

UNIVERSITY OF CAPE TOWN

**DIABETES AND HYPERTENSION IN PREGNANCY: ASSOCIATION
WITH ADVERSE BIRTH OUTCOMES AMONG PREGNANT WOMEN
LIVING WITH AND WITHOUT HIV IN CAPE TOWN, SOUTH
AFRICA (2017 – 2019):
A RETROSPECTIVE STUDY**

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Dissertation submitted in partial fulfilment of the requirements for the degree of

**Master of Public Health
(Epidemiology and Biostatistics)**

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PREAMBLE

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My sincerest gratitude goes to my parents and immediate family for all the sacrifices they have made and their unconditional support throughout my academic life. In particular, I thank my dear brother Paul Lehloa who polished the path and inspired me to make it this far.

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ABSTRACT

Background

Research suggests that human immunodeficiency virus (HIV) and antiretroviral therapy (ART) increases the likelihood of having hypertension and diabetes. In pregnancy, maternal exposures such as HIV and ART, hypertension, and diabetes are associated with adverse birth outcomes. However, studies tend to explore these factors in isolation. In South Africa, there is a high prevalence of HIV and obesity, thus a high risk of hypertension and diabetes. This study sought to explore the interplay of these non-communicable diseases (NCDs) with HIV in pregnancy and the prevalence of adverse birth outcomes.

Methods

A retrospective secondary data analysis of data collected from pregnant women where questionnaires, body anthropometrics and birth outcomes were obtained in an urban antenatal facility was conducted. A total of 470 (48%) participants living with HIV and 505 (52%) without HIV were included in this analysis. The prevalence of hypertension and diabetes was reported as overall and stratified by body mass index (BMI) and HIV status in the population. Pregnancy exposures of interest were HIV, hypertension, diabetes, HIV and hypertension, HIV and diabetes, and ART initiated during and pre-pregnancy. Factors associated with hypertension and diabetes were assessed using regression analysis although we could not retrieve the models on diabetes due to sample size restrictions. The adverse birth outcomes of interest were small for gestational age (SGA), large for gestational age (LGA), preterm delivery (PTD), low birthweight (LBW), and high birthweight (HBW). Median and interquartile range, proportions, and regression analysis were used to analyse adverse birth outcomes.

Results

Overall hypertension was approximately 9% whereas diabetes was 2% in this population. Although we could not achieve statistical significance, obese women living with HIV (WLHIV) had higher hypertension prevalence compared to normal weight WLHIV (14% vs 2%). A unit increase in gravidity, parity and age were significantly associated with increased odds of having hypertension (gravidity OR 1.02; 95% confidence interval (CI): 1.01 – 1.04, parity OR 1.02; 95% CI: 1.01 – 1.04, age OR 95% CI: 1.00 – 1.01). Being obese was significantly associated with increased odds of having hypertension (OR 1.07; 95% CI: 1.02

– 1.13). While there were some associations between increased LBW, PTD and SGA and HIV and ART initiation timing, statistical significance could not be achieved. Hypertension was significantly associated with more LBW and PTD (LBW aOR 2.05; 95% CI: 1.14 – 3.68, PTD aOR 4.67; 95% CI: 2.63 - 8.15). WLHIV and diabetes had a significantly higher prevalence of PTD (26% vs 9%) compared to WLHIV only. There were no appreciable differences in the prevalence of diabetes by HIV status. Stratifying by BMI, total diabetes was significantly higher in the obese group (3%) compared to the normal weight (1%) and overweight group (1%). LBW prevalence was significantly higher in diabetic pregnancies than in non-diabetic pregnancies (30% vs 10%). A higher SGA, LGA, HBW and LBW were recorded for WLHIV and diabetes compared to WLHIV only (SGA: 43% vs 11%, LGA 28% vs 8%; HBW: 14% vs 4%, LBW: 43% vs 11%).

Conclusion

The findings suggest that a double burden of HIV plus an additional non-communicable disease needs to be closely monitored to prevent increased poor birth outcomes. Extensive dietary and physical activity plans need to be incorporated to mitigate the occurrence of NCDs and poor birth outcomes in this high BMI population especially in WLHIV. The prevalence of diabetes and hypertension in WLHIV needs to be further studied, especially in the HIV-burdened Southern African settings.

LIST OF ABBREVIATIONS

A

ANC	Antenatal Care
ART	Antiretroviral Therapy
AGA	Appropriate Gestational Age

B

BMI	Body Mass Index
BDS	Birth Defects Surveillance

C

CD4	Cluster of differentiation-4, T lymphocyte
CI	Confidence Interval

G

GA	Gestational Age
GDM	Gestational Diabetes Mellitus

H

HIV	Human Immunodeficiency Virus
HAART	Highly Active Antiretroviral Therapy

I

IQR	Inter-Quartile Range
IUGR	Intrauterine Growth Restriction

L

LBW	Low Birth Weight
LGA	Large for Gestational Age
LMIC	Low-Middle-Income Countries

M

MOU	Midwife Obstetric Unit
MCR	Maternity Case Records

N

NCD	Non-Communicable Diseases
NNRTI	Non-nucleoside reverse-transcriptase inhibitor

O

OR	Odds Ratio
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P

PER	Pregnancy Exposure Register
PI	Protease Inhibitor
PMTCT	Prevention of Mother-to-Child Transmission
PTD	Preterm Delivery

S

SD	Standard Deviation
SGA	Small for Gestational Age
SSA	Sub-Saharan Africa

W

WHO	World Health Organization
WLHIV	Women living with HIV
WNLHIV	Women not living with HIV

ORGANIZATION OF THE DISSERTATION

Part 1: Protocol

This part outlines the field background literature, rationale, objectives, research methodology, statistical analysis to be carried out, ethical considerations and references.

Part 2: Journal manuscript

Formatted using submission guidelines of BMC Pregnancy and Hypertension peer-reviewed journal. This part outlines the background, methodology used in the study, results, and a discussion.

Part 3: Appendices

This part includes results supplementary tables, ethical approval documents, and submission guidelines for BMC pregnancy and hypertension.

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PART 1: RESEARCH PROTOCOL

1. INTRODUCTION

1.1 Background

Hypertensive disorders of pregnancy and diabetes are two of the most common conditions closely monitored during pregnancy due to associated sequelae that threaten pregnancy, thereby contributing to maternal and child morbidity or mortality. The prevalence of hypertensive disorders of pregnancy is estimated to affect 10-15% of pregnancies globally (1,2). Perinatal medicine classifies these disorders into categories of gestational hypertension, pre-eclampsia, eclampsia, and chronic hypertension as conditions of concern related to elevated blood pressure (3). In normotensive pregnancies, blood pressure is expected to lower steadily until the middle of the second trimester and then peak steadily until the end of term (4). Because of the possibility of multiple abnormal trajectories that may occur, measurements are taken at each antenatal visit to determine high-risk pregnancies. South African guidelines for maternal care indicative of blood pressure that is outside the norms is to initiate them with either Alpha-methyldopa, low-dose aspirin or Magnesium sulphate depending on the level of risk (4). These women are then followed up much more frequently in between routine antenatal care (ANC), usually at primary health care facilities.

Hypertension and diabetes can either be chronic or occur transiently during pregnancy. Research has shown that due to shared metabolic pathways between hypertension and diabetes, women with a history of hypertension are at twice the risk of developing diabetes (5,6). Hypertensive disorders of pregnancy have a co-prevalence of 4% with gestational diabetes mellitus (GDM) (7). Frequent screening for diabetes is recommended particularly for women with risk factors of diabetes such as insulin resistance, a history of maternal diabetes, family history of diabetes and overweight (8). According to the International Classification of Disease (ICD-10), diabetes is confirmed if fasting blood glucose is 126mg/dL (7.0 mmol/L) or higher (9). Either glucose tolerance screening or glucose tolerance test is used to test for GDM depending on the setting and available resources (10). During pregnancy, changes occur in the body that affect the uptake and use of glucose, consequently worsening chronic diabetes or inducing gestational diabetes. Such include gestational weight gain and a build-up of glucose in the bloodstream due to hormone secretions of the placenta that render insulin inactive (10).

Hypertension and diabetes complications in pregnancy are associated with adverse birth outcomes. Poorly managed diabetes and glucose intolerance have been linked to neonatal

jaundice, respiratory distress syndrome, stillbirths, high birthweight (HBW), large for gestational age (LGA) and very early or late births (8,11). Consistently high fasting blood glucose of 6.7mmol/l heightens the risks of these conditions (8). On the other hand, hypertension in pregnancy is associated with an increased risk of small for gestational age (SGA) (12), preterm delivery (PTD), emergency C-section, neural tube defects and heart defects (13-16). Some studies cite long neonatal intensive care unit stays and intrauterine growth restrictions (IUGR) to be common negative birth outcomes in hypertensive pregnancies (17,18).

Both hypertension and diabetes are mediated by metabolic syndrome which is closely linked to obesity. Obesity is a major risk factor for hypertension and diabetes among other non-communicable diseases (NCDs) (19). Low and middle-income countries (LMICs) have seen a triple growth in obesity and double disease burden of NCDs (19) thereby, changing the narrative of obesity being primarily a problem of developed countries. Several factors account for these trends including modern diets, reduced physical activity due to improved transport modes, and urbanisation (19). Additionally, there is evidence that childhood poverty, malnutrition and stunting which are common in South Saharan Africa (SSA) result in adult abdominal fat and obesity which might account for the vast growth of NCDs in poor LMICs (20). Furthermore, cultural views regard heavy body size in women as portraits of beauty, health and affluence (21).

South Africa, a middle-income country is similarly experiencing a rise in obesity. Around the year 2016, 88% of women and 34% of males were in the category of overweight/obese/severely obese (22). There are notable gender disparities in overweight/obesity data, with females having increased from 56% to 68% and males from 29% to 31% in the period of 1998 to 2016 globally (22). In 2019, the country was ranked on the World Health Organisation (WHO) report as one of the unhealthiest on Earth, battling the highest obesity and probability of dying from diabetes, cancers and cardiovascular diseases (23). South African studies show a high prevalence of obesity at presentation for ANC visits. A study from Johannesburg Hospital South Africa found the prevalence of obesity among pregnant women to be at 44% (24). A corresponding higher occurrence of GDM and urinary tract infections and late and preterm labour were more common in these women (24).

In addition to the burden of obesity and NCDs in SSA, South Africa ranks amongst countries riddled with the highest prevalence of human immunodeficiency virus (HIV) in the world

(25). Subsequently, the country has the largest Antiretroviral therapy (ART) program. With recent vertical health system interventions that implemented early treatment to achieve complete viral suppression, underweight, commonly known as HIV wasting has been eradicated through ART. In pregnant women, the test and treat coupled with prevention of mother-to-child transmission (PMTCT) bears boastful results of babies being born without HIV from mothers living with HIV. This approach also called option B+ was first implemented by WHO for all pregnant women who test positive regardless of their Cluster of differentiation-4, T lymphocyte (CD4) count (26,27). However, some ART sub-types have been linked to obesity, hypertension and diabetes which could potentially add to the sheer worldwide growth of NCDs (28,29). The relationship between ART and associated weight gain accompanying metabolic disarrangements and NCDs is a growing topic in public health. Moreover, these drugs are additionally associated with high blood pressure and related complications such as pre-eclampsia (21,24,25).

HIV has been independently associated with birth outcomes such as low birthweight (LBW) largely in women who are not virally suppressed (30,31). Furthermore, this group of women has been shown to experience higher rates of stillbirths and neonatal deaths than women not living with HIV (WNLHIV) (32). A study conducted in Nairobi demonstrated that women living with HIV (WLHIV) were 3 times more likely to have low birthweight babies long before the advent of universal ART (33). A high prevalence of stillbirths is also reported in areas that were highly impacted by HIV for extended periods reinforcing that HIV alone has significant negative results in pregnancy (32). Some recent studies have observed links between certain classes of ART and adverse birth outcomes in pregnancy. Groups such as highly active antiretroviral therapy (HAART) and protease inhibitors (PIs) have been associated with the risk of PTD, LGA, SGA and stillbirths (29,34).

Pregnancy exposures play a profound role in immediate birth outcomes and long-term health outcomes well into adulthood. Such exposures make up the environment of the foetus which may be either nurturing or harmful. Studies on epigenetics have pointed out that hypertension and diabetes are some of the exposures that can influence gene expression for the late-life risk of developing the same conditions in adulthood (35,36). The process of epigenetic methylation mediates the association between adult risk of metabolic conditions including diabetes and hypertension and exposure to pregnancy hypertension and diabetes (35,37,38). Analysis of placental tissue confirms the presence of such biological markers that alter gene expression between women with these metabolic conditions and healthy comparator subjects

(37-39). These have led to conclusions that gestational hypertension and diabetes may inflate the risk of future hypertension and diabetes mellitus in the offspring of cohorts (37,39).

With the whole world grappling with the increasing growth of NCDs, related morbidity and mortality, the direct burden that HIV and ART add to the prevalence of hypertension and diabetes must be mapped and understood. This is a dilemma for women with HIV who are then faced with a double burden of disease and their offspring who will in turn add to future NCD burden. Given the increasing population of pregnant women who are both obese and receiving ART in Cape Town, South Africa, we aim to investigate the prevalence of diabetes and hypertension and birth outcomes in a population of this group undergoing routine ANC in this setting.

1.2 Rationale

Obesity is increasingly common among people living with HIV on ART, a paradigm shift from the historic view of HIV as a wasting disease (40,41). This is a concern since obesity is the predecessor of multiple metabolic disarrangement conditions such as hypertension and diabetes (42). Additionally, some studies have shown ART regimens such as PIs to be associated with gestational hypertension and diabetes in pregnant women and subsequent chronic hypertension and diabetes (28,43,44). This implies a double burden of disease in people living with HIV especially in South Africa where HIV is prevalent at presentation at ANC facilities. However, there is limited data on the impact of these recent obesity trends on the burden of hypertension and diabetes. Therefore, this study aims to assess the prevalence of diabetes and hypertension by HIV status as well as factors associated with these conditions in pregnant women in Cape Town, South Africa.

