**0.008**
Gestational Age at Booking										
	<20 weeks		reference			reference			reference	
	>20 weeks	1.5	0.8-2.9	**0.174**	1.1	0.4-2.7	0.886	2.3	0.9-5.7	0.078

Table 4.7b Adjusted odds ratios for factors associated with low-birth-weight deliveries

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Prematurity		4.6	2.2-9.7	**0.000**	8	2.5-25.7	0.001	3.3	1.2-9.4	0.021
HIV Status										
	Neg		reference							
	Pos	0.9	0.5-1.6	0.715						
ART Timing										
	Pre-conception					reference				
	Post-conception				0.3	0.05-2.1	0.244			

In the multivariate analysis level of education, maternal comorbidities, parity and prematurity remained significant for HIV negative women while parity also became significant for the HIV positive women in addition to prematurity.

Maternal age, place of residence, HIV status, ART timing for HIV positive women and gestational age at booking all remained insignificant with p values above 0.05. In the multivariate analysis when stratified by HIV status the odds ratios are different for the two HIV groups and are also different from the odds ratio for the combined population for all independent variables except for parity. This shows that HIV status is an effect modifier in the occurrence of low-birth-weight deliveries.

Another interesting finding is that place of residence and level of education are not significantly associated with low-birth-weight deliveries for the HIV positive cohort. Also of note is that rural and peri-urban residence had high odds of delivering a low-birth weight infant when compared to urban delivery with almost 5 times and 9 times higher odds respectively. This however was not statistically significant.

The logistic regression model for low birth weight for both populations showed a good fit on postestimation. The results of the post estimations are shown in **table 4.8** below:

Table 4.8 Post estimation of the logistic regression model for low birth weight

Post estimation test	**All populations**	**HIV positive**	**HIV negative**
Pearson chi-square (goodness of fit)	p=0.2198	p=0.5466	p=0.2944
Area under the curve	73.38%	76,29%	78,58%
Link test (_hatsq)	p=0.939	p=0.289	p=0.422

The chi-square test and link test (_hatsq) p values were all above 0.05 meaning they were not statistically significant and hence the null hypothesis for the goodness of fit of the models could not be rejected and hence it is concluded that the models were a good fit.

The area under the curve for the regression model was above 75% for both HIV positive and HIV negative populations again showing that the regression model for these stratified populations were a good fit. When the populations were combined the area under the curve of the regression model was lower than 75% and this signifies that there could be other factors affecting low birth weight deliveries in the general population that the study did not look at.

4.4.2 Still births

Tables 4.9 and **4.10** below show the univariate and multivariate odds ratios for the various factors associated with still births for the combined population and the disaggregated HIV groups.

Table 4.9a Unadjusted odds ratios for factors associated with still births

Variable	Category	All populations			HIV Positive			HIV Negative		
		OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Number with outcome			10			2			8	
N			603			304			299	
Age										
	<20		reference			collinearity			reference	
	20-34	1.9	0.2-16.2	0.544				1.9	0.2-17.3	0.567
	35+	2.9	0.3-27.8	0.367				6.1	0.6-60.3	0.123
Residence						collinearity				
	Rural		collinearity						collinearity	
	Peri-Urban	2.2	0.5-10.6	0.332				3.3	0.6-17.5	0.155
	Urban		reference						reference	
Level of Education										
	None	2.2	0.4-11.4	0.364	5.1	0.3-83.9	0.254	1.4	0.2-13.5	0.749
	Primary	0.71	0.17-3	0.64				0.9	0.2-4	0.875
	Secondary +		reference			reference			reference	
Maternal Comorbidity										
	No		reference			collinearity			reference	
	Yes	3.2	0.4-26.4	0.283				3.3	0.4-29.2	0.279

Table 4.9b Unadjusted odds ratios for factors associated with still births

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Parity										
	Nulli		reference			reference			reference	
	Multi	0.8	0.2-2.8	0.704	0.4	0.02-5.7	0.465	1.24	0.3-5.3	0.773
Gestational Age at Booking										
	<20 weeks		reference			reference			reference	
	>20 weeks	0.7	0.2-2.4	0.567	0.7	0.04-10.9	0.784	0.7	0.2-2.9	0.635
Prematurity		2.6	0.5-12.6	0.234	collinearity			3	0.6-15.6	0.189
HIV Status										
	Neg		reference							
	Pos	0.2	0.05-1.1	0.073						
ART Timing										
	Pre-conception					collinearity				
	Post-conception									

In the unadjusted model various variables including age, rural residence, maternal comorbidities, premature delivery and timing of ART initiation were dropped for the HIV positive population because of collinearity. For the HIV negative population rural residence was dropped from the model because of collinearity as well. This means that these variables were highly corelated with each other and this is possibly due to the very few observations noted especially for the HIV positive cohort where only 2 still births were recorded in this sub population.

There were higher odds of delivering still born infants with increasing maternal age, peri-urban residence, no maternal education, the presence of a maternal comorbidity and premature delivery. When stratified by HIV status the odds for no maternal education were higher for HIV positive women at 5 times higher odds compared to 40% higher odds for HIV negative women.

However, none of these factors analysed were statistically significant in the univariate analysis for still births.