Exposure to metabolic conditions during pregnancy presents a distinct public health vulnerability as they are not only a threat to maternal health but also that of offspring. Perinatal exposures such as diabetes and hypertension are implicated in foetal programming and are associated with poor pregnancy and birth outcomes (45). Poor birth outcomes including LBW, SGA, LGA and PTD have been observed in women living without HIV with these conditions (15,46). HIV/ART have also been shown to have negative impacts on birth outcomes. Despite the rise in NCDs in HIV-prevalent countries in sub-Saharan Africa, the context of the interplay between HIV/ART and obesity-related complications, particularly diabetes and hypertension in modulating birth outcomes is lacking. Therefore, the secondary

aim of this study is to examine the combined effects of HIV/ART, hypertension, and diabetes on birth outcomes.

1.3 Aims and objectives

Aim

To investigate the prevalence and factors associated with diabetes and hypertension; and associations with adverse birth outcomes among women living with and without HIV in Cape Town, SA

Objectives

1. To examine the prevalence of chronic and gestational diabetes and hypertension in pregnant women by HIV and BMI status.
2. To examine factors associated with diabetes and hypertension in pregnant women.
3. To assess the association of diabetes, hypertension and HIV with adverse birth outcomes.

2. METHODOLOGY

2.1 Study design

The current study will be a secondary analysis of data collected in the parent study titled “B Positive” whose principal aim was to monitor the WHO Option B+ PMTCT effectiveness and impact at a population level in the entire Western Cape Province, South Africa. The parent study was a post-intervention evaluation of expanded ART access in pregnancy. The cohort formed part of the Pregnancy Exposure Register (PER) and Birth Defects Surveillance (BDS) whose purposes are in the names.

The proposed study will draw on “B Positive” cohort data collected in the period between 2017 to 2019 in pregnant WLHIV and WNLHIV attending their first ANC visit at the Gugulethu clinic.

2.2 Study setting

This study focuses on the Gugulethu Midwife Obstetric Unit (MOU), serving low-risk pregnant women and escalating risky pregnancies to its referral sites Mowbray MOU and Groote Schuur Hospital. Gugulethu MOU is a primary care facility that serves a low-income population of around 5000 pregnancies per annum. The prevalence of HIV on presentation to antenatal care in the Western Cape is high with a seroprevalence of 30% as of 2014 (47).

However, there has been a decline in antenatal prevalence in the entire Western Cape province from 2014 to 2017 from 18.7 to 18.0, an indirect positive development with regards to achieving the 90 90 90 targets (48). The commonality of obesity in child-bearing age across South Africa (22) and the prevalence of HIV particularly in this setting makes it convenient to understand the outcomes of the two and related NCDs hypertension and diabetes on birth outcomes.

2.3 Study population and sampling

Gugulethu MOU participated in the PER study which has approximately 5000 pregnancies per annum. A nested cohort study of 989 WLHIV, and WNLHIV, starting or continuing ART were recruited for a more comprehensive analysis of ART and PMTCT outcomes from the PER study. All children of the mentioned pregnancies were included in the collection of birth outcomes. Enrolled women were ≥ 18 years of age and intended to reside in Cape Town for at least 1 year post-partum and were willing to consent to the study.

2.4 Data collection

Interviews/Questionnaires

Several interview methods were used to collect data in the parent study at multiple points of contact. Face-to-face interviews were used during the first antenatal visit to gather information from all consenting participants and again twice during pregnancy during their visits to the research facility at Gugulethu.

Rigorously prepared questionnaires were administered by trained staff in participants' mother-tongue predominantly isiXhosa to collect extensive information on dietary demographic and clinical data, concomitant medications with related acute or chronic conditions, drug abuse, food intake, mental health and ART origination experiences (see Appendix 3 for maternal Audit form, maternal demographics, maternal ART/HIV history forms, maternal medication use and side effects and obstetric data collections forms).

Intensive clinical measurements

Vital information such as blood pressure and BMI-related information such as height and weight were measured by a trained study nurse.

Maternity Case Records (MCR)

The documents contain information on every aspect of pregnancy and delivery gathered at every medical visit. Pregnancy exposures such as alcohol use during pregnancy, chronic

medication and reports of pregnancy/birth outcome examination are routinely recorded. Data was abstracted retrospectively from these documents.

Table 1:1 List of variables to be included in the analysis

Variable	Scale	Categories
Maternal variables		
Age (years)	Numerical – Continuous Categorical - Ordinal	Mean (standard deviation, SD) /median (interquartile range, IQR) <24, 25-29, >30
Education	Categorical - Binary	Finished high school, Did not finish high school
Employment Status	Categorical - Binary	Employed, Not Employed
Socio-economic Status	Categorical - Ordinal	Lowest, Medium, Highest
BMI	Numerical – continuous Categorical – ordinal	Mean (SD)/median (IQR) Normal, Overweight, Obese
Gravidity	Numerical – Discrete Categorical - Ordinal	Quartile Category Proportions 1, 2, >3
Gestational age (GA) at presentation	Numerical – Continuous	Mean (SD)/ Median (IQR)
Parity	Numerical – Discrete Categorical - Ordinal	Quartile Category Proportions 0, 1, >2
HIV status	Categorical – binary	Living with HIV Not living with HIV
ART status	Categorical – binary	ART initiation during pregnancy ART initiated before pregnancy Not living with HIV
Completed High School	Categorical – binary	Yes, No
Alcohol use	Categorical - Ordinal	Yes, No

Smoking status	Categorical - Ordinal	Yes, No
ART regimen	Categorical - Nominal	Non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based, PI-based
CD4 cell count	Numerical – Continuous	Mean(SD)/Median (IQR)
	Categorical - Ordinal	<300, 301-600, >600
Pregnancy outcomes		
GA at delivery (weeks)	Categorical - Ordinal	PTD (<37) Full-term delivery (≥37)
Birth weight (g)	Numerical – continuous	Mean (SD)/median (IQR)
	Categorical – ordinal	Low (<2500), normal (2500 -3999g), high (≥4000g)
Size for Gestational Age	Categorical - Ordinal	Small (SGA) <10 percentile Appropriate (AGA): ≥10 up to 90 th percentile Large (LGA) >90 th percentile

Maternal Exposures of Interest

Hypertension: participants will be classified according to:

- Chronic hypertension - detected before the week of presentation for ANC
- Gestational hypertension – First detected at presentation for ANC or ≥24 weeks GA
- No hypertension

Diabetes mellitus: participants will be classified into:

- Chronic diabetes - detected before the week of presentation for ANC
- Gestational Diabetes – First detected at presentation for ANC or ≥24 weeks GA
- No diabetes

HIV status:

- Living with HIV

- Not living with HIV

ART status. The exposure will be categorised into the following:

- ART initiated pre-pregnancy
- ART initiated during pregnancy (both newly tested and ART naïve participants)
- Not HIV infected

BMI

- Normal (18.5-24.9 kg/m²)
- Overweight (25-29.9 kg/m²)
- Obese (≥ 30 kg/m²)

Outcomes of interest

- Birthweight

The outcome will be categorised into 3 groups: LBW <2500g, normal birthweight ≥ 2500 g ranging to 3999g and HBW ≥ 4000 g.

- Size for gestational age

Size for gestational age will be divided into SGA (babies in the <10 percentile), appropriate size (AGA: babies in the ≥ 10 up to 90th percentile) and LGA (>90th percentile). These are the norms developed by the INTERGROWTH-21st Project Standards (49). Calculations will be derived based on infant GA, birthweight and sex inputted into the INTERGROWTH-21st Project online tool.

- GA at birth

This outcome will be categorized into 2 groups: preterm (<37 gestational weeks) and full-term (≥ 37 gestational weeks) with the primary focus on preterm births. In the parent study, two options were used to derive maternal GA according to availability and priority of measurement accuracy. In the absence of an ultrasound or for women who presented for their first ANC late, the first day of the last menstrual period and symphysis-fundal height were used to estimate maternal GA as ultrasound accuracy declines for late presentations. In this study, three data components will be used to confirm GA at delivery for the neonates in the study. Those will be maternal GA at booking into the ANC, the date it was estimated and the delivery date obtained from clinic records.

2.5 Data management and analysis plan

Data safety

Database entries will be limited to anonymous participant identification numbers, and reference to tracing information (located in a locked cabinet in the project office) will be made as necessary by the project coordinator. No personal identification information such as names will be stored with the data. All data is stored in a password-protected database.

Data Analysis

The statistical and data analysis will be carried out in R-4.1.1 for Windows (32/64 bit). Continuous variables will be summarized using the means and SD for normally distributed variables; or the median and IQR for skewed distributions. Categorical variables will be described using proportions, Chi-squared analysis, or the Kruskal-Wallis test. The overall prevalence of the adverse birth outcomes (PTD, LBW, HBW, LGA and SGA) across the exposure groups will be computed.

Associations (as stated in Aim 3) will be analysed and adjusted for relevant confounders and effect modifiers. The analysis will focus on the following exposure comparisons:

- WLHIV and WNLHIV across the whole study
- Among WLHIV: those with hypertension and those with no hypertension
- Among WLHIV: those with diabetes and those with no diabetes

For each of the exposure combinations, descriptive statistics will be used to show the prevalence of the adverse birth outcomes (PTD, LBW, HBW, LGA and SGA). An analysis of regression models will allow us to estimate the relationship between HIV status alone and in combination with diabetes and hypertension and adverse outcomes of interest in pregnancy. Potential confounders determined *a priori* will be adjusted for.

3. ETHICAL CONSIDERATIONS

3.1 Informed consent

Since the study is a secondary research analysis, there will be no requirement for obtaining consent as participants had already consented that their information can be used for research and academic purposes within the bounds that their identity is protected. The burden in this study is to ensure that participants' information is kept safe, and this will be addressed as stated in the risks and benefits below for safeguarding the ethical principle of respect for

persons. However, necessary and ethical steps will also be taken to obtain the data from the rightful custodians of the data being the parent study researchers at the University of Cape Town and the Provincial Government of Western Cape. University of Cape Town Human Research Ethics Committee had approved the parent study (HREC 541/2015) and the Provincial Government of Western Cape (REFWC_2016RP6_286) (see appendix 2 for ethical clearance documents and informed consent for the parent study). This study will seek ethical clearance from the University of Cape Town Human Research Ethics Committee.

3.2 Privacy and Confidentiality

There shall not be any risk of loss of confidentiality in this study as the data used is de-identified. 5 digits codes were created in place of names for each participant to protect their identity. Other measures *ensured* in the parent study to *ensure the* security of data and confidentiality include:

- Data collection staff was thoroughly trained on how to obtain informed consent and collect data
- The paper-based MCRs and folders will not leave the site where the delivery occurred. They will be stored as is typically the case at those facilities.
- Data capture will take place electronically directly into Redcap electronic database (password protected) where personal identifying information will be excluded.

3.3 Risks and benefits

There are no direct benefits to the participants of this study as this is a retrospective analysis. There is minimal risk of loss of privacy, but this has already been addressed in the parent study through the use of identifiers. Additionally, data is stored in a password-protected database. However, the derived information and benefits can extend to all pregnant women of this community and women of similar characteristics of hypertension, diabetes, and HIV in similar settings. Information obtained can be used to inform their health management and make recommendations.

3.4 Reporting and Implementation

The study results will be submitted for peer review, updated, and published. The findings may also be shared with the community healthcare practitioners in Cape Town antenatal care centres and presented at conferences.

3.5 Logistics

Table 1:2 Study Timeline

Milestone	Time (Months)					
	December 2021	March 2022	June 2022	August 2022	December 2022	February 2023
Protocol Submission for ethical clearance						
Data Extraction						
Clean and merge data						
Data analysis						
Thesis and manuscript write-up						
Submission of the draft manuscript						
Finalise thesis and submit for marking						

3.6 Budget

This analysis is part of the requirements of the Master of Public Health and there shall not be any payment required to the student.

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1 PART 2: MANUSCRIPT

**Diabetes and hypertension in pregnancy: Association with adverse birth
outcomes among pregnant women living with and without HIV in Cape
Town, South Africa (2017 – 2019):**

A retrospective study

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1. ABSTRACT

Background

Although human immunodeficiency virus (HIV) and antiretroviral therapy (ART) has been implicated in increasing the likelihood of hypertension and diabetes, and all these conditions have been associated with adverse birth outcomes, studies tend to explore them in isolation. We explored the interplay of these non-communicable diseases (NCDs) with HIV/ART and adverse birth outcomes in South Africa where there is a high HIV burden.

Methods

A retrospective study was conducted on data collected from pregnant women where questionnaires, body anthropometrics, and birth outcomes were obtained in an urban South African facility. 470 participants living with HIV and 505 without HIV were included in this analysis. Hypertension and diabetes were studied by HIV and BMI status. Factors associated with hypertension and diabetes were assessed using regression. Medians, proportions, and regressions were used to estimate small for gestational age (SGA), large for gestational age (LGA), preterm delivery (PTD), low birthweight (LBW), and high birthweight (HBW).

Results

Although not significantly different, obese women living with HIV (WLHIV) had higher hypertension than normal weight WLHIV (14% vs 2%). A unit increase in gravidity, parity, age and being obese were significantly associated with increased odds of having hypertension (gravidity OR 1.02; 95% CI: 1.01 – 1.04, parity OR 1.02; 95% CI: 1.01 – 1.04, age OR 95% CI: 1.00 – 1.01, obesity OR 1.07; 95% CI: 1.02 – 1.13). Hypertension was significantly associated with more LBW and PTD (LBW aOR 2.05; 95% CI: 1.14 – 3.68, PTD aOR 4.67; 95% CI: 2.63 - 8.15). Women living with HIV (WLHIV) and diabetes had a significantly higher prevalence of PTD (26% vs 9%) compared to WLHIV only. Chronic diabetes was significantly higher in the obese group (3%) compared to the normal weight (1%) and

40 overweight group. A higher SGA, LGA, HBW and LBW were recorded for WLHIV and
41 diabetes compared to WLHIV only (SGA: 43% vs 11%, LGA 28% vs 8%: HBW: 14% vs
42 4%, LBW: 43% vs 11%).

43 **Conclusion**

44 The findings suggest that a double burden of HIV plus an additional non-communicable
45 disease needs to be closely monitored to prevent increased poor birth outcomes. The
46 prevalence of NCDs in WLHIV needs to be further studied, especially in HIV-burdened
47 South Africa.

48 **Keywords:** Pregnancy, obesity, Hypertension, Diabetes, HIV, adverse birth outcomes

2. BACKGROUND

Diabetes and hypertension are among the leading obstetric threats that contribute to increased risk of mortality, morbidity, and poor birth outcomes (50-52). The current global nutritional transition and urbanization have led to the worldwide spread of obesity and an increased risk of non-communicable diseases (NCDs) such as hypertension and diabetes (53,54).

Additionally, research in the context of South Africa and Sub-Saharan Africa (SSA) has made links between NCDs and the use of antiretroviral therapy (ART) (55,56).

Population groups, such as pregnant women, may be at a heightened risk of these NCDs compounded by ART use, gestational weight gain, gestational hypertension, and diabetes to acquire chronic hypertension and diabetes. A study conducted in Zambia indicates that women on ART are at a higher risk of gestational hypertension than both women not living with HIV (WNLHIV) and treatment-naïve women living with HIV (WLHIV) (57).

While HIV remains endemic in the low and middle-income countries (LMICs), ART use has improved outcomes for people living with HIV, eradicated wasting and led to higher survival rates and, thus a high prevalence of HIV (58). However, ART use has also been linked to a conglomerate of conditions ranging from hampered liver function and metabolic conditions such as lipodystrophy, and dyslipidaemia, all leading up to large belly circumference, obesity, and consequently NCDs (59-61).

Diabetes mellitus is estimated to be 10% among people with HIV on lifelong ART, an excess of 3.8% above the general population inclusive of infected individuals not taking ART (62,63). Pregnant WLHIV have also been reported to be at an inflated risk for gestational diabetes mellitus (GDM) (64). Multiple mechanisms linking HIV infection and gestational diabetes mellitus such as viral insults altering placental hormones that promote insulin resistance have been elucidated (64,65). HIV infection alone has also been linked to hypertensive disorders of pregnancy (66,67).

74 Diabetes, hypertension, and HIV are individually associated with adverse birth outcomes.
75 Diabetes pregnancy outcomes include foetal macrosomia, large for gestational age (LGA),
76 preterm delivery (PTD), bilirubinaemia, risk of caesarean section, and neonatal jaundice
77 (68,69). Hypertensive pregnancies are associated with stillbirths, PTD, small size for
78 gestational age (SGA), neonatal deaths, and maternal mortality (70-73). ART and HIV
79 pregnancy exposures are associated with PTD, low birth weight (LBW), and SGA (74-76).
80 The prevalence of HIV at first antenatal care (ANC) in Cape Town is estimated to be 18.8%,
81 a 0.8% increase from 2017 (77).

82 Owing to the literature on ART-related hypertension and diabetes, women presenting for
83 ANC could be more likely to have a higher prevalence of these conditions emanating from a
84 high body mass index (BMI), HIV, and ART use. The triple burden of HIV, hypertension,
85 and diabetes instigates the urgency to study the burden of negative birth outcomes contrasting
86 WNLHIV in this setting. The vast existing literature has explored exposure to HIV/ART,
87 diabetes and hypertension separately. There is limited research on the combined impact of
88 this triple burden on birth outcomes. Therefore, in this study, we examined the prevalence of
89 hypertension and diabetes at ANC by HIV and BMI status and associated negative birth
90 outcomes in Cape Town, South Africa.

METHODS

3.1 Study design

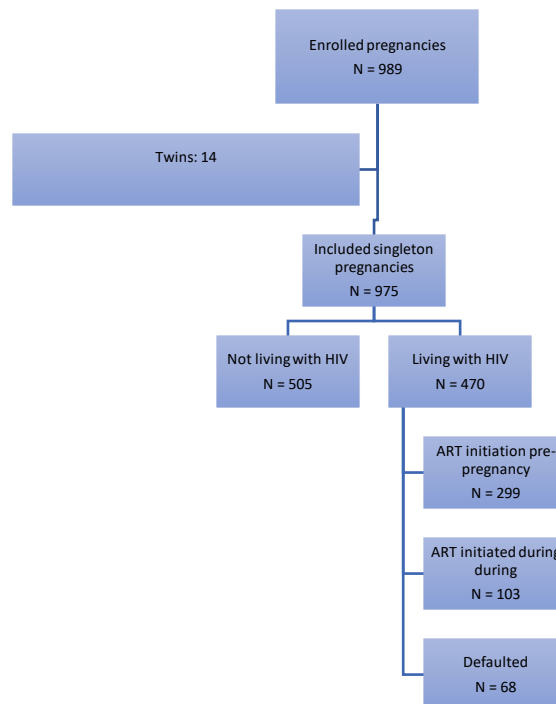
The current study was a secondary analysis of data collected in a prospective cohort study titled “B Positive” whose principal aim was to monitor the World Health Organisation (WHO) Option B+ Prevention of Mother-to-child transmission (PMTCT) effectiveness and impact at a population level in the entire Western Cape Province. The parent study data was collected in the period between 2017 to 2019 in pregnant women living with HIV and without HIV attending their first antenatal care.

3.2 Study setting

The parent study participants were recruited from Gugulethu Midwife Obstetric Unit (MOU), a primary care facility that serves a low-income population of around 5000 pregnancies per annum. The prevalence of HIV on presentation to antenatal care in the Western Cape is high with a seroprevalence of 30% as of 2014 (78). The commonality of obesity in child-bearing age across South Africa (79) and the prevalence of HIV, particularly in this setting, makes it convenient to understand the outcomes of the two and related NCDs, hypertension and diabetes on birth outcomes, per our secondary study aims.

3.3 Characteristics of Participants

A cohort of 989 women living with and without HIV, starting or continuing ART, were consecutively recruited for a more comprehensive analysis of ART and PMTCT outcomes in the parent study. Birth outcomes from all children of the aforementioned pregnancies were comprehensively recorded. The analysis included women ≥ 18 years of age with live singleton pregnancies booking for the first ANC in the period between January 2017 and July 2019. Excluded were pregnancies bearing more than one baby and those born by underweight women since the study focuses on obesity-related hypertension and diabetes.



115 *Figure 2:1* Flow diagram of included participants

116 3.4 Study procedures and data collection

117 The parent study was approved by the University of Cape Town (UCT) Faculty of Health
 118 Sciences Research Ethics Committee (HREC 541/2015) and the Western Cape Department of
 119 Health (REFWC_2016RP6_286) (Appendix 2). Written informed consent was obtained from
 120 all participants (Appendix 2). Ethical approval for the current study was obtained from the
 121 UCT-HREC (345/2022) (Appendix 2). Since the study was a secondary research analysis,
 122 obtaining participants' consent was not a requirement.

123 The parent study collected vital information such as blood pressure and BMI-related
 124 information such as height and weight, measured by a trained study nurse. Other methods of
 125 obtaining data included rigorously prepared questionnaires, and interviews administered by
 126 trained staff. The questionnaires collected extensive information on dietary, demographic and
 127 clinical data, concomitant medications with related conditions, substance use and ART

experiences (see Appendix 3 for questionnaires and data abstraction forms). Lastly, data was abstracted from maternity case records (MCR) which contain pregnancy exposures, medical information and delivery outcomes gathered at every medical visit and kept at the delivery site.

Hypertension, diabetes, weight, height and HIV/ART

The study abstraction forms were used to retrieve weight, height, hypertension, diabetes, HIV and ART use information that ANC nurses and practitioners routinely measure and store in MCR and other patient files. Some of this information was directly obtained by the study personnel from women booking for the first ANC wherever possible. Weight and height measurements were used to calculate BMI, which was categorized into normal (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²) and obese (≥ 30 kg/m²) by HIV status. Diabetes and hypertension statuses were categorized by gestational and chronic hypertension.

Gestational age (GA), birthweight, and Size for gestational age assessment

Two options were used to derive maternal GA at first presentation according to availability and priority of measurement accuracy. In the absence of ultrasound or for women who presented for their first ANC late, the first day of the last menstrual period and symphysis-fundal height were used to estimate maternal GA as ultrasound accuracy declines for late presentations. Three data components were used to confirm GA at delivery for the neonates in the study. Those were the maternal GA at booking into the ANC, the date it was estimated and the delivery date obtained from clinic records in the following formula:

Delivery GA = Maternal GA at first presentation + (delivery date – date at first presentation)

Delivery GA was categorised into preterm delivery (<37 gestational weeks) and full-term (≥ 37 gestational weeks). Infant birth weight and sex were obtained from data abstracted from

medical records. Infant birth weight was categorised into low (<2500g), normal (2500g – 3999g) and high ($\geq$ 4000g) (80). Size for gestational age categories were: SGA (<10th), AGA (10-90th) and LGA (>90th) measured in percentiles categorised according to the INTERGROWTH-21st Project norms (81). Calculations were derived based on infant GA, birthweight and sex inputted into the INTERGROWTH-21st Project online calculating tool (81).

3.5 Data analysis

The statistical and data analysis was carried out in R-4.1.1 for Windows (64-bit). Continuous variables were summarized using the median and interquartile range (IQR). Categorical variables were described using proportions and Chi-squared analysis. The prevalence of diabetes and hypertension in pregnant women by HIV and BMI was reported. Additionally, the prevalence of adverse birth outcomes across the exposure groups was computed. Analysis was carried out based on the following exposure combinations: HIV only, hypertension only, diabetes only, HIV and hypertension, HIV and diabetes, and ART initiated during and pre-pregnancy. Adjusted and unadjusted regression models were used to estimate the effects of these exposures on birth outcomes using odds ratios (OR) and confidence intervals (CI).

4. RESULTS

This analysis included a total of 975 women who had given birth to live singletons. Of the 470 (48%) women living with HIV, 74 (16%) had normal weight, 125 (27%) overweight and 222 (47%) obesity (Table 2.1). Of the 505 (52%) not living with HIV, 81 (16%) had normal weight, 123 (24%) overweight and 239 (47%) obesity. 64% of WLHIV had initiated ART pre-pregnancy, and 36% during pregnancy. Normal weight was equally distributed in both WLHIV and WNLHIV (30%). Overweight was higher in women living with HIV (28% vs 21%) whereas obesity was higher in WNLHIV (47% vs 40%) (Table 2.1).

Table 2.1 also makes a comparison of the baseline characteristics of included women by HIV status. Compared to women not living with HIV, women living with HIV were of older age (median 31 vs 27 years), of higher gravidity (≥ 3 vs 2), and more likely to have not completed matric (71% vs 64%). Alcohol use during pregnancy was equally reported in both the HIV group and the comparator group. Both groups were likely to have presented for their first ANC visit in the second trimester.

Maternal characteristics	Total N = 975 (%)	HIV status		Chi ² P
		HIV + N = 470 (%)	HIV – N = 505 (%)	
Age, years				<0.001
≤24	208 (21)	58 (12)	150 (30)	
≥25 – 29	285 (29)	122 (26)	163 (32)	
≥30	482 (49)	290 (62)	192 (38)	
Median IQR	29 (25-33)	31 (26-35)	27 (23-32)	
GA at presentation (weeks)				0.051
(≤13) 1 st trimester	292 (30)	154 (33)	138 (27)	
(14-28) 2 nd trimester	621 (64)	292 (62)	329 (65)	
(>28) 3 rd trimester	60 (6)	22 (5)	38 (6)	
Median (IQR)	17 (13-22)	17 (12-22)	18 (13-23)	
Missing	2 (0.2)	2 (0.4)	0	
Gravidity				<0.001
1	204 (21)	69 (15)	135 (27)	
2	284 (29)	125 (26)	159 (31)	
≥3	287 (50)	276 (59)	211 (42)	
Median (IQR)	2 (2-3)	3 (2-3)	2 (1-3)	
Parity				<0.001
0	249 (26)	83 (18)	166 (33)	
1	329 (33)	159 (39)	167 (33)	
≥2	400 (41)	228 (49)	172 (34)	
Median (IQR)	1 (0-2)	1 (1-2)	1 (0-2)	
Alcohol use				0.985
Yes	88 (9)	43 (9)	45 (9)	
No	885 (91)	426 (91)	459 (91)	
Missing	2 (0.2)	1 (0.2)	1 (0.2)	
Education				0.001
Completed matric.	312 (32)	129 (27)	183 (36)	
Matric not completed.	639 (66)	336 (71)	303 (64)	
Missing	24 (2)	5 (1)	19 (4)	
Employment status				0.649
Yes	417 (43)	197 (42)	220 (44)	
No	558 (57)	273 (58)	285 (56)	
ART initiation status				N/A
During pregnancy	171 (18)	171 (36)	N/A	
Pre-pregnancy	299 (31)	299 (64)		
BMI				0.819
Normal	155 (16)	74 (16)	81 (16)	
Overweight	248 (25)	125 (27)	123 (24)	
Obese	461 (47)	222 (47)	239 (47)	
Missing	111 (11)	49 (10)	62 (12)	
Median (IQR)	30.5 (26.4 - 35.9)	31(26-35)	31(27-37)	

NB: Some percentage values may not add to 100 due to rounding off.

Legend: Maternal baseline characteristics by HIV status expressed as proportions (%) of the included participants

Hypertension

The total estimated hypertension by HIV status in this population was 8% in WLHIV and 9% in the comparator group of WNLHIV although not statistically significant (Supplementary Table 3.4). Stratifying by BMI, total hypertension was higher in obese WLHIV compared to normal weight WLHIV (14% vs 2%) although this difference was not statistically significant (Table 2.2). The distribution of hypertension was equal in overweight participants regardless of HIV status (7%) (Table 2.2).

Chronic hypertension was higher in obese WLHIV than in the group of normal weight WLHIV (9% vs 1%, $P = 0.955$) (results not statistically significant). In the overweight group, chronic hypertension was higher in overweight WLHIV compared to overweight WNLHIV (4% vs 1%). Gestational hypertension was more prevalent in the obese WLHIV group (5%) than in the overweight (3%) and normal weight group (1%) ($p = 0.955$).