Table 4.10a Adjusted odds ratios for factors associated with still births

Variable	Category	All populations			HIV Positive			HIV Negative		
		OR	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Number with outcome			10			2			8	
N			603			304			299	
Age										
	<20		reference						reference	
	20-34	4.5	0.5-45.1	0.198		collinearity		3.2	0.3-36	0.342
	35+	8.7	0.6-129.5	0.116				4.1	0.7-188.4	0.095
Residence										
	Rural	collinearity				collinearity			collinearity	
	Peri-Urban	2.7	0.5-14.5	0.26				3.4	0.5-20.8	0.193
	Urban		reference						reference	
Level of Education										
	None	2.5	0.4-14.3	0.32	6.2	0.3-124.7	0.229	1.6	0.2-16.6	0.698
	Primary	0.7	0.2-2.9	0.59				0.9	0.2-4.4	0.902
	Secondary +		reference						reference	
Maternal Comorbidity										
	No		reference			collinearity			reference	
	Yes	2.2	0.2-25.1	0.525				1.8	0.1-26.8	0.664

Table 4.10b Adjusted odds ratios for factors associated with still births

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Parity										
	Nulli		reference			reference			reference	
	Multi	0.4	0.1-2.1	0.307	0.3	0.01-9.4	0.488	0.5	0.1-3.1	0.444
Gestational Age at Booking										
	<20 weeks		reference			reference			reference	
	>20 weeks	0.9	0.2-3.5	0.898	1.8	0.05-63.9	0.736	0.9	0.2-3.9	0.84
Prematurity		2.2	0.4-12.4	0.36		collinearity		2.8	0.4-18.3	0.277
HIV Status										
	Neg		reference							
	Pos	0.2	0.05-1.2	0.079						
ART Timing										
	Pre-conception					collinearity				
	post-conception									

In the adjusted model for stillbirth deliveries the odds for delivering a still born infant for the combined cohort increased from at least 2 times higher odds for the 20–34-year age group and at least 3 times higher odds for the 35 years and older age group to at least 4 times and 8 times higher odds respectively. This change was not evident for the other variables. This was however not statistically significant. All the variables in the multivariate analysis for all the populations were not statistically significant.

The post estimation findings for the logistic model for still births is shown below:

Table 4.11 Post estimation for the logistic regression model for still births

Post estimation test	**All populations**	**HIV positive**	**HIV negative**
Pearson chi-square (goodness of fit)	p=0.9999	No observations	p=0.9068
Area under the curve	75.73%	No observations	72.03%
Link test (_hatsq)	p=0.507	p=0.37	p=0.484

For the combined population the model was a good fit with all the three different post-estimation showing this as shown in the table. Not enough observations were available for the HIV positive cohort and the post estimation tests show this. The area under the curve for the HIV negative women was below 75% and this shows that there may be

other factors beyond those analysed under the study that could explain still births in this subpopulation.

4.4.3 Preterm deliveries

While preterm deliveries were analysed as a predictor variable in the analysis for low-birth-weight deliveries and still births the factors associated with preterm births were also analysed separately. **Tables 4.12** and **4.13** below show the univariate and multivariate analyses done for preterm deliveries.

Table 4.12a Unadjusted odds ratios for factors associated with preterm deliveries

Variable	Category	All populations OR	95% CI	p value	HIV Positive OR	95% CI	p value	HIV Negative OR	95% CI	p value
Number with Outcome			54			23			31	
N			603			304			299	
Age										
	<20		reference			reference			reference	
	20-34	0.6	0.3-1.1	0.09	0.7	0.2-2.6	0.598	0.6	0.3-1.3	0.197
	35+	0.7	0.3-1.5	0.314	1.1	0.3-4.6	0.861	0.4	0.1-1.6	0.221
Residence										
	Rural	2.6	1.03-6.8	0.046	2.1	0.6-7.4	0.238	3.2	0.7-13.9	0.122
	Peri-Urban	1.4	0.3-6	0.663	0.8	0.1-8.3	0.867	2.1	0.3-16.2	0.462
	Urban		reference			reference			reference	
Level of Education										
	None	0.9	0.3-2.6	0.812	0.5	0.1-4.4	0.562	1.2	0.3-4.3	0.829
	Primary	1.3	0.7-2.4	0.35	1.8	0.7-4.4	0.191	1.0	0.5-2.3	0.943
	Secondary +		reference			reference				
Maternal Comorbidity										
	No		reference						reference	
	Yes	3	0.8-7.7	0.111		collinearity		4.3	1.2-14.8	**0.022**
Parity										
	Nulli		reference			reference			reference	
	Multi	1	0.5-1.7	0.889	1.8	0.6-5.3	0.318	0.8	0.4-1.6	0.483

Table 4.12a Unadjusted odds ratios for factors associated with preterm deliveries

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Gestational Age at Booking										
	<20 weeks		reference			reference			reference	
	>20 weeks	0.8	0.5-1.4	0.419	0.7	0.3-1.7	0.456	0.9	0.4-1.8	0.689
HIV Status										
	Neg		reference							
	Pos	0.7	0.4-1.2	0.23						
ART Timing										
	Pre-conception					reference				
	Post-conception				1.8	0.6-5.3	0.318			

In the unadjusted model for preterm deliveries the presence of a maternal comorbidity was dropped from the analysis for HIV positive women because of collinearity. This means that maternal comorbidity was strongly correlated with another variable in the model.

For the combined population women residing in rural areas had at least two times higher odds of delivering prematurely when compared with those in the urban areas. This was up to 6 times higher odds and was statistically significant. For HIV negative women higher odds of delivering prematurely were noted for women with a maternal comorbidity with at least 4 times higher noted for this population when compared with those with no maternal comorbidity. This ranged from 20% higher odds to up to 14 times higher odds and was statistically significant.

Higher odds for delivering prematurely were noted in HIV positive women who resided in rural areas (2.1), had primary level education, were multiparous and in those starting ART after conceiving (1.8 for all three variables). These however did not reach statistical significance.

Table 4.13a Adjusted odds ratios for factors associated with preterm deliveries.