195 **Table 2:2** Prevalence of chronic and gestational hypertension by HIV and BMI status

	HIV- N = 505						HIV + N = 470					
	Normal N = 150 (%)	Over- weight N = 108 (%)	Obese N (%) 235	Missing BMI N = 12 (%)	Total N = 505 (%)	<i>Chi² P</i>	Normal N = 141(%)	Over- weight N = 132 (%)	Obese N = 188 (%)	Missing BMI N = 9 (%)	<i>Chi² P</i>	Total N = 470(%)
Chronic	3 (2)	1 (1)	10 (4)	0	14 (3)	0.409	1 (1)	5 (4)	16 (9)	0	0.955	22 (5)
Gestational	9 (6)	6 (6)	16 (7)	0	31 (6)		1 (1)	4 (3)	11 (5)	1 (11)		17 (3)
Total	12 (8)	7 (7)	26 (11)	0	45 (9)		2 (2)	9 (7)	27 (14)	1 (11)		39 (8)
hypertension												
Missing	0	0	0	0	0		0	0	0	0		0
hypertension												
Normotensive	138 (92)	101 (93)	209 (89)	12	460 (91)		139 (98)	123 (93)	161 (86)	8 (89)		431 (92)

Legend: Prevalence of chronic and gestational hypertension by HIV and BMI status in pregnancy (n = 975)

196 **Diabetes**

197 The total estimated prevalence of diabetes in this population was 2%. Stratified by HIV
 198 status, participants living with HIV had a lower prevalence of diabetes compared to
 199 participants in the comparator group (2% vs 3%) (Supplementary Table 3.3) although not
 200 statistically significant. Stratified by both HIV and BMI status, diabetes was equally 2% in
 201 obese WLHIV and overweight WLHIV whereas there was no diabetes in the normal weight
 202 group of WLHIV.

203 Stratifying by BMI only, total diabetes (regardless of the timing of diagnosis) was
 204 significantly higher in the obese group (3%) compared to the normal weight (1%) and
 205 overweight group (1%) (Supplementary Table 3.1). Gestational hypertension was estimated
 206 at 2% in obese participants living with HIV (Table 2.3).

Five patients (0.5%) were found to have both NCDs and HIV across the study, four of which were obese and one normal weight. One had developed both GDM and gestational hypertension whereas 3 had chronic hypertension and developed GDM. No further analysis could be carried out on these patients' birth outcomes for lack of statistical power.

Table 2:3 Prevalence of chronic and gestational diabetes by HIV and BMI status

	HIV- N = 505					HIV + N = 470						
	Normal N = 150 (%)	Over- weight N = 108 (%)	Obese N = 235 (%)	Missing BMI N = 12 (%)	<i>Chi</i> ² <i>P</i>	Total N = 505 (%)	Normal N = 141 (%)	Over- weight N = 132 (%)	Obese N = 288 (%)	Missing BMI N = 9 (%)	<i>Chi</i> ² <i>P</i>	Total N = 470 (%)
Chronic	0	0	4 (2)	0	0.546	4 (1)	0	3 (2)	1 (0)	0	0.225	4 (1)
Gestational	3 (2)	0	6 (2)	0		9 (2)	0	0	3 (2)	0		3 (1)
Total diabetes	3 (2)	0	10 (4)	0		13 (3)	0	3 (2)	4 (2)	0		7 (2)
Missing diabetes status	1 (1)	0	0	0		0	0	0	0	0		0
Not diabetic	146 (97)	108	137 (96)	12		491 (97)	141	129 (98)	284 (98)	9		463 (98)

Legend: Percentage proportion (%) of chronic and gestational diabetes by HIV and BMI status in pregnancy (n = 975)

Factors associated with having hypertension and diabetes in pregnancy.

Hypertension: HIV infection was associated with decreased odds of hypertension (OR 0.99; 95% CI: 0.96 – 1.03) though the results were not statistically significant (Table 2.4). Starting ART before pregnancy and starting during pregnancy did not seem to influence hypertension (ART initiated pre-pregnancy OR 1.00; 95% CI: 0.96 – 1.04; ART initiated during pregnancy OR 0.99; 95% CI: 0.94 – 1.04) though the results were not statistically significant. Alcohol use was associated with increased odds of having hypertension (alcohol OR 1.03; 95% CI: 0.97 – 1.10). However, these results were not statistically significant.

220 A year increase in age was significantly associated with a 1.01 increase in the odds of having
221 hypertension (95% CI: 1.00 – 1.01). A unit increase in gravidity and parity was significantly
222 associated with increased odds of having hypertension (gravidity OR 1.02; 95% CI: 1.01 –
223 1.04, parity OR 1.02; 95% CI: 1.01 – 1.04). Being obese was significantly associated with
224 increased odds of having hypertension (OR 1.07; 95% CI: 1.02 – 1.13).

225 Being overweight, employed, and educated, though not statistically significant were
226 associated with decreased odds of having hypertension (overweight OR 0.99; 95% CI: 0.94 -
227 1.05, being employed OR 0.98; 95% CI: 0.94 - 1.01, education OR 0.97; 95% CI: 0.93 -
228 1.01). Maternal GA at ANC presentation was not associated with hypertension (OR 1.00;
229 95% CI: 0.97 – 1.00).

230 A maximally adjusted regression model was run including all the variables that were
231 significant in the univariable model and the following results were obtained:

232 The association between age and hypertension; gravidity and hypertension did not change in
233 the adjusted model (Table 2.4). A unit increase in parity was associated with decreased but
234 non-significant odds of having hypertension in the adjusted model (aOR 0.98; 95% CI: 0.95 -
235 1.02). A trend towards a positive association between obese BMI and hypertension was
236 observed (aOR 1.05; 95% CI: 0.97 - 1.10). No regression analysis was explored on factors
237 associated with diabetes because the prevalence was too small to run the models.

238 *Table 2:4* Univariable and adjusted logistic regression of baseline factors associated with
 239 hypertension

	Hypertension: unadjusted models (Ref. category: no hypertension)		Hypertension: adjusted models (Ref. category: no hypertension).	
	OR (95% CI)	P values	aOR (95% CI)	P values
HIV (yes)	0.99 (0.96 - 1.03)	0.734		
HIV (no)	Reference			
Age	1.01 (1.00 - 1.01)	< 0.001	1.01 (1.00 - 1.01)	< 0.001
Gravidity	1.02 (1.01 - 1.04)	0.004	1.02 (0.98 - 1.05)	0.361
Parity	1.02 (1.01 - 1.04)	0.008	0.98 (0.95 - 1.02)	0.355
BMI (overweight)	0.99 (0.94 - 1.05)	0.691		
BMI (obese)	1.07 (1.02 - 1.13)	0.007	1.04 (0.99 - 1.10)	0.093
Normal	Reference		Reference	
(Started ART pre-pregnancy)	1.00 (0.96 - 1.04)	0.916		
(Started during pregnancy)	0.99 (0.94 - 1.04)	0.599		
No HIV	Reference			
Alcohol (yes)	1.03 (0.97 - 1.10)	0.139		
Alcohol (no)	Reference			
Employed (yes)	0.98 (0.94 - 1.01)	0.172		
Employed (no)	Reference			
Finished high school.	0.97 (0.93 - 1.01)	0.128		
Did not finish high school	Reference			
GA at the first ANC visit	1.00 (0.99 - 1.00)	0.376		

Note: Only the variables which were significantly associated with hypertension in the univariable model were included in the maximally adjusted model. These variables were age, gravidity, parity, and obesity.

Legend: Univariable and adjusted logistic regression of baseline factors associated with having hypertension in the cohort

240 Adverse birth outcomes

241 The prevalence of birth outcomes by hypertension and diabetes status were calculated
 242 yielding the tables below. In this analysis, we had a small prevalence of hypertension and
 243 diabetes to carry out birth outcomes analysis by chronicity of NCDs or whether the
 244 conditions were gestational. Therefore, analysis was based on total hypertension and total
 245 diabetes regardless of the type.

246 *Table 2:5* Proportion of baby outcomes by hypertension status

	Maternal hypertension status			
	Hypertensive N = 84 (%)	Normotensive N = 891 (%)	Totals N = 975 (%)	<i>Chi</i> ²
GA (weeks)				
Pre-term (<37 weeks)	24 (29)	66 (7)	90 (9)	<0.001
Full-term (≥37 weeks)	59 (70)	750 (84)	809 (83)	
Missing	1 (1)	75 (9)	76 (8)	
Birthweight (g)				
Low (<2500g)	18 (21)	83 (9)	101 (10)	0.002
High (≥4000g)	0 (0)	39 (4)	39 (4)	
Normal (2500 – 3999g)	65 (77)	678 (76)	743 (76)	
Median [IQR]	2940 [2580 – 3295]	3195 [2889 – 3480]	3189 [2870 – 3470]	
Missing	1 (1)	91 (10)	92 (9)	
Size for gestational age				
Small (<10 th percentile)	14 (17)	86 (10)	100 (10)	0.065
Appropriate (10-90 th percentile)	64 (76)	628 (70)	692 (71)	
Large (>90 th Percentile)	4 (5)	90 (10)	94 (10)	
Missing	2 (2)	87 (10)	89 (11)	

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Proportion of baby outcomes by maternal hypertension status in the cohort of pregnant women at an ANC facility in Cape Town, South Africa

247 Table 2:6 Proportion of baby outcomes by diabetes status

	Maternal diabetes status				
	Diabetic N = 20 (%)	Non-diabetic N = 954 (%)	Missing N = 1	Totals N = 975 (%)	Chi ²
GA (weeks)					
Pre-term (<37 weeks)	3 (15)	87 (9)		90 (9)	0.646
Full-term (≥37 weeks)	16 (80)	792 (83)	1	809 (83)	
Missing	1 (5)	75 (8)		76 (8)	
Birthweight (g)					
Low (<2500g)	6 (30)	95 (10)		101 (10)	0.019
High (≥4000g)	1 (5)	38 (4)		39 (4)	
Normal (2500 – 3999g)	12 (60)	730 (77)	1	743 (76)	
Median [IQR]	3090 [2400-3530]	3180 [2870 -3470]		3189 [2870 – 3470]	
Missing	1 (5)	91 (10)		92 (9)	
Size for gestational age					
Small (<10 th percentile)	4 (20)	96 (10)		100 (10)	0.098
Appropriate (10-90 th percentile)	11 (55)	680 (71)	1	692 (71)	
Large (>90 th percentile)	4 (20)	90 (9)		94 (10)	
Missing	1 (5)	88 (9)		89 (11)	

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Proportion of baby outcomes by maternal diabetes status in the cohort of pregnant women at an ANC facility in Cape Town, South Africa

248 Low birthweight:

249 The total estimated low birthweight in the population was 10%. Comparing birthweight
 250 outcomes between WLHIV (N = 470) and WNLHIV (N = 505), the HIV group had a higher
 251 incidence of low birthweight (11% vs 9%) although not statistically significant

(Supplementary Table 3.7). Hypertensive pregnancies had a statistically higher low birthweight than normotensive pregnancies (21% vs 9 %) (Table 2.5). Babies born from participants with both hypertension and HIV had a higher prevalence of LBW (23%) compared to babies born from participants with HIV only (10%). Between diabetic and non-diabetic pregnancies, LBW was significantly higher in diabetic pregnancies (30% vs 10%, $p = 0.019$) (Table 2.6). A significantly higher LBW was recorded for pregnancies with both diabetes and HIV compared to WLHIV only (43% vs 11%).

Multinomial regression analysis showed increased odds of having a low birthweight baby for participants living with HIV compared to those not living with HIV (OR 1.26; 95% CI: 0.83 – 1.90) though the results were not statistically significant (Table 2.7). Adjusting for HIV, maternal age, maternal GA at first presentation, and parity resulted in the odds of 1.16 (95% CI: 0.75 – 1.80) for living with HIV compared to not living with HIV.

Having hypertension significantly increased the odds of low birthweight by 2.26 (95% CI: 1.28 – 4.00). Adjusting for maternal age, parity and HIV, the odds of low birthweight remained significant but slightly lower (aOR 2.05; 95% CI: 1.14 – 3.68). A sub-group analysis of birth outcomes by ART initiation time was carried out between the 171 women who initiated ART during pregnancy and the 299 who entered ANC on ART. Initiating ART during pregnancy was associated with increased odds of having LBW (aOR 1.18; 95% CI: 0.66 – 2.11) whereas the association was reversed for ART initiated pre-pregnancy (aOR 0.97; 95% CI: 0.59 – 1.61) using ART inexperienced group as reference i.e WNLHIV (Supplementary Table 3.6).

High birthweight:

The total estimated prevalence of HBW was 4% and was only recorded from normotensive participants (Table 2.5). Because of this imbalance, regression analysis could not be carried

out between hypertension and HBW. The prevalence of high HBW did not differ by HIV status and was 4% for both groups. There was no recorded high birthweight from participants living with both HIV and hypertension (Table 2.8). HBW did not differ considerably between diabetic compared to non-diabetic pregnancies (5% vs 4%, $p = 0.019$). Between pregnancies with both diabetes and HIV compared to pregnancies with only HIV, HBW was significantly higher (14% vs 4%).

The association between HIV and HBW was not significant in either the univariable or multivariable model adjusting for hypertension, maternal GA at the first week of presentation, and age (crude OR 0.94; 95% CI: 0.49 – 1.79, aOR 0.99; 95% CI: 0.50 – 1.95). Sub-groups of ART initiation timing showed increased odds of HBW in both women who initiated ART before (aOR 1.11; 95% CI: 0.46 – 2.68) and during pregnancy (aOR 1.08; 95% CI: 0.49 – 2.41) (using ART inexperienced group as reference i.e WNLHIV) although the results were not statistically significant.

Small for gestational age:

The total estimated prevalence of SGA was 10%. There was a marked difference in hypertension status with hypertensive pregnancies having a higher prevalence compared to normotensive pregnancies (17% vs 10%, $p = 0.065$) but the odds ratios were not statistically significant (OR 1.60; 95% CI: 0.86 – 2.97). Adjusting for maternal age, HIV, and parity, resulted in the odds of 1.56 (95% CI: 0.83 – 2.95). Participants living with both HIV and hypertension had a higher prevalence of SGA compared to those with HIV only (18% vs 10%) though not statistically significant. SGA was higher in diabetic pregnancies compared to non-diabetic pregnancies (20% vs 10%) (Table 2.6) though not statistically significant. A higher SGA was recorded for pregnancies with both conditions compared to WLHIV only (43% vs 11%).