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Number with outcome			54			23			31	
N			603			304			299	
Age										
	<20		reference			reference			reference	
	20-34	0.6	0.2-1.3	0.163	0.7	0.1-3.6	0.623	0.7	0.2-1.8	0.427
	35+	0.6	0.2-1.6	0.273	0.9	0.1-5.7	0.877	0.5	0.1-2.2	0.318
Residence										
	Rural	2.3	0.9-6.1	0.094	2.1	0.6-7.6	0.275	2.8	0.6-12.7	0.181
	Peri-Urban	1.3	0.3-5.5	0.77	0.6	0.05-6.6	0.679	1.9	0.2-14.8	0.542
	Urban		reference			reference			reference	
Level of Education										
	None	0.9	0.3-2.8	0.882	0.6	0.1-4.9	0.615	1.2	0.3-4.5	0.837
	Primary	1.3	0.7-2.3	0.423	1.9	0.7-4.7	0.165	0.9	0.4-2.1	0.86
	Secondary +		reference			reference			reference	
Maternal Comorbidity										
	No		reference			reference			reference	
	Yes	2.1	0.6-6.6	0.225		collinearity		3.7	1.02-13.4	**0.047**
Parity										
	Nulli		reference			reference			reference	
	Multi	1.4	0.7-3.1	0.361	4.9	0.9-27	0.067	1	0.4-2.7	0.995

Table 4.13b Adjusted odds ratios for factors associated with preterm deliveries.

		All populations			HIV Positive			HIV Negative		
Variable	**Category**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Gestational Age at Booking										
	<20 weeks		reference			reference			reference	
	>20 weeks	0.9	0.5-1.5	0.602	0.8	0.3-2	0.652	1	0.4-2.2	0.993
HIV Status										
	Neg		reference							
	Pos	0.8	0.4-1.4	0.444						
ART Timing										
	Pre-conception					reference				
	Post-conception				5.2	0.9-29.7	0.063			

In the adjusted model only the presence of a maternal comorbidity was significantly associated with premature delivery for HIV negative women. The odds of a delivering prematurely were almost 4 times those of women with no existing comorbidity going up to almost 13 times higher odds.

In the HIV positive population multiparity and starting ART post conceiving were associated with almost 5 times higher odds noted for these subgroups. These odds were much higher than those seen in the univariate model (1.8) and those seen for HIV negative women (1 for parity) suggesting that these variables are possible effect modifiers in the relationship between premature deliveries and HIV status. These were however not statistically significant.

The results of the post estimation for the logistic regression models for preterm deliveries are shown in **table 4.14** below:

Table 4.14 Post estimation for the logistic regression model for preterm deliveries

Post estimation test	All populations	HIV positive	HIV negative
Pearson chi-square (goodness of fit)	p=0.4581	0.0834	p=0.6409
Area under the curve	64.2%	71.4%	66%
Link test (_hatsq)	p=0.651	p=0.194	p=0.346

The Pearson chi-square and the _hatsq p values were not statistically significant for all the three different populations and show that generally the models were a good fit. The areas under the curve were however all below 75% showing that in general there are other factors that can lead to preterm deliveries that were not explored in this study.

4.5 Summary

This chapter presented the findings of this retrospective cohort study. 9% of the delivering women had a low-birth-weight delivery and preterm delivery and the still birth rate was 16 per 1000 births. There were no differences in adverse birth outcomes by HIV status in both the unadjusted and adjusted models. Low birth weight deliveries were associated with low level of education, the presence of maternal comorbidities, nulliparity, and premature deliveries while preterm deliveries were significantly

associated with the presence of maternal comorbidities. None of the explored factors were significantly associated with stillbirths.

CHAPTER 5 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This main objective of this retrospective cohort study was to determine if there are differences in adverse birth outcomes by HIV status in Masvingo province. This chapter discusses the findings of the study in relation to findings in similar settings, offers some recommendations and ends with suggesting some potential research areas.

5.2 Discussion

The demographic characteristics of the study participants are revealing of the general state of maternal health care services in the province. The proportion of women booking before 20 weeks of gestation, generally regarded as early booking was significantly lower than those booking late at 41%. Utilization of antenatal care services has been previously noted to be poor in rural settings in Zimbabwe as Mutowo, Yazbek, van der Wath, and Maree (2021) note.

The reasons for poor utilization of antenatal care services include among others distance from primary care facilities, lack of knowledge among maternal services users, lack of spousal or family involvement, fear of HIV in testing in women or their partners and household responsibilities among others. Being a predominantly rural province with the majority of facilities being in rural areas the picture previously noted elsewhere is also applicable in the province.

Yahaya et al (2024) noted a link between poor utilization of antenatal care services and still birth deliveries while Chasekwa et al (2022) noted a link between poor utilization of antenatal care services and adverse outcomes including still births, low birth weight deliveries and preterm deliveries.

In this study we noted that hypertensive disorders of pregnancy were present in 2% of the pregnancies and syphilis infection in pregnancy in 1% of the study sample. This is different from the globally noted 5-8% prevalence of hypertensive diseases of pregnancy and in Zimbabwe this has been previously reported at 19.4% (Muti, Tshimanga, Gombe, Bangure, and Chonzi, 2015). Syphilis seroprevalence has been previously reported at 2.5% of all pregnancies (Pham et al, 2005). These differences may be due to poor documentation in the source registers used in this study but may also reflect poor access to these tests.

Syphilis testing is commonly done at the same sitting as HIV testing for those with unknown or previously known HIV negative results at booking and is usually present as a dual testing kit. Availability of standalone syphilis test kits can sometimes be a challenge in facilities. Availability of blood pressure machines at primary care facilities is sometimes a challenge and women may go through their pregnancy with no blood pressure testing.

Both syphilis and hypertensive diseases of pregnancy are recognized risk factors of adverse birth outcomes with higher risk of still births and preterm deliveries noted (Yahaya et al, 2024). In Zimbabwe pregnancy induced hypertension has also been noted to be among the top 5 causes of maternal mortality, giving even more need for regular testing in pregnancy.

5.2.1 Prevalence of adverse birth outcomes

In this study we note that low birth weight deliveries accounted for 9% of all deliveries. This is in keeping with program data from the District Health Information System (DHIS) which shows that from 17 738 deliveries in 2024 in the province a total of 1 433, which is 8%, were low birth weight deliveries. It also tallies with findings from

the Multiple Indicators Cluster Survey (MICS) of 2019 which showed that low birth weight deliveries accounted for 8.7% of all deliveries in the sampled population (ZimStat, 2019). Chasekwa et al (2021) also noted that low birth weight deliveries accounted 9.8% of all deliveries. This shows that our study sample closely represented the population from which they were drawn.

These figures are lower than the 15-20% estimates from the World Health Organization but also remain high considering the goal to have reduced low birth weight deliveries by 30% by 2025 (WHO 2014). Low birth weight deliveries are associated with multiple short term and long-term consequences for the infants delivered with a low birth weight. In the short-term low birth weight is associated with high fetal and neonatal mortality and morbidity and in the medium to long term period it is associated with inhibited physical and cognitive development and a higher risk of non-communicable diseases.

The stillbirth rate that we observed in this study of 16 per 1000 births is also similar to rates observed by Chasekwa et al (2021) of 2.3% and those by the National Institute for Health Research (2021) who also reported 16 per 1000 deliveries. Still birth deliveries are a source of maternal grief and grief for the whole family and community and can lead to stigma and discrimination for the woman affected.

Preterm deliveries accounted for 9% of all deliveries in this study. This is much lower than the 18.2% reported previously by Chasekwa et al (2022). In this study calculation of gestational age at delivery was mainly based on using the date of the last known menstrual period by the pregnant women and as this depends on recall there is a possibility that preterm deliveries were underreported in this study. Preterm deliveries

are the leading cause of death in children under 5 years and in the fight to reduce child mortality rates addressing the factors associated with prematurity is key.

5.2.2 HIV Status and adverse birth outcomes

The key finding from our study is that HIV status was not significantly associated with adverse birth outcomes. These findings closely mirror those of Mugo et al (2022) and Dadhwal et al (2017) but are also in direct contrast to those of Tukei et al (2021), Worku et al (2022) and Slogrove et al (2024).

A key distinguishing feature of our study is that it looks at women who are taking a dolutegravir based regimen as part of their first line. All previous studies on the subject have looked at non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor-based (PI) ART or compared dolutegravir based ART with other regimens but to our knowledge no studies have compared outcomes for HIV positive women taking dolutegravir based ART and HIV negative women. Dolutegravir, an integrase strand transfer inhibitor, is fairly new and currently is part of the recommended first line regimen by WHO. It is hailed for superior viral suppression and for having a high genetic barrier to resistance when compared to NNRTI based ART.

A second distinguishing feature of this study is that it enrolled women who were virally suppressed and clinically stable in their pregnancy. This contrasts with studies by Tukei and Slogrove where some participants' virological status was unknown at the time of delivery. From Mugo and Dadhwal's work it is notable that the majority of women were either virally suppressed or had a high CD4 cell count, hallmarks of being clinically stable. These features seem to suggest that for HIV positive women being clinically stable, immunologically sound, having viral suppression and the use of an efficacious ART regimen may be key to good outcomes during the maternal period.

Another key finding in this study is that timing of ART was not associated with birth outcomes. This is in keeping with the findings of Dadabhai et al (2019). For still births this is also in keeping with the findings of Quinn et al (2022). In their study however, Quinn et al noted that ART initiation before the 20th week of gestation was associated with higher risk of preterm deliveries. The ART regimen that was used in their study was an NNRTI based regimen. Again, this would seem to suggest that being on an ART regimen, even one started during the pregnancy, and having viral suppression may be key to better outcomes compared to no ART. It is possible that the dolutegravir based ART offers direct benefits in and of itself, but more research would be required on that.

In the adjusted models by HIV status, it is notable that while level of education and maternal comorbidities were significant for low-birth-weight deliveries for HIV negative women, the same factors were not significant for HIV positive women who in general for all adverse outcomes showed very different patterns to those noted for HIV negative women. For level of education, it may be that HIV positive women have more frequent contact with health care facilities as they get their ART refills and other services, and they may get more health education on a variety of topics and hence their level of education and place of residence may not affect the occurrence of adverse birth outcomes.

It may be paramount to assess the risk factors for adverse birth outcomes in HIV positive women as a standalone group to assess the risk factor patterns for this group. It is quite possible that exposure to antiretroviral therapy or other factors peculiar to HIV positive women may give a different risk factor profile for this subpopulation.

5.2.3 Factors associated with adverse birth outcomes

The main factors associated with low-birth-weight deliveries in this study were level of education, parity, the presence of maternal comorbidities and premature delivery. Feresu, Harlow, and Woelk (2015) have previously demonstrated that rural residence, lack of antenatal care, maternal comorbidities like pregnancy induced hypertension and anaemia and preterm labour are some factors related to a high risk of low-birth-weight deliveries.

In this study rural residence was associated with higher odds for low-birth-weight delivery but this did not reach statistical significance. Rural based women may find it hard to attend to antenatal care regularly because of longer distances to health care facilities and because of poor socio-economic status and poorer nutrition when compared with their urban counterparts and maternal nutrition is a noted factor in low-birth-weight deliveries (WHO 2025).

Nulliparity has been previously associated with low-birth-weight deliveries. Garces et al (2020) and Lin, Lu, Chen, Li and Guo (2021) demonstrated that compared to multiparous women nulliparous women had a higher risk of delivering low birth weight infants. This goes to show the need for adequate antenatal care and giving special attention to nulliparous women to try and address these adverse outcomes in this population.

Low level of education can be a multifactorial risk factor. Women with lower level of education may not utilize antenatal care services appropriately as Mutowo et al (2021) note. In addition, because of low level of education they may be of low socioeconomic status and may not access highly nutritious foods that are important for the foetus to

grow. This may also be related to poor knowledge on the food groups that are required for a balanced diet for fetal growth.

Maternal comorbidities are a well noted factor in development of adverse birth outcomes. Pregnancy induced hypertension has been implicated in preterm deliveries, intrauterine growth restriction and intra-uterine fetal death (Muti et al, 2015), outcomes that this study explored. It is quite possible that maternal comorbidities are underreported in this study because of undertesting.