A decrease in the odds of SGA was recorded for those with HIV compared to those not living with HIV (OR 0.71; 95% CI: 0.46 – 1.10) but was statistically not significant. However, adjusting for GA at the first week of ANC, maternal age, hypertension, and parity resulted in increased odds of SGA (aOR 1.09; 95% CI: 0.70 – 1.69). The results were not statistically significant. Sub-group analysis of ART initiation timing showed a 3% less likelihood of SGA in pre-pregnancy-initiated ART participants and a 1% more likelihood of SGA in participants who initiated ART during pregnancy compared to WNLHIV. The results were not statistically significant in both groups (Supplementary Table 3.6).

Large for gestational age:

LGA in the population was estimated at 10%. A greater percentage of normotensive pregnancies had a higher prevalence of LGA compared to hypertensive pregnancies (10% vs 5%,) (Table 2.5) though not statistically significant. Compared by HIV, a larger proportion of LGA appeared from WNLHIV (11%) compared to those living with WLHIV (8%) though not statistically significant (Supplementary Table 3.7). There was no recorded LGA from participants living with both HIV and hypertension. However, pregnancies with both diabetes and HIV had higher LGA (28%) compared to pregnancies with HIV only (8%) (Table 2.9).

Having hypertension was associated with decreased odds of LGA (OR 0.44; 95% CI: 0.16 – 1.23). The association did not change indicatively following adjustment for maternal age, HIV, and parity (OR 0.45; 95% CI: 0.16 – 1.26) (Table 2.7). LGA was higher for diabetic pregnancies compared to non-diabetic pregnancies (20% vs 9%, $p = 0.098$) (Table 2.6).

HIV was associated with increased odds of LGA although the results were not statistically significant (OR 1.13; 95% CI: 0.75 – 1.73). Following adjustment for age, parity, and maternal GA at presentation, HIV infection was associated with decreased odds of LGA (aOR 0.73; 95% CI: 0.46 – 1.14) but the results were not statistically significant. LGA did not

differ by the timing of ART initiation compared to people not living with HIV (initiated pre-pregnancy aOR 0.71; 95% CI: 0.37 – 1.35 versus ART initiated during pregnancy aOR 0.75; 95% CI: 0.44 – 1.29).

Preterm delivery:

The total estimated PTD was approximately 10%. The hypertensive pregnancies had a statistically higher PTD (29%) compared to normotensive deliveries (7%) (Table 2.5).

Stratified by HIV status, no considerable difference in PTD was observed in those living with HIV compared to those not living with HIV (10% vs 9%, $p = 0.832$) (Supplementary Table 3.7). Having both conditions resulted in a significantly higher prevalence of PTD (26%) compared to pregnancies with HIV only (9%). PTD was higher in diabetic pregnancies compared to non-diabetic pregnancies (15% vs 9%, $p = 0.646$). The outcome was likewise higher between pregnancies that had both diabetes and HIV compared to pregnancies with HIV only (14% vs 10%), though statistical significance could not be achieved. We observed that 2 babies with PTD were born from pregnancies that concurrently had both NCDS and HIV. However, it is essential to acknowledge that no analysis could be undertaken for this specific exposure combination due to inherent statistical power limitations.

Having hypertension during pregnancy was associated with significantly increased odds of PTD (OR 4.62; 95% CI: 2.67 – 7.83). These associations increased following adjustment for age, BMI, parity, and gravidity (aOR 4.67; 95% CI: 2.63 - 8.15) (Table 2.7).

HIV was associated with increased PTD (OR 1.07; 95% CI: 0.69 - 1.66, aOR 1.02; 95% CI: 0.65 - 1.58, adjusted for maternal BMI and gravidity). Initiating ART during pregnancy was associated with more preterm delivery (aOR 1.05; 95% CI: 0.56 – 1.88) whereas initiating pre-pregnancy was associated with less PTD compared to people not living with HIV (aOR 0.83; 95% CI: 0.49 – 1.40).

348 *Table 2:7* Univariable and adjusted odds of adverse birth outcomes by HIV and hypertension
349 status

Adverse Birth outcomes	Hypertension (Ref. category: no hypertension)				HIV (Ref. category: not living with HIV)			
	OR	<i>P</i>	aOR	<i>P</i>	OR	<i>P</i>	aOR	<i>P</i>
Size for gestational age								
Small (<10th percentile)	1.60 (0.86 - 2.97)	0.140	1.56 (0.83 - 2.95)	0.168	0.71 (0.46 - 1.10)	0.555	1.09 (0.70 - 1.69)	0.696
Large (>90th percentile)	0.44 (0.16 - 1.23)	0.116	0.45 (0.16 - 1.26)	0.129	1.13 (0.75 - 1.73)	0.127	0.73 (0.46 - 1.14)	0.168
Appropriate	Ref.		Ref.		Ref.		Ref.	
GA								
PTD < 37weeks	4.62 (2.67 - 7.84)	<0.001	4.67 (2.63 - 8.15)	<0.001	1.07 (0.69 - 1.66)	0.747	1.02 (0.65 - 1.58)	0.946
Term	Ref.		Ref.		Ref.		Ref.	
Birthweight								
High (≥4000g)	-	-	-	0.000	0.94 (0.49 - 1.79)	0.844	0.99 (0.50 - 1.96)	0.981
Low (<2500g)	2.26 (1.28 - 4.00)	0.005	2.05 (1.14 - 3.68)	0.016	1.26 (0.83 - 1.90)	0.284	1.16 (0.75 - 1.80)	0.504
Normal	Ref.		Ref.		Ref.		Ref.	

NB: GA and Hypertension logistic regression model: adjusted for BMI, gravidity, parity, and age.

GA and HIV logistic regression model: adjusted for maternal BMI and gravidity.

Size for GA and Hypertension multinomial model: adjusted for maternal age, HIV status and parity.

Size for GA and HIV multinomial models: adjusted for GA at the first week at ANC, hypertension, maternal age and parity.

Birthweight and Hypertension multinomial regression models: adjusted for maternal age, parity, and HIV status.

Birthweight and HIV multinomial models: adjusted for maternal age, GA at the first week of ANC and hypertension.

We could not run a model of HBW because there were no HBW births from participants with hypertension.

Legend: Univariable and adjusted odds of adverse birth outcomes by HIV and hypertension status among mothers with live singleton births (975)

350 *Table 2:8 Birth outcome frequencies by maternal HIV & hypertension status*

Birth Outcomes	Total N=975 (%)	Not living with HIV				Living with HIV			
		Hypertension status				Hypertension status			
		No hypertension N = 460(%)	Hypertension N = 45 (%)	Total N = 505 (%)	Chi ²	No hypertension N = 431 (%)	Hypertensi on N = 39 (%)	Totals N = 470 (%)	Chi ²
GA (weeks)					<0.001				0.003
PTD (<37)	90 (9)	31 (7)	14 (31)	45 (9)		35 (9)	10 (26)	45 (100)	
Term (≥37)	809 (83)	389 (85)	30 (67)	419 (83)		361 (83)	29 (74)	390 (83)	
Missing	76 (8)	40 (8)	1 (2)	41 (8)		35 (8)	0	35 (7)	
Birthweight (g)									
LBW <2500	101 (10)	38 (8)	9 (20)	47 (9)	0.026	45 (10)	9 (23)	54 (11)	0.058
HBW (≥4000)	39 (4)	21 (5)	0	21 (4)		18 (4)	0	18 (4)	
Normal (2500 - 3999)	743 (76)	353 (77)	35 (78)	388 (77)		325 (75)	30 (77)	355 (76)	
Median [IQR]	3189 [2870 – 3470]	3240 [2940 -3520]	3105 [2639 - 3350]	3220 [2920 -3505]		3140 [2840 -3442]	2910 [2552 – 3248]	3140 [2805 – 3420]	
Missing	92 (9)	48 (10)	1 (2)	49 (10)		43 (10)	0	43 (9)	
Size for gestational age									
SGA (<10th)	100 (10)	41 (9)	7 (16)	48 (10)	0.408	45 (10)	7 (18)	52 (11)	0.079
Appropriate (10-90th)	692 (71)	321 (70)	33 (73)	354 (70)		307 (71)	31 (79)	338 (72)	
LGA (>90th)	94 (10)	52 (11)	4 (9)	56 (11)		38 (9)	0	38 (8)	
Median (IQR)									
Missing	89 (11)	46 (10)	1 (2)	47 (9)		41 (10)	1 (3)	41 (9)	

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Percentage proportion (%) of birth outcomes of children born from mothers with hypertension and HIV at an ANC facility in Cape Town, South Africa

351 Table 2:9 Birth outcomes frequencies by maternal HIV & diabetes status

Birth outcomes	Totals N = 975 (%)	Not Living with HIV		Living with HIV					
		Diabetes status		Diabetes status					
		No Diabetes N = 492(%)	Diabetes N = 13 (%)	Totals N = 505 (%)	<i>Chi</i> ²	No Diabetes N = 463 (%)	Diabetes N = 7 (%)	Totals N = 470 (%)	<i>Chi</i> ²
GA (weeks)									
PTD (<37)	90 (9)	43 (9)	2 (16)	45 (9)	0.742	44 (10)	1 (14)	45 (10)	1.000
Term (≥37)	809 (83)	409 (83)	10 (77)	419 (83)		384 (83)	6 (86)	390 (83)	
Missing	76 (8)	40 (8)	1 (7)	41 (8)		35 (7)	0	35 (7)	
Birthweight (g)									
LBW (<2500)	101 (10)	44 (9)	3 (23)	47 (9)	0.194	51 (11)	3 (43)	54 (11)	0.016
HBW (≥4000)	39 (4)	21 (4)	0	21 (4)		17 (4)	1 (14)	18 (4)	
Normal (2500 - 3999)	743 (76)	379 (77)	9 (69)	388 (77)		352 (76)	3 (43)	355 (76)	
Median [IQR]	3189 [2870 – 3470]	3220 [2920 – 3520]	3055 [2604 – 3450]	3220 [2920 -3505]		3140 [2810 – 3420]	3275 [2400 – 3930]	3140 [2805 – 3420]	
Missing	92 (9)	48 (10)	1 (8)	49 (10)		43 (9)	0	43 (9)	
Size for gestational age									
SGA (<10th)	100 (10)	47 (10)	1 (8)	48 (10)	0.879	49 (11)	3 (43)	52 (11)	0.004
Appropriate (10-90th)	692 (71)	345 (70)	9 (69)	354 (70)		336 (73)	2 (28)	338 (72)	
LGA (>90th)	94 (10)	54 (11)	2 (15)	56 (11)		36 (8)	2 (28)	38 (8)	
Missing	89 (11)	46 (9)	1 (8)	47 (9)		42 (9)	0	42 (9)	

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Percentage proportion (%) of birth outcomes of children born from women with diabetes and HIV at an ANC facility in Cape Town, South Africa

5. DISCUSSION

The aim of this study was to investigate the prevalence of hypertension and diabetes in WLHIV in relation to their BMI, in comparison to WNLHIV. Furthermore, this study investigated factors associated with hypertension and assessed if hypertension and HIV were associated with adverse birth outcomes among women seeking antenatal care in Cape Town, South Africa.

The prevalence of hypertension was found to be relatively similar between WLHIV and WNLHIV. However, obesity accounted more for NCDs (hypertension and diabetes) than HIV in this setting, but a higher burden of NCDs was observed in women who had both HIV and obesity. We found that age, parity, and gravidity were the factors associated with having hypertension. When studied separately, hypertension and HIV were associated with PTD, LBW, and SGA. Furthermore, a double burden of HIV and an additional NCD of either hypertension or diabetes resulted in a higher occurrence of adverse birth outcomes.

Diabetes and hypertension prevalence in pregnant women in relation to BMI and HIV

HIV

In this study, we found no difference in the prevalence of total hypertension, between participants living with HIV and those not living with HIV. Furthermore, ART initiation timing did not show an association with total hypertension. On further analysis stratifying by type of hypertension, we found that the prevalence of chronic hypertension was higher in WLHIV than in WNLHIV, although not statistically significant. This could be attributed to long-term exposure to ART and HIV infection inflammatory response as indicated in literature (82-85). While the prevalence of gestational hypertension was higher among WNLHIV compared to WLHIV, it is noteworthy that all five cases of pre-eclampsia recorded were from WLHIV. These findings may suggest a clinical risk of hypertension complications

in pregnant WLHIV, underscoring the importance of enhanced monitoring protocols to mitigate adverse pregnancy and birth outcomes.

While our study could not yield any discernable differences between GDM and chronic diabetes by HIV status, research has demonstrated that pregnant WLHIV remain at a compounded vulnerability to GDM due to dysregulation of placental hormones by ART and the virus (66,86,87). This is in addition to the risk of GDM in the general pregnant population due to pregnancy insulin resistance and hyperinsulinemia that come with gestational weight gain (61,88). This body of research underscores the compelling necessity of integrating GDM screening into the routine ANC protocols for pregnant WLHIV in Southern Africa, as an additional dimension to the already existing risk-based screening and testing procedures (64).

BMI

Generally, a high prevalence of obesity was observed among the participants regardless of HIV status. Other South African studies indicated that most women present at ANC with an unhealthy BMI and an overall elevated level of obesity in the country (79,89). In this study, we found that a sedentary lifestyle was common during pregnancy regardless of HIV status. This factor together with urbanization and its accompanying dietary transition in the LMICs may explain the high obesity prevalence observed in low-income settings such as ours (54). Although not statistically significant, chronic hypertension prevalence was higher in obese women than in overweight and normal-weight women. Overall diabetes was significantly highest in obese participants than in normal weight and overweight participants as is the case elsewhere (90,91). We also found that gestational hypertension and diabetes occurred the most in obese women than in overweight and normal-weight women. These results agree

with findings from recent literature that women who conceived and present for ANC with a high BMI are at a higher risk of gestational diabetes and hypertension (92-94).

HIV and BMI

We compared the prevalence of hypertension or diabetes by both BMI status and HIV to determine if there could be a higher prevalence of NCDs from this exposure combination. When looking at women who had both high BMI and HIV, the prevalence of chronic hypertension was highest in obese WLHIV, although the results were not statistically significant. This indicates a double burden and risk for hypertension in women living with HIV in South Africa as obesity continues to grow. Recent literature has shown links between the elevated prevalence of NCDs such as hypertension in people living with HIV and the mediative role of ART-related obesity (95,96). One study conducted in China demonstrated abdominal fat increment at each ART follow-up visit and associations with incident hypertension (97). Hence, the intersection of obesity and NCD with ART in the context of maternal health among women living with HIV remains a persistent concern. Addressing this issue may necessitate additional interventions, particularly in light of the 2018 World Health Organization (WHO) guidance advocating the transition from protease inhibitor (PI) and non-nucleoside reverse-transcriptase inhibitor (NNRTI) based ART regimens to dolutegravir DTG based regimens in South Africa, which has been associated with an increased risk of obesity (98,99).

Factors associated with hypertension.

The second objective of this study was to investigate factors associated with having hypertension in the cohort of pregnant women seeking antenatal care in Cape Town South Africa. We found that factors significantly associated with having hypertension were age,

parity, gravidity, and obesity. Although child-bearing women tend to be of lower age categories, the effects of age on hypertension can still be inferred from our findings (100). Recent literature points out that trends in hypertension in younger adults may be due to psychosocial factors and lifestyle (101). Since parity and gravidity are correlated with age, we adjusted for age yet did not see much change in effect size, indicating that these factors were independently associated with hypertension in our study as they are elsewhere(102-104).

Adverse birth outcomes

HIV/ART

In this study, our results showed that having HIV was associated with more LBW, PTD, and SGA deliveries but less LGA and HBW, although these associations were not statistically significant. Higher LBW, PTD and SGA findings in WLHIV on ART have also been reported by other studies (105-107). The mechanisms implicated in these outcomes include reduced assimilation of nutrients due to HIV thus resulting in intra-uterine growth restrictions that lead to fetal microsomia, inflammatory responses that trigger preterm births and ART-related hormonal imbalances such as reduced progesterone (86,108,109).

LGA and HBW are predominantly the product of high gestational weight gain, high maternal baseline BMI (110), comorbidities such as diabetes (68,69) and long-term exposure to ART subtypes such as dolutegravir and tenofovir suspected to promote significant weight gain (99,111). Reduced LGA and HBW in WLHIV observed in this study may potentially be explained by lifestyle alterations and education that WLHIV received due to interacting more with the healthcare system in relation to HIV infection and ARV treatment.

In this study initiating ART during pregnancy was associated with more PTD and LBW than in WNLHIV as is the case in a study by Short et al. (112), although our findings were not

statistically significant. Whether ART initiation before or during pregnancy is associated with more adverse birth outcomes remains a contentious issue (113-115). However, one study postulates that ART initiation before pregnancy is a major risk factor, linking it to placental vascular malperfusion commonly occurring in long-term ART-exposed pregnant women (116). Our results are comparable to those observed pre-ART revolution and this can be explained in part by not having achieved complete viral suppression during the initial stages of conception (76,117). This could indicate an underlying need to strengthen ART adherence and retention programs in low-income settings to ensure that people living with HIV are encouraged to regularly take their medication to achieve viral suppression. ART adherence regardless of conception can prevent vertical transmission from mother-to-child especially in late ANC presentation pregnancies.

Most studies investigating the impact of ART on birth outcomes have not considered the GA at which women started ART during pregnancy. Like most toxic in-utero exposures, ART toxicity could differ depending on the trimester of exposure. Therefore, the results of this study should also be interpreted with caution as we did not consider GA due to a small sample size.

Hypertension

In this study, we found LBW to be consistently associated with having hypertension, with hypertensive pregnancies twice as likely to deliver LBW babies compared to normotensive pregnancies. Hypertensive pregnancies have been associated with an increased likelihood of LBW in previous literature (71-73). Our results also revealed that having hypertension was significantly associated with more PTD than no hypertension. PTD was more than 4 times likely in hypertensive pregnancies than in normotensive pregnancies. The results agree with most studies of hypertensive disorders during pregnancy (73,118). We also discovered a

significantly high prevalence of PTD in pregnancies with both hypertension and HIV. SGA prevalence was higher in pregnancies with hypertension than in normotensive pregnancies as is the case elsewhere (71-73). The prevalence was highest when women had HIV in addition (43%) versus HIV only (10%) though not statistically significant. These results have concerning health implications in this population and similar settings in South Africa. The implications are of clinical concern, particularly with a high prevalence of obesity. The coexistence of high obesity rates, a significant HIV burden, and an increased prevalence of hypertension underscores the potential for compounded health risks and the need for comprehensive medical attention and interventions to address these complex health challenges in this particular population. Maternal and neonatal health morbidity carries a substantial economic burden in both the short and long-term. Adverse birth outcomes, including PTD and LBW, can lead to a heightened risk of health conditions such as congenital hearing loss, poor vision, developmental delays, cerebral palsy and intellectual difficulties (119,120).

Diabetes

In this study, LBW and HBW were significantly higher in diabetic pregnancies than in non-diabetic pregnancies. Moreover, SGA, LGA, and PTD were higher in diabetic pregnancies compared to non-diabetic pregnancies. However, the results were not statistically significant due to a small prevalence of diabetes in the population. Our results are comparable to studies done elsewhere indicating the risk of these negative birth outcomes and other congenital birth anomalies resulting from diabetes exposure during pregnancy (121,122). However, SGA is not very prevalent in diabetic pregnancies unless there are other conditions mediating the pathway such as placental damage (123). Our observations may be attributable to chance as we had a very narrow sample of diabetic pregnancies rather than an indication of clinical significance.

Yet another concerning finding was the higher prevalence of birth outcomes where both diabetes and HIV were present during pregnancy. A higher SGA was recorded for pregnancies with both conditions compared to pregnancies with neither (43% vs 10%). LBW and HBW were significantly recorded for pregnancies with both diabetes and HIV compared to WLHIV only (43% vs 11% and 14% vs 4% respectively). PTD outcome was likewise higher between pregnancies that had both diabetes and HIV compared to pregnancies with HIV only (14% vs 10%). The observed occurrence of SGA infants in this exposure combination may be more attributable to the influence of HIV rather than being ascribed to diabetes. This potential connection may be explained by intrauterine growth restrictions associated with HIV or other factors not investigated here (124). Nonetheless, more research is needed to understand the compounded effects of HIV on diabetes in increasing the risk of adverse birth outcomes. HBW in diabetes occurs due to a high glucose maternal glucose passing through the placenta resulting in foetal overgrowth (124,125).

Strengths and limitations

There are a few limitations in this study to be considered when interpreting the findings. One is that we did not study the maternal exposures by the exact gestational timing of exposure during pregnancy. Due to a small sample size, we could not exactly dissect the pregnancy ART initiation timing by trimesters. Likewise, we could not disentangle the effects of gestational versus chronic hypertension and diabetes on birth outcomes. However, this study has unique strengths such as being able to compare birth outcomes using different exposure combinations: HIV only, hypertension only, diabetes only, HIV and hypertension, HIV and diabetes, and ART initiated during and pre-pregnancy. Because this study used secondary data collected for another study not curated specifically for our research questions, we had some incomplete data in areas that are crucial to this analysis such as the 11% BMI

missingness, one of the two main categorising variables of our study. Challenges related to data transformation surfaced when addressing variables, particularly in cases where a classification decision was required for discerning whether a certain NCD should be categorized as chronic or gestational. This complexity was particularly notable when this information was abstracted but not confirmed from participants who initiated their first ANC visits at a later stage. Consequently, it is important to acknowledge that the measurement of these variables may be subject to bias.

6. CONCLUSION

PTD and LBW appear to be consistently associated with hypertension. Larger studies may be required to understand the aetiology of LGA and HBW in diabetes, hypertension, and HIV-exposed pregnancies while disentangling the effect of obesity in similar settings. The findings suggest that a double burden of HIV plus an additional non-communicable disease needs to be closely monitored to prevent increased poor birth outcomes. More studies with bigger sample sizes on the timing of ART initiation and birth outcomes need to be considered in the South African setting. The prevalence of diabetes and hypertension in women living with HIV needs to be further studied, especially in Southern African settings where there is a high burden of HIV. Obesity remains a higher risk factor for diabetes. There is a consistent need to intervene with dietary and weight plans for people living with HIV on ART, to prevent excessive weight gain and risk to NCDs. Additionally, more statistical methods need to be employed to understand the interaction between NCDs and HIV in pregnancy.

7. LIST OF ABBREVIATIONS

ANC	Antenatal Care
ART	Antiretroviral Therapy
AGA	Appropriate Gestational Age

543	BMI	Body Mass Index
544	CI	Confidence Interval
545	GA	Gestational Age
546	GDM	Gestational Diabetes Mellitus
547	HIV	Human Immunodeficiency Virus
548	IQR	Inter-Quartile Range
549	LBW	Low Birth Weight
550	LGA	Large for Gestational Age
551	LMIC	Low-Middle Income Countries
552	MOU	Midwife Obstetric Unit
553	MCR	Maternity Case Records
554	NCD	Non-Communicable Diseases
555	NNRTI.	Non-nucleoside reverse-transcriptase inhibitor
556	OR	Odds Ratio
557	PI	Protease Inhibitor
558	PMTCT	Prevention of Mother-to-Child Transmission
559	PTD	Preterm Delivery
560	SGA	Small for Gestational Age
561	SSA	Sub-Saharan Africa
562	WHO	World Health Organization

563 WLHIV Women living with HIV

564 WNLHIV Women not living with HIV

565 **8. DECLARATIONS**

566 **Ethics approval and consent to participate**

567 This study followed the guidelines laid down in the Declaration of Helsinki and all

568 procedures involving research study participants were approved by relevant ethical bodies.

569 The current study analysed primary data from a parent study titled B Positive approved by

570 relevant bodies.

571 Since the study is a secondary research analysis, there was no requirement for obtaining

572 informed consent as participants had already consented that their information could be used

573 for research and academic purposes. University of Cape Town Human Research Ethics

574 Committee had approved the parent study (HREC 541/2015) as well as the Western Cape

575 Department of Health (REFWC_2016RP6_286). This current study sought ethical clearance

576 from the University of Cape Town Human Research Ethics Committee (HREC 345/2022).

577 **Consent for publication**

578 Not applicable

579 **Availability of data and materials**

580 The data analysed in this study will be available to external investigators both in the

581 supplementary materials of the published article and upon request from the corresponding

582 author.

583 **Competing interests**

584 The authors declare that they have no competing interests.

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590 **Authors contributions**

591 AJL conceptualised the research question, conducted the design and analysis of data, and
592 wrote the manuscript under the supervision and guidance of HPM. Additionally, HPM gave
593 access to the primary data analysed in this study. All authors reviewed, edited, and approved
594 the final manuscript.

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956

PART 3: APPENDICES

1. MANUSCRIPT SUPPLEMENTARY MATERIAL

Table 3:1 Prevalence of chronic and gestational diabetes by BMI status

Diabetes type	BMI				Chi ² P	Total N = 975(%)
	Normal N = 291 (%)	Overweight N = 240 (%)	Obese N = 423 (%)	Missing N = 21(%)		
Chronic	0	3 (1)	5 (1)		0.037	8 (0.8)
Gestational	3 (1)	0	9 (2)			12 (1)
Total diabetes	3 (1)	3 (1)	14 (3)			20 (2)
Missing diabetes status	1 (0.3)	0	0	0		1 (0.1)
Not diabetic	287 (98)	237 (98)	409 (97)	21		954 (98)

Note: P value for gestational vs chronic diabetes

Some percentage values may not add to 100 due to rounding off!

Table 3:2 Prevalence of chronic and gestational hypertension by BMI status

Hypertension type	BMI				Chi ² P	Total N= 975 (%)
	Normal N = 291 (%)	Overweight N = 240 (%)	Obese N = 423 (%)	Missing N = 21 (%)		
Chronic	4 (1)	6 (3)	26 (6)		0.3378	36 (3)
Gestational	10 (3)	10 (4)	27 (6)	1 (5)		48 (5)
Total Hypertension	14 (5)	16 (7)	53 (12)	1(5)		84 (8)
Normotensive	277 (95)	224 (93)	370 (88)	20 (95)		891 (92)

Note: P value for gestational vs chronic hypertension

Table 3:3 Prevalence of chronic and gestational diabetes by HIV status

	Living with HIV N = 470 (%)	Not living with HIV N = 505 (%)	Chi² P	Total N= 975 (%)
Chronic	4 (1)	4 (1)	0.331	8 (1)
Gestational	3 (1)	9 (2)		12 (1)
Total Diabetes	7 (2)	13 (3)		20 (2)
Missing diabetes	0	1 (0.2)		1 (0.1)
Normotensive	463 (99)	491 (97)		954 (98)

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Percentage proportion (%) of types of diabetes by HIV status from the population of pregnant women at an ANC facility in Cape Town, South Africa

Table 3:4 Prevalence of chronic and gestational hypertension by HIV status

	Living with HIV N = 470 (%)	Not living with HIV N = 505 (%)	Chi² P	Total N= 975 (%)
Chronic	22 (5)	14 (3)	0.821	36 (4)
Gestational	17 (4)	31 (6)		48 (5)
Total hypertension	39 (8)	45 (9)		84 (9)
Missing hypertension	0	0		0
Normotensive	431 (92)	460 (91)		891 (91)

Legend: Percentage proportion (%) of types of hypertension by HIV status from the population of pregnant women at an ANC facility in Cape Town, South Africa

Table 3:5 Prevalence of birth outcomes by the timing of ART initiation

Birth outcomes	Living with HIV N = 470		Not living with HIV	Chi ² P
	ART initiated during pregnancy N = 171 (%)	ART initiated pre-pregnancy N = 299 (%)	N = 505 (%)	
GA (weeks)				0.945
Pre-term (<37)	16 (9)	29 (10)	45 (9)	
Full-term (≥37)	136 (80)	254 (85)	419 (83)	
Missing	19 (11)	16 (5)	41 (8)	
Birthweight (g)				0.857
Low (<2500)	19 (11)	35 (12)	47 (9)	
High (≥4000)	7 (4)	11 (4)	21 (4)	
Normal (2500 - 3999)	125 (73)	230 (77)	388 (77)	
Median [IQR]	3100 [2745-3475]	3140 [2840-3420]	3220 [2920 -3505]	
Missing	20 (12)	23 (8)	49 (10)	
Size for gestational age				0.486
Small (<10th)	16 (9)	36 (12)	48 (10)	
Appropriate (10-90th)	119 (62)	219 (73)	354 (70)	
Large (>90th)	14 (8)	24 (8)	56 (11)	
Missing	22 (13)	20 (7)	47 (9)	

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Prevalence of birth outcomes by timing of ART initiation.