In this study none of the factors analysed for stillbirth deliveries showed statistical significance. Higher odds for still birth deliveries were noted for higher maternal age, peri-urban residence, no education and the presence of a maternal comorbidity. The NIHR (2021) showed that previous history of a still birth delivery, maternal medical complications and fewer than 4 antenatal visits were strongly associated with stillbirth deliveries in Zimbabwe. Advanced maternal age has also been cited by Dongarwar, Aggawarl, Barning, and Salihu (2019) as being a risk factor for still birth delivery. This goes to show the need for early booking and close monitoring of women with previous still births for the development of any medical complications that may lead to pregnancy loss.

For preterm deliveries the main noted associated factor was maternal comorbidities. Parity, rural residence and starting ART after conception were associated with higher odds of delivering prematurely even though this didn't reach statistical significance. Starting ART after conception but before 20 weeks of gestation has been previously noted by Quinn et al (2022) to be associated with higher risk of preterm delivery when compared to pre-conception ART and this may need to be researched further to identify the reasons for this.

The logistic regression model post estimation showed that the models were generally a good fit but for still birth for HIV positive women and for both cohorts for preterm deliveries it was evident that other factors could also be responsible for the adverse birth outcomes. Factors such as number of antenatal care visits and maternal nutritional status were not assessed in this study and these have been previously shown to be associated with adverse birth outcomes (Yahaya et al, 2024).

This study only looked at birth outcomes at the time of delivery but did not look at outcomes in the immediate or long term post-natal period. Outcomes for HIV exposed and non-exposed infants may be different in the long term, and it may be key for this to be researched.

5.3 Limitations of the study

- This was a retrospective cohort study using secondary data and hence had limited control over which variables to use in the analysis. It is possible that there are other factors associated with adverse outcomes that were not explored in this study.
- The study limited itself to HIV positive women on dolutegravir based first line antiretroviral therapy and as such the results may not apply to other antiretroviral regimens.
- The study was done in Masvingo province, and the results may only be generalizable to this setting.
- Estimated gestational age was calculated based on the last known menstrual period for the woman which can be subject to recall bias.

5.3 Conclusions

The use of dolutegravir based first line antiretroviral therapy may lead to comparable birth outcomes between HIV positive women who are viral suppressed and HIV negative women. ART timing does not seem to affect these results. There is need to encourage early booking and close monitoring for women for maternal comorbidities to try and ensure they are closely managed, and adverse outcomes can be prevented. More still needs to be done to improve maternal and neonatal health within the province if the country is to attain the sustainable development goals of reducing neonatal and under 5 mortalities by 2030.

5.4 Implications

At the peak of the HIV/AIDS pandemic mortality and morbidity were higher among HIV positive individuals compared to HIV negative individuals and this translated to maternal and neonatal health. Evidence from this study shows that adverse birth outcomes for women on dolutegravir based first line therapy are comparable with HIV negative women. This has several implications on public health.

Dolutegravir based first line ART may need to continue to be recommended for women of childbearing age even when there are regimen changes until the new regimens have been shown to have a beneficial effect on birth outcomes. Achieving viral suppression seems to be the important aspect for women on ART and hence close virological monitoring for women of childbearing age both prior to and during pregnancy may need to be emphasised to ensure adverse birth outcomes are prevented.

The study showed slightly different risk factor patterns for HIV negative women and HIV positive women which may show a need for more research on the risk factors for adverse birth outcomes for HIV positive women as a standalone cohort.

5.5 Recommendations

The recommendations from this study are summarized in **table 5.1** below.

Table 5.1 Recommendations from the study

Finding	Recommendation	Timeline	Responsible authority
HIV positive women on the currently recommended first line ART regimen have comparable outcomes with HIV negative women.	If first line ART regimens are to be changed it is recommended that DTG based first line be maintained for women of childbearing age unless and until evidence exists to show that the new regimens have beneficial effects for maternal and neonatal health.	Ongoing	MOHCC
ART timing is not associated with adverse outcomes	Increase awareness among women of childbearing age of the benefits of ART for their health and their infants irrespective of when ART is initiated	Immediate	MOHCC, Media houses
Pregnant women continue to book their pregnancies late	Increase awareness among women of childbearing age on the benefits of early booking and attending the requisite number of antenatal care visits	Immediate	MOHCC, media houses
Pregnant women continue to book their pregnancies late	Address access to health care sites issues for women especially in rural areas through offering more sites or integrated outreaches that include antenatal care services for women in hard-to-reach areas	Immediate	MOHCC, Development partners
Poor access to testing for non-communicable diseases	Increase availability of blood pressure machines and glucose testing machines to increase access to and identification of women with PIH and gestational diabetes so that proper care may be given to these women.	Immediate	MOHCC

5.6 Suggestions for Further Research

- A prospective cohort study that looks at outcomes beyond delivery into the early and late post-natal periods.
- A larger scale study to look at risk factors for adverse outcomes among HIV positive women
- A cohort study to assess factors associated with stillbirths in Masvingo Province

List of References

Abadiga, M., Mosisa, G., Tsegaye, R., Oluma, A., Abdisa, E., & Bekele, T. (2022). Determinants of adverse birth outcomes among women delivered in public hospitals of Ethiopia, 2020. *Archives of Public Health, 80*(12). doi:10.1186/s13690-021-00776-0

Bruce-Brand, C., Wright, C., & Schubert, P. (2021). HIV, Placental Pathology, and Birth Outcomes—a Brief Overview. *The Journal of Infectious Diseases, 224*(S6), S683-S690. doi:10.1093/infdis/jiab240

Chaibva, B., Olorunju, S., Nyadundu, S., & Beke, A. (2019). Adverse pregnancy outcomes, 'stillbirths and early neonatal deaths' in Mutare district, Zimbabwe (2014): a descriptive study. *BMC Pregnancy and Child Birth, 19*(86). doi:10.1186/s12884-019-2229-3

Chasekwa, B., Ntozini, R., Church, J., Majo, F., Tavengwa, N., & Mutasa, B. L. (2022). Prevalence, risk factors and short-term consequences of adverse birth outcomes in Zimbabwean pregnant women: a secondary analysis of a cluster-randomized trial. *International Journal of Epidemiology, 61*(S7), 1785-1799. doi:10.1093/ije/dyab248

Chibura, T., Twabi, H., Maluleke, K., & Musekiwa, A. (2024). Trends and factors associated with adverse pregnancy outcomes in Zimbabwe, 2005 - 2015. *South African Medical, 114*(6). doi:10.7196/SAMJ.2024.v114i6b.1399

Dadabhai, S., Gadama, L., Chamanga, R., Kawalazira, R., Katumbi, C., B, M., . . . Taha, T. (2019). Pregnancy outcomes in the era of universal antiretroviral treatment in sub-Saharan Africa (POISE Study). *Journal of Acquired Immune Deficiency Syndrome, 80*(1), 7-14. doi:10.1097/QAI.0000000000001875.