Table 3:6 Adjusted associations between ART initiation timing and adverse outcomes

Adverse birth outcomes	<i>Living with HIV</i>			
	<i>N = 470</i>			
	ART initiated during pregnancy (Ref. category: not living with HIV)	<i>P value</i>	ART initiated pre- pregnancy (Ref. category: not living with HIV)	<i>P value</i>
	aOR	<i>P</i>	aOR	<i>P</i>
PTD (<37 weeks)	1.05 (0.56 - 1.88)	0.885	0.83 (0.49 - 1.40)	0.495
Term (≥37)	Ref.		Ref.	
LBW (<2500g)	1.18 (0.66 - 2.11)	0.567	0.97 (0.59 - 1.61)	0.908
HBW (≥4000g)	1.11 (0.46 - 2.68)	0.844	1.08 (0.49 - 2.41)	0.821
Normal (2500 – 3999g)	Ref.		Ref.	
SGA (<10th)	0.97 (0.52 - 1.78)	0.722	1.10 (0.66 - 1.82)	0.916
LGA (>90th)	0.71 (0.37 - 1.35)	0.306	0.75 (0.44 - 1.29)	0.299
Appropriate (10-90th)	Ref.		Ref.	

Nb: GA logistic regression models: adjusted for maternal age and BMI.

Size for GA and birthweight multinomial models: adjusted for maternal BMI and maternal age.

Table 3:7 Prevalence of birth outcomes by HIV status

Birth outcomes	Living with HIV N = 470 (%)	Not living with HIV N = 505 (%)	Chi² P	Totals N = 975 (%)
GA (weeks)				
Pre-term (<37)	45 (10)	45 (9)	0.832	90 (9)
Full-term (≥37)	390 (83)	419 (83)		809 (83)
Missing	35 (7)	41 (8)		76 (8)
Birthweight (g)				
Low (<2500)	54 (11)	47 (9)	0.541	101 (10)
High (≥4000)	18 (4)	21 (4)		39 (4)
Normal (2500 - 3999)	355 (76)	388 (77)		743 (76)
Median [IQR]	3140 [2805 – 3420]	3220 [2920 -3505]		3189 [2870 – 3470]
Missing	43 (9)	49 (10)		92 (9)
Size for gestational age				
Small (<10th)	52 (11)	48 (10)	0.227	100 (10)
Appropriate (10-90th)	338 (72)	354 (70)		692 (71)
Large (>90th)	38 (8)	56 (11)		94 (10)
Missing	42 (9)	47 (9)		89 (11)

NB: Some percentage values may not add to 100 due to rounding off!

Legend: Percentage proportion (%) of birth outcomes by maternal HIV status from the population of pregnant women at an ANC facility in Cape Town, South Africa

2. ETHICAL APPROVAL AND INFORMED CONSENT DOCUMENTS



UNIVERSITY OF CAPE TOWN
UNIBESITHI YAKHEKAPA • UNIVERSITEIT VAN KAPSTAD

**HUMAN RESEARCH
ETHICS COMMITTEE**

08 JUL 2022

HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN



ACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☒ Approved	Annual progress report	Approved until/next renewal date	30-8-23
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Signed by candidate	Date Signed 11/7/22

Note: Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.
Please clarify your plan for research-related activities during COVID-19 lockdown.
Please use the latest form found on our website:
<http://www.health.uct.ac.za/fhs/research/humanethics/forms>

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	08 July 2022		
HREC REF Number	749/2015	Current Ethics Approval was granted until	30 Aug 2022
Protocol title	B positive: a population-based evaluation of expanded (anti-retroviral therapy) ART access in pregnancy		
Protocol number (if applicable)	5.0		
Are there any sub-studies linked to this study?		☒ Yes	☐ No
If yes, could you please provide the HREC Reference number for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.		HREC REF: 541/2015 (separate FHS016 enclosed)	
Principal Investigator	Emma Kalk		
Department / Office Internal Mail Address	Centre for Infectious Disease Epidemiology & Research, School of Public Health & Family Medicine, 5 th floor Falmouth Building, UCT FHS, Anzio Road		



1.1 Does this protocol receive US Federal funding?	☒ Yes	☐ No	
1.2 If the study receives US Federal Funding, does the annual report require full committee approval?	☐ Yes	☒ No	
Note: Any annual approvals for Full Committee review MUST be submitted on the monthly HREC submission dates. (Please send electronic copy for full committee review to hrec-submission@uct.ac.za)			
If yes in 1.2 please complete section 1.3 below for invoicing purposes			
1.3 Ethics Renewal Fee			
Please (tick ✓) appropriate box for billing purposes:			
Submission Type	Description	New fee (Vat Incl.)	tick ✓
Research funded solely from UCT departmental/divisional/group budget	Annual evaluation of research progress report for re-certification	R0,00	☐
Non-sponsored student research for degree purposes at UCT/Other Universities & Colleges	Annual evaluation of research progress report for re-certification	R0,00	☐
Annual re-certification / Progress report (FHS016 Form)	Clinical Trial & International Grant Funded Research - Annual evaluation of research progress report for re-certification for Full Committee Approval	R7000,00	☐
Annual re-certification / Progress report (FHS016 Form)	Clinical Trial & International Grant Funded Research - Annual evaluation of research progress report for re-certification for Expedited review	R3 710,00	☐
Annual re-certification / Progress report (FHS016 Form)	National grant funded research - Annual evaluation of research progress report for re-certification for Full Committee Approval	R6000,00	☐
Annual re-certification / Progress report (FHS016 Form)	National Grant funded research for Annual evaluation of research progress report for re-certification for Expedited review	R1 500,00	☐
NB: Protocols funded by UCT (e.g. departmental funding / student research) and by certain grant funding organizations (e.g. MRC, NRF, CANSA,) are exempt from these charges.			
Please provide details for Invoicing, either complete section 1 or 2 :			
1. Invoice billing – Directly to Sponsor			
Sponsor's name			
Billing Address of Sponsor:			
Vat Number:			
Contact person			
Telephone number			



Email Address	
2. Internal Journal Billing:	
Fund Number:	
Cost Centre Number:	
Account Holder Name:	
Division of Account Holder:	

2. List of documentation for approval

I submitted a letter to HREC with regard to sharing data with the National Pregnancy Exposure Registry, Ubomi Buhle (HREC REF: R039/2021) in February and followed up in June 2022. This is in keeping with an amendment to this protocol approved in April 2020. I am enclosing this letter and related documentation with this submission.

1. Letter to HREC dated 31 January 2022
2. Ubomi Buhle poster
3. Ubomi Buhle patient information leaflet
4. Ubomi Buhle sticker.

If approved, this will be affixed to the Maternity Case Record (MCR) and will greatly facilitate identifying participants with pregnancy outcomes at hospital (as opposed to the MOU). The MCR is a patient-held clinical record of pregnancy and is retained at the site of delivery. Our current method of identifying PER participants for data collection is more time-consuming as there is a delay in identifying and requesting folders for participants.

Please could you provide feedback regarding the proposed collaboration and the use of the Ubomi Buhle documents?

3. Protocol status (tick ✓)

☒	Open Enrolment (PER)
☒	Closed to enrolment (tick ✓) (cohort study)
☒	Research-related activities are ongoing
☐	Research-related activities are complete, long-term follow-up only
☐	Research-related activities are complete, data analysis only
☐	Main study is complete but sub-study research-related activities are ongoing
☐	Study is closed → Please submit a Study Closure Form (FHS010)

4. Enrolment

Number of participants enrolled to date	995
Number of participants enrolled, since last HREC Progress report (continuing review)	0
Additional number of participants still required	0



5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	49
---	----

6. Cumulative summary of participants

Total number of participants who provided consent	995
Number of participants determined to be ineligible (i.e. after screening)	6
Number of participants currently active on the study	0
Number of participants completed study (without events leading to withdrawal)	694 completed 4 postnatal visits 699 completed at least 1 postnatal visit
Number of participants withdrawn at participants' request (i.e. changed their mind)	14 not interested
Number of participants withdrawn by PI due to toxicity or adverse events	Miscarriage 19 TOP 4 Ectopic 3 Stillbirth 22 Neonatal death 9 Maternal death 6 Total: 63
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	0
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up.	224
There have been no changes since the last report. The cohort component of the project is complete with only analysis and write-up continuing.	
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:

See attached sheet.

8. Protocol violations and exceptions (tick ✓ all that apply)

☒	No prior violations or exceptions have occurred since the original approval
☐	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved
☐	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

☐	No Prior amendments have been made since the original approval
☒	Prior amendments have been reported since the last review and have already been approved
☐	New protocol changes/ amendments are requested as part of this continuing review (See note below)

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS006).

Specific changes in the amended protocol and consent/assent forms must be **bolded**, *italicised* or tracked and all changes must include a rationale.

10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.

N/A. There have been no changes since the last report. The cohort component of the project is complete with only analysis and write-up continuing.

10.2 Have participants received appropriate treatment/ follow-up/ referral when indicated (e.g. in the case of abnormal or incidental clinical findings, distress or anxiety)?

☐ Yes ☐ No ☒ Not applicable

If yes, please describe:


11. Summary of Monitoring and Audit Activities (tick ✓)

11.1 Was this study monitored or audited by an external agency (e.g. SAHPRA, FDA)?					
☐ Yes		☒ No		☐ Not applicable	

11.2 Did a Data and Safety Monitoring Board publish a report?					
☐ Yes		☐ No		☒ Not applicable	

11.3 If yes, please identify the agency and attach a summary of the findings.					
Agency Name		Report attached	☐ Yes	☐ No	☐ Not applicable
		DSMB report attached	☐ Yes	☐ No	☐ Not applicable

11.4 Has there been any agency, institutional or other inquiry into non-compliance in this study, or any finding of non-compliance concerning a member of the research team?					
☐ Yes		☒ No			
If yes, please explain:					

12. Level of risk (tick ✓)

12.1 In light of your experience of this research, please indicate whether the level of risk to participants has:	
☐	Increased
☐	Decreased
☒	Shown no change
If there has been a change, please explain:	

12.2 Please provide a narrative summary of recent relevant literature that may have a bearing on the level of risk.	
The study complies with the requirements of the Health Act and POPI Act introduced in July 2021.	



13. Insurance

Please confirm that valid no fault insurance is still in place? (tick ✓)		
☐ Yes	☐ No	☒ Not Applicable – N/A
If yes, please complete the following:		
Insurer's name:		
Policy no.		*Coverage Period: .
For UCT sponsored studies please liaise the Insurance office via fhs.sponsorship@uct.ac.za regarding the required documentation and information required obtain a renewed UCT No-fault Insurance Certificate.		

14. Statement of conflict of interest

Has there been any change in the conflict of interest status of this protocol since the original approval? (tick ✓)	
☐ Yes	☒ No
If yes, please explain and if necessary, attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form FHS013):	
Change of PI was approved in 2021 and new Col completed at that time. There have been no further changes.	

15. Signature

My signature certifies that the above is complete and correct.		
Signature of PI	Signed by candidate	Date 08 July 2022



Western Cape
Government

Health



GROOTE SCHUUR HOSPITAL

Enquiries: DrBernadette Eick

E-mail : Bernadette.Eick@westerncape.gov.za

Professor Andrew Boule
Centre for Infectious Disease Epidemiology & Research
School of Public Health & Family Medicine

E-mail: Andrew.Boule@uct.ac.za / Emma.Kalk@uct.ac.za

Dear Professor Boule

RESEARCH PROJECT EXTENSION: A Population Based Evaluation of Expanded (Anti-Retroviral Therapy) ART Access in Pregnancy ('B- Positive')

Your recent communication to the hospital refers.

The extension of your research is approved in accordance with UCT Ethics clearance, until **30 August 2018**.

As previously mentioned:

- a) Your research may not interfere with normal patient care.
- b) Hospital staff may not be asked to assist with the research.
- c) No hospital consumables and stationary may be used.
- d) No patient folders may be removed from the premises or be inaccessible.**
- e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
- f) Confidentiality must be maintained at all times.
- g) Once the research is complete, please submit a copy of the publication or report.

I would like to wish you every success with the project.

Yours sincerely

Signed by candidate

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER

Date: 1 November 2017

BE/vms

C.C. Mr L. Naidoo, Professor E. Weimann, Professor Denny, Professor Anthony

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FHS016: Annual Progress Report / Renewal

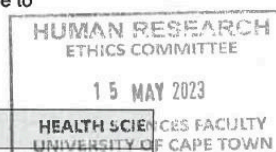
HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☒ Approved	Annual progress report	Approved until/next renewal date	30/6/2024
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee	Signed by candidate	Date Signed	17/5/2023

Note: Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.

Please clarify your plan for research-related activities during COVID-19 lockdown.