Dadhwal, V., Sharma, A., Khoiwal, K., Deka, D., Sarkar, P., & Vanamail, P. (2017). Pregnancy Outcomes in HIV-Infected Women: Experience from a Tertiary Care Center in India. *International Journal of MCH and AIDS, 6*(1), 75-81. doi:21106.ijma.196

Dongarwar, D., Aggarwal, A., Barning, K., & Salihu, H. (2020). Stillbirths among Advanced Maternal Age Women in the United States: 2003-2017. *Int J MCH AIDS, 9*(1), 153-156. doi: 10.21106/ijma.346

Fentie, E., Yeshita, H., & Bokie, M. (2022). Low birth weight and associated factors among HIV positive and negative mothers delivered in northwest Amhara region referral hospitals, Ethiopia,2020 a comparative crossectional study. *PLoS One*. doi:10.1371/journal.pone.0263812

Feresu, S., Harlow, S., & Woelk, G. (2015). Risk Factors for Low Birthweight in Zimbabwean Women: A Secondary Data Analysis. *PLOS One, 10*(6), 1-17. doi:10.1371/journal.pone.0129705

Friis, H., Gomo, E., Nyazema, N., Ndhlovu, P., Krarup, H., Kaestel, P., & Michaelsen, K. (2004). Maternal body composition, HIV infection and other predictors of gestation length and birth size in Zimbabwe. *British Journal of Nutrition, 92*, 833-840. doi:10.1079/BJN20041275

Garces, A., Perez, W., Harrison, M., Hwang, K., Nolem, T., Goldenberch, R., . . . Hambridge, K. (2020). Association of parity with birthweight and neonatal death in five sites: The Global Network's Maternal Newborn Health Registry study. *Reproductive Health, 17*(Suppl 3), 182-189. doi:10.1186/s12978-020-01025-3

Ikumi, N. a. (2022). Preterm Birth in Women With HIV: The role of the placenta. *Frontiers in Global Women's Health, 3*. doi:10.3389/fgwh.2022.820759

Ikumi, N., Matjila, M., Gray, C., Anumba, D., & Pillay, K. (2021). Placental pathology in women with HIV. *Placenta*, 27-36.

Lin, L., Lu, C., Chen, W., Li, C., & Guo, V. (2021). Parity and the risks of adverse birth outcomes: a retrospective study among Chinese. *BMC Pregnancy and Childbirth, 21*. doi:10.1186/s12884-021-03718-4

Lookman, S., Brummel, S., Ziemba, L., Stranix-Chibanda, L., McCathy, K., Coletti, A., . . . Currier, J. (2021). Efficacy and safety of dolutegravir- and tenofovir alafenamide fumarate-containing HIV antiretroviral treatment regimens started in pregnancy: a randomised controlled trial. *Lancet*, 1276-1292.

Moseholm, E., Katzenstein, T., Pedersen, G., Johansen, I., Wienecke, L., Storgaard, M., . . . Weis, N. (2022). Use of antiretroviral therapy in pregnancy and association with birth outcome among women living with HIV in Denmark: A nationwide, population-based. *HIV Medicine, 23*, 1007-1018. doi:10.1111/hiv.13304

Msukwa, M., Kesier, O., Jahn, A., Van Oosterhout, J., Edmonds, A., Phiri, N., . . . Estill, J. (2019). Timing of combination antiretroviral therapy (cART) initiation is not associated with stillbirth among HIV-infected pregnant women in Malawi. *Trop Med Int Health, 24*(6), 727-735. doi:10.1111/tmi.13233

Mugo, C., Nduati, R., Osoro, E., Nyawanda, B., Mirieri, H., Hunsperger, E., . . . Wamalwa, D. (2022). Comparable Pregnancy Outcomes for HIV-Uninfected and HIV-Infected Women on Antiretroviral Treatment in Kenya. *The Journal of Infectious Diseases, 226*, 678-686. doi:10.1093/infdis/jiac128

Murray, C., Portwood, C., Sexton, H., Kumarendran, M., Brandon, Z., Kirtley, S., & Hemelaar, J. (2023). Adverse perinatal outcomes attributable to HIV in sub-Saharan Africa from 1990 to 2020: Systematic review and meta-analyses. *Communications medicine*. doi:10.1038/s43856-023-00331-8

Muti, M., Tshimanga, M., Gombe, N., Bangure, D., & Chonzi, P. (2015). Prevalence of pregnancy induced hypertension and pregnancy outcomes among women

seeking maternity services in Harare, Zimbabwe. *BMC Cardiovascular Disorders, 15*. doi:10.1186/s12872-015-0110-5

Mutowo, J., Yazbek, M., van der Wath, A., & Maree, C. (2021). Barriers to using antenatal care services in a rural district in Zimbabwe. *International Journal of Africa Nursing Sciences, 15*. doi:10.1016/j.ijans.2021.100319

Ohuma, E., Moller, A., Bradley, E., Chakwera, S., Hussain-Alkhateeb, L., Lewin, A., . . . Moran, A. (2023). National, regional, and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis. *The Lancet*, 1261-1271.

Perneger, T., Courvoisier, D., Hudelson, P., & Gayet-Ageron, A. (2015). Sample size for pre-tests of questionnaires. *Qual Life Res, 24*(1), 147-151. doi:doi: 10.1007/s11136-014-0752-2

Pham, L., Woelk, G., Ning, Y., Madzime, S., Mudzamiri, S., Mahomed, K., & Willliams, M. (2005). Seroprevalence and risk factors of syphilis infection in pregnant women delivering at Harare Maternity Hospital, Zimbabwe. *Central African Journal of Medicine, 51*(3-4), 24-30. Retrieved from https://www.researchgate.net/publication/5952640_Seroprevalence_and_risk_factors_of_syphilis_infection_in_pregnant_women_delivering_at_Harare_Maternity_Hospital_Zimbabwe

Quinn, M., Wiliams, P., Muhihi, A., Duggan, C., Ulenga, N., Al-Beity, F., . . . Sudfeld, C. (2022). Timing of Antiretroviral Therapy Initiation and Birth Outcomes Among Pregnant Women With Human Immunodeficiency Virus in Tanzania. *The Journal of Infectious Diseases, 226*, 687-695. doi:10.1093/infdis/jiac224

Research, N. I. (2021). *Global Health Research Group on Stillbirth Prevention and Management in Sub-Saharan Africa: Zimbabwe Report 2021.* NIHR.

Setia, M. S. (2016). Methodology Series Module 1: Cohort Studies. *Indian J Dermatol.* , 21–25.

Shinar, S., Agrawal, S., Ryu, M., Walmsley, S., Serghides, L., Yudin, M., & Murphy, K. (2021). Perinatal outcomes in women living with HIV-1 and receiving antiretroviral therapy- a systematic review and meta-analysis. *Acta Obstetricia et Gynecologica Scandinavica, 101*, 168-182. doi:10.1111/aogs.14282

Slogrove, A., Bovu, A., de Beer, S., Phelanyane, F., Williams, P., Heekes, A., . . . Boulle, A. (2024). Maternal and birth outcomes in pregnant people with and without HIV in the Western Cape, South Africa. *AIDS, 38*, 59-67. doi:10.1097/QAD.0000000000003728

Tamirat, K., Sisay, M., Tesema, G., & Tessema, Z. (2021). Determinants of adverse birth outcome in Sub-Saharan Africa: analysis of recent demographic and health surveys. *BMC Public Health*.

Thompson, K., Meyers, D., Lee, Y., Cu-Uvin, S., & Wilson, I. (2022). HIV-Positive and HIV-Negative Women with Medicaid Have Similar Rates of Stillbirth and Preterm Birth. *Women's Health Reports, 3*(1), 1-9. doi:10.1089/whr.2021.0068

Ticconi, C., Mapfumo, M., Dorrucci, M., Naha, N., Tarira, E., Pietropolli, A., & Rezza, G. (2003). Effect of maternal HIV and malaria infection on pregnancy and perinatal outcome in Zimbabwe. *Journal of Acquired Immune Deficiency Syndrome, 34*(3), 289-274.

Tripathy, J. P. (2013). Secondary Data Analysis: Ethical Issues and Challenges. *Iran J Public Health.* , 1478–1479.

Tukei, V., Hoffman, H., Greenberg, L., Thabelo, R., Nchephe, M., Mots'oane, T., . . . Tiam, A. (2021). Adverse Pregnancy Outcomes Among HIV-positive Women in the Era of Universal Antiretroviral Therapy Remain Elevated Compared With HIV-negative Women. *The Paediatric Infectious Diseases Journal, 40*(9), 821-826. doi:10.1097/INF.0000000000003174

Twabi, H., Manda, S., & Small, D. (2020). Assessing the effects of maternal HIV infection on pregnancy outcomes using cross-sectional data in Malawi. *BMC Public Health, 20*. doi:10.1186/s12889-020-09046-0

UN. (2024). *3 Ensure healthy lives and promote well-being for all at all ages.* Retrieved from Sustainable Development Goals: https://sdgs.un.org/goals/goal3

UNAIDS. (2020). *Progress towards the Start Free, Stay Free, AIDS Free targets: 2020 report.* Geneva: UNAIDS.

UNAIDS. (2023, July 13). *New report from UNAIDS shows that AIDS can be ended by 2030 and outlines the path to get there*. Retrieved from UNAIDS: https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2023/july/unaids-global-aids-update

UNICEF. (2023). *Country Office Annual Report 2023: Zimbabwe.* Retrieved from https://www.unicef.org/media/152316/file/Zimbabwe-2023-COAR.pdf

Wedi, C., Kirtley, S., Hopewell, S., Corrigan, R., Kennedy, S., & Hemelaar, J. (2016). Perinatal Outcomes associated with maternal HIV infection: a systematic review and meta-analysis. *The Lancet HIV, 3*, 33-48. doi:10.1016/S2352-3018(15)00207-6

WHO. (2014). *Low birth weight policy brief.* Geneva: WHO.

WHO. (2023). *Preterm birth*. Retrieved from World Health Organization: https://www.who.int/news-room/fact-sheets/detail/preterm-birth

WHO. (2024). *Low Birth Weight*. Retrieved from WHO: https://www.who.int/data/nutrition/nlis/info/low-birth-

weight#:~:text=Low%20birth%20weight%20has%20been,2500%20grams%20(5.5%20pounds).

WHO. (2024). *Stillbirth*. Retrieved from World Health Organization: https://www.who.int/health-topics/stillbirth#tab=tab_1

WHO. (2025). *Low Birth Weight.* Retrieved from https://www.who.int/data/nutrition/nlis/info/low-birth-weight

Worku, W., Azale, T., Ayele, T., & Mekonnen, D. (2022). Effects of HIV Infection on Pregnancy Outcomes among women attending antenatal care in referral hospitals of the Amhara Regional State, Ethiopia: A prospective cohort study. *International Journal of Women's health, 14*, 1405-1423. doi:10.2147/IJWH.S382685

Worku, W., Azale, T., Ayele, T., & Mekonnen, D. (2022). Effects of HIV Infection on Pregnancy Outcomes Among Women Attending Antenatal Care in Referral Hospitals of the Amhara Regional State, Ethiopia: A Prospective Cohort Study. *International Journal of Women's Health*, 1405-1423.

Yahaya, H., Adeyemo, Q., & Kumah, A. (2024). Adverse perinatal outcomes and their associated determinants in Sub-Saharan Africa. *Journal of Medicine, Surgery, and Public Health, 3*. doi:10.1016/j.glmedi.2024.100124

Yang, L., Cambou, M., Segura, E., De Melo, M., Santos, B., Varella, I., & Nielsen-Saines, K. (2022). Patterns of pregnancy loss among women living with and without HIV in Brazil, 2008−2018. *AJOG Global Reports, 13*. doi:10.1016/j.xagr.2022.100121

Yingjuan, L., Peng, J., Liu, Y., Xia, W., Chen, S., Yongcheng, S., & Lin, Y. (2023). Association between maternal HIV infection and the risks of preterm birth and low birth weight in Chengdu, China: a propensity score matching approach. *BMJ Open, 13*. doi:10.1136/bmjopen-2022-071205

Zash, R., Jacobson, D., Diseko, M., Mayondi, G., Mmalane, M., Essex, M., . . . Shapiro, R. (2017). Comparative Safety of Antiretroviral Treatment Regimens in Pregnancy. *JAMA Pediatr, 171*(10). doi:10.1001/jamapediatrics.2017.2222

Zash, R., Jacobson, D., Diseko, M., Mayondi, G., Mmalane, M., Essex, M., . . . Shapiro, R. (2018). Comparative safety of dolutegravir-based or efavirenz-based antiretroviral treatment started during pregnancy in Botswana: an observational study. *Lancet Global Health, 6*(7), 804-810. doi: 10.1016/S2214-109X(18)30218-3

ZimStat. (2016). *Zimbabwe Demographic and Health Survey 2015.* Harare: ZimStat.

ZimStat. (2023). *Zimbabwe 2022 Population and Housing Census Report.* Harare: Zimbabwe Statistical Agency.

ZimStat, & UNICEF. (2019). *Multiple Indicator Cluster Survey: 2019 SURVEY FINDINGS REPORT.* Harare: ZimStat and UNICEF.

Appendices

Appendix 1: Data collection table

DISTRICT:													
Name of Facility:													
Date of data collection:									Total number of birth records:				
ANC Number (UIC)	Patient Age	Place of residence (Rural, urban, peri-urban)	Level of education	Maternal comorbidities	HIV Status	Duration on ART	Viral load at booking	Parity	Gestational Age at booking	Gestational Age at Delivery	Birth Weight	Fetal status at delivery (Live birth or still birth)	APGAR Score

Appendix 2: AUREC Approval letter

AFRICA UNIVERSITY
A United Methodist-Related Institution
"Investing in Africa's future"
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)

P.O. Box 1320 Mutare, Zimbabwe, Off Nyanga Road, Old Mutare-Tel (+263-20) 60075/60026/61611 Fax: (+263 20) 61785 Website: www.africau.edu

Ref: AU 3577/25 22 January, 2025

VITALIS GUVAVA
C/O Africa University
Box 1320
MUTARE

RE: **DISPARITIES IN BIRTH OUTCOMES BETWEEN HIV-NEGATIVE AND HIV-POSITIVE WOMEN UNDERGOING ANTIRETROVIRAL THERAPY IN MASVINGO PROVINCE, JANUARY 2023- DECEMBER 2024**

Thank you for the above-titled proposal you submitted to the Africa University Research Ethics Committee for review. Please be advised that AUREC has reviewed and approved your application to conduct the above research.

The approval is based on the following.

a) Research proposal

- **APPROVAL NUMBER** AUREC 3577/25
  This number should be used on all correspondences, consent forms, and appropriate document
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** January 24, 2025
- **EXPIRATION DATE** January 24, 2026
- **TYPE OF MEETING**: Expedited
  After the expiration date, this research may only continue upon renewal. A progress report on a standard AUREC form should be submitted a month before the expiration date for renewal purposes.
- **SERIOUS ADVERSE EVENTS** All serious problems concerning subject safety must be reported to AUREC within 3 working days on the standard AUREC form.
- **MODIFICATIONS** Prior AUREC approval is required before implementing any changes in the proposal (including changes in the consent documents)
- **TERMINATION OF STUDY** Upon termination of the study a report has to be submitted to AUREC.

AFRICA UNIVERSITY
RESEARCH ETHICS COMMITTEE (AUREC)
APPROVED
P.O. BOX 1320, MUTARE, ZIMBABWE

Yours Faithfully

MARY CHINZOU
FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE

Appendix 3 PMD approval letter

Telephone: 263 - 39-262465

Telegraphic Address
E-mail: masvingopmd@gmail.com
Fax: 265145/262411
Internet:

ZIMBABWE

Reference:
EC Number:
MINISTRY OF HEALTH &
CHILD CARE
P O Box 147
MASVINGO

9 January 2025

Dr Vitalis Guvava
JF Kapnek Zimbabwe
42 Bates Avenue
Milton Park
Harare

RE: DISPARITIES IN BIRTH OUTCOMES BETWEEN HIV-NEGATIVE AND HIV-POSITIVE WOMEN UNDERGOING ANTIRETROVIRAL THERAPY IN MASVINGO PROVINCE, JANUARY 2023- DECEMBER 2024

Reference is made to the application you made for approval of the above-named study to be conducted in Chiredzi, Masvingo, and Mwenezi Districts of Masvingo province.
We are pleased to let you know that the study is approved. We look forward to getting feedback from you once the study is completed and to know about the findings and how they can help improve neonatal and child health outcomes in the province and the country at large.

Yours sincerely,

PROVINCIAL MEDICAL DIRECTOR
MUSAMA BUILDING
1 JAN 2025
P.O. BOX 147, MASVINGO
ZIMBABWE

DR A. SHAMU
(PMD MASVINGO)