Please use the latest form found on our website:

<http://www.health.uct.ac.za/fhs/research/humanethics/forms>



Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	12 May 2023		
HREC REF Number	UCT-HREC (345/2022)	Current Ethics Approval was granted until	30 June 2023
Protocol title	DIABETES AND HYPERTENSION IN PREGNANCY: ASSOCIATION WITH ADVERSE BIRTH OUTCOMES AMONG PREGNANT WOMEN LIVING WITH AND WITHOUT HIV IN CAPE TOWN, SOUTH AFRICA		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes	☒ No	
If yes, could you please provide the HREC Reference number for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.			
Principal Investigator	Dr Hlengiwe Madlala		



Department / Office Internal Mail Address	Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, University of Cape Town, Falmouth Building, Anzio Road, Observatory, Cape Town, South Africa, 7925; hlengiwe.madlala@myuct.ac.za
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1.1 Does this protocol receive US Federal funding?	☐ Yes	☒ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval?	☐ Yes	☐ No
Note: Any annual approvals for Full Committee review MUST be submitted on the monthly HREC submission dates. (Please send electronic copy for full committee review to hrec-submission@uct.ac.za)		

If yes in 1.2 please complete section 1.3 below for invoicing purposes

1.3 Ethics Renewal Fee

Please (tick ✓) appropriate box for billing purposes:

Submission Type	Description	New fee (Vat Incl.)	tick ✓
Research funded solely from UCT departmental/divisional/group budget	Annual evaluation of research progress report for re-certification	R0,00	☐
Non-sponsored student research for degree purposes at UCT/Other Universities & Colleges	Annual evaluation of research progress report for re-certification	R0,00	☒
Annual re-certification / Progress report (FHS016 Form)	Clinical Trial & International Grant Funded Research - Annual evaluation of research progress report for re-certification for Full Committee Approval	R7000,00	☐
Annual re-certification / Progress report (FHS016 Form)	Clinical Trial & International Grant Funded Research - Annual evaluation of research progress report for re-certification for Expedited review	R3 710.00	☐
Annual re-certification / Progress report (FHS016 Form)	National grant funded research - Annual evaluation of research progress report for re-certification for Full Committee Approval	R6000.00	☐
Annual re-certification / Progress report (FHS016 Form)	National Grant funded research for Annual evaluation of research progress report for re-certification for Expedited review	R1 500,00	☐

NB: Protocols funded by UCT (e.g. departmental funding / student research) and by certain grant funding organizations (e.g. MRC, NRF, CANSA,) are exempt from these charges.

Please provide details for Invoicing, either complete section 1 or 2 :

1. Invoice billing – Directly to Sponsor



Sponsor's name	
Billing Address of Sponsor:	
Vat Number:	
Contact person	
Telephone number	
Email Address	
2. Internal Journal Billing:	
Fund Number:	
Cost Centre Number:	
Account Holder Name:	
Division of Account Holder:	

2. List of documentation for approval

None

3. Protocol status (tick ✓)

☐	Open Enrolment
☐	Closed to enrolment (tick ✓)
☐	Research-related activities are ongoing
☐	Research-related activities are complete, long-term follow-up only
☒	Research-related activities are complete, data analysis only
☐	Main study is complete but sub-study research-related activities are ongoing
☐	Study is closed → Please submit a Study Closure Form (FHS010)

4. Enrolment

Number of participants enrolled to date	989
Number of participants enrolled, since last HREC Progress report (continuing review)	0



Additional number of participants still required	0
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5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	N/A
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6. Cumulative summary of participants

Total number of participants who provided consent	989
Number of participants determined to be ineligible (i.e. after screening)	N/A
Number of participants currently active on the study	N/A
Number of participants completed study (without events leading to withdrawal)	989
Number of participants withdrawn at participants' request (i.e. changed their mind)	N/A
Number of participants withdrawn by PI due to toxicity or adverse events	N/A
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	N/A
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up.	N/A
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	N/A

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:
This is a secondary data analysis of data collected between 2017 and 2019 from Gugulethu maternal obstetric unit. Currently the data has been analysed and we are writing the discussion of the data in the manuscript. We intend to submit to UCT towards a master's in public health degree for marking in July 2023. Because this protocol is a retrospective secondary data analysis of data long collected, there was no enrolment or contact with participants of any nature.

8. Protocol violations and exceptions (tick ✓ all that apply)



☒	No prior violations or exceptions have occurred since the original approval
☐	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved
☐	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

☒	No Prior amendments have been made since the original approval
☐	Prior amendments have been reported since the last review and have already been approved
☐	New protocol changes/ amendments are requested as part of this continuing review (See note below)

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS006).

Specific changes in the amended protocol and consent/assent forms must be **bolded**, *italicised* or tracked and all changes must include a rationale.

10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.
N/A

10.2 Have participants received appropriate treatment/ follow-up/ referral when indicated (e.g. in the case of abnormal or incidental clinical findings, distress or anxiety)?		
☐ Yes	☐ No	☒ Not applicable
If yes, please describe:		

11. Summary of Monitoring and Audit Activities (tick ✓)

11.1 Was this study monitored or audited by an external agency (e.g. SAHPRA, FDA)?		
☐ Yes	☐ No	☒ Not applicable
11.2 Did a Data and Safety Monitoring Board publish a report?		
☐ Yes	☐ No	☒ Not applicable



11.3 If yes, please identify the agency and attach a summary of the findings.				
Agency Name		Report attached	☐ Yes	☐ No
		DSMB report attached	☐ Yes	☐ No
			☒ Not applicable	☐ Not applicable

11.4 Has there been any agency, institutional or other inquiry into non-compliance in this study, or any finding of non-compliance concerning a member of the research team?	
☐ Yes	☒ No
If yes, please explain:	

12. Level of risk (tick ✓)

12.1 In light of your experience of this research, please indicate whether the level of risk to participants has:	
☐	Increased
☐	Decreased
☒	Shown no change
If there has been a change, please explain:	

12.2 Please provide a narrative summary of recent relevant literature that may have a bearing on the level of risk.
None yet



13. Insurance

Please confirm that valid no fault insurance is still in place? (tick ✓)			
☐ Yes	☐ No	☒ Not Applicable – N/A	
If yes, please complete the following:			
Insurer's name:			
Policy no.		*Coverage Period:	
For UCT sponsored studies please liaise the Insurance office via fhs.sponsorship@uct.ac.za regarding the required documentation and information required obtain a renewed UCT No-fault Insurance Certificate.			

14. Statement of conflict of interest

Has there been any change in the conflict of interest status of this protocol since the original approval? (tick ✓)	
☐ Yes	☒ No
If yes, please explain and if necessary, attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form FHS013):	

15. Signature

My signature certifies that the above is complete and correct.			
Signature of PI	Signed by candidate Dr Hlengiwe Madlala	Date	12 May 2023

B POSITIVE SENTINEL COHORT – PREGNANT WOMEN **INFORMATION AND INFORMED CONSENT**

WHAT IS THE PURPOSE OF THIS STUDY?

We are researchers from the University of Cape Town (UCT) and we are asking you to participate in a study we are conducting at the Gugulethu Midwife Obstetric Unit (MOU) and its referral centres. The purpose of this study is to understand and monitor the health of pregnant women and how they are cared for at health facilities during pregnancy and after they deliver their baby. It includes women's mental and physical health and any medicines and remedies that are taken during pregnancy.

We know that it is important for their own health as well as that of their baby, that pregnant women receive all the care and treatment they need both during pregnancy and after delivery. Information learned in this study will help us to improve health services for pregnant women.

You are being asked to take part in this study because you are pregnant and you are getting your pregnancy care here at the Gugulethu MOU. The purpose of this consent form is to give you information to help you decide if you want to take part in this study.

WHAT DO I HAVE TO DO IF I AGREE TO TAKE PART?

If you agree to take part, you will come in for **up to 7 study visits**. The first visit will take place today while you are in the clinic, and then up to two more before delivery depending on how far your pregnancy is. These visits will occur after your routine ANC clinic visit. After you have given birth, the next visit will occur within one week of delivering your baby and again when your baby is about 6 weeks, 6 months and 12 months old. These study visits are separate from the usual clinic visits that you will have for your pregnancy or your baby's health but we can time the study visits so that they take place on the same days as your usual pregnancy and baby checkups. The first visit today will take about 90 minutes and each of the subsequent visits will take about 60 minutes.

At the visits that are conducted while you are pregnant, you will do the following:

- Answer questions about your pregnancy and related healthcare issues/problems
- Answer questions about any other health concerns or ailments
- Discuss any chronic health conditions (if present)
- Discuss any medicines and remedies you are taking
- Answer questions to assess whether you are stressed or unhappy (depressed)
- Discuss some aspects of your personal relationships
- Answer questions about the care you are receiving

If we feel there are any serious problems, we will refer you to the relevant specialized care.

One-week after delivery

One week after you give birth to your baby, you will come to the clinic for a visit that will include the following:

- A repeat of some of the questions discussed previously (health, medicines, stress)
- Questions about your delivery, your baby's health and feeding.

At the other visits after your baby is born (6 weeks, 6 months and 12 months old) you will do the following:

- Answer questions about your recent health and any health concerns
- Answer questions about your baby's health, feeding practices and immunizations

- Discuss any problems with taking chronic medications
- Answer questions to assess whether you are stressed or unhappy (depressed)
- Discuss some aspects of your personal relationships
- Answer questions about the care you are receiving

Review of medical records

As part of this study, we will also be looking at and taking information from your antenatal, obstetric, medical, and laboratory records. We will also be looking at and taking information from the health care records of your baby after she or he is born. From these records, we are interested in learning about the pregnancy care you received, medicines you took as well as information about your delivery and your baby's health. All data that we review and abstract is confidential and no participant names are recorded on study documents.

Follow-up of missed visits

You will be asked to provide contact information so that we may get in touch with you during the study. Study staff will talk with you about the best way to contact you. In the event that you miss one of the scheduled study visits, a member of the study staff will contact you in order to find another day and time to complete your visit. If you repeatedly miss study visits or the staff is unable to contact you using the information that you provide, it may be necessary to visit you at home in order to reschedule the missed study visit.

Contact for future study

After the completion of the visit one week after delivery, we will speak to you again to make sure you are happy to be involved in further research.

WHAT ARE THE POTENTIAL RISKS?

You may feel uncomfortable about some of the personal questions you are asked. You may refuse to answer any question that you do not want to answer. There is some risk in sharing personal and medical information. We will be careful to keep all your information as private as possible.

WHAT ARE THE POTENTIAL BENEFITS?

There is no direct benefit to you if you take part in this study. The information gained in this study may help to improve healthcare services for pregnant women and their babies in Cape Town, the Western Cape Province, and across South Africa.

WHAT ARE THE ALTERNATIVES TO TAKING PART?

The alternative to taking part in this study is to continue with your usual health care. If you decide not to participate in this study, your usual health care will not be changed in any way.

WHAT ABOUT CONFIDENTIALITY?

If you agree to take part, all information collected during the study will be kept strictly confidential. Your name will not be written on the study forms and will not be used in connection with any information or lab samples that are collected as part of the study.

All study materials will be stored in locked filing cabinets. Only study staff and personnel involved in routine audits will have access to these materials. All staff involved in data collection and management will get specific training in confidentiality.

Even with these procedures in place if the study staff learns that you are at risk of hurting yourself or someone else or of possible child abuse and/or neglect, study staff will tell the proper authorities.

ARE THERE ANY COSTS?

There is no cost for being in this study.

CAN I LEAVE THE STUDY?

You have the right to decide not to take part in the study, to refuse to answer any questions, or to withdraw from the study at any time without any penalty. It will have no effect on the care that you receive at the Gugulethu MOU or any other health facility.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

There is no payment for participation. At the end of each visit, you will be given a R100 grocery voucher, R20 for transport, and food and drink while you are at the visit.

If you are HIV infected, you will be asked to provide a dried blood spot (DBS) sample at each visit. This involves a prick on the tip of your finger with a sterile lancet, and the drops of blood are used to fill a maximum of five spots on a filter paper.

The DBS sample will be stored and used to check on your immune system (the part of your body that fights infections like HIV) and ARV levels at a later time. Results from these tests are purely for research and will not be available to you, the clinic, or the study staff. If the health care providers at the clinic need to check your blood, they will take a separate blood sample. When it is stored, your blood and test results will not have your name or any other way of identifying you attached to it.

Please initial below to indicate whether or not you give permission for us to take DBS sample from you. You may still remain in the study, even if you choose not to give a sample.

_____ (initial) I agree to have DBS sample as part of this research.

_____ (initial) I do NOT agree to have a DBS sample as part of this research.

FUTURE USE OF SAMPLES:

If you are HIV-infected and agree, some of the blood drawn from you (DBS sample) as part of the study may be used for future HIV-related research. At this time, we cannot provide details of when this testing may be conducted, or exactly what tests we would like to do. However, additional testing will not be done using these stored samples without the approval of the appropriate research ethics committees involved in this research.

If you agree to let us keep your stored sample from you for future research, they may be kept in a locked freezer for up to 5 years. If we do use these samples in the future, the names of other identifiers will not be included with this information (as with the rest of the information we collect for this study).

Please initial below to indicate whether or not you give permission for these samples to be used for future research. You may still remain in the study, no matter which you choose.

_____ (initial) I agree to have my blood stored for future research.

_____ (initial) I do NOT agree to have my blood stored for future research.

DO YOU HAVE ANY QUESTIONS?

If there is anything that is unclear or if you need further information, please ask us and we will provide it.

Do you have any questions?

FOR ADDITIONAL INFORMATION:

If you have any questions or have any problems while taking part in this research study, you should contact:

Professor Landon Myer
School of Public Health and Family Medicine
Faculty of Health Sciences
University of Cape Town
Tel: 021 406-6661
Email: Landon.Myer@uct.ac.za

Professor Andrew Boule
School of Public Health and Family Medicine
Faculty of Health Sciences
University of Cape Town
Tel 021 406-6715
Email: Andrew.Boule@uct.ac.za

If you have any questions about your rights as a research participant, you may contact the following member of the ethics committee:

Prof Marc Blockman
Chair, Human Research Ethics Committee
Faculty of Health Sciences, University of Cape Town
Tel: 021 406-6338

SIGNATURE PAGE

For participant to complete (please tick):

- ☐ I have read the information in this document (or it has been read to me). I have been offered a copy of this consent form. I was encouraged and given time to ask questions and all my questions about the study and my participation in it have been answered. I freely consent to be in this research study and agree to participate and know that I may withdraw at any time. My being in the study is voluntary. I understand that whether or not I participate will not affect my health care services received today, or at any time in the future.
- ☐ I agree that the study team can access my medical records at this hospital or another hospital if necessary for this study. My information will be kept confidential.
- ☐ I agree to provide contact information for myself which will be kept confidential by the study team.
- ☐ I agree to be called on my telephone during the course of the study

Participant Name (Please print)	Participant Signature	Date/Time
---------------------------------	-----------------------	-----------

Interviewer Name (Please print)	Interviewer Signature	Date/Time
---------------------------------	-----------------------	-----------

If this consent form is read to the participant because the participant is unable to read the form or if the participant must use a thumbprint to sign his/her name, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant. The participant freely consented to be in the research study.

Witness Name (Please print)	Witness Signature	Date/Time
-----------------------------	-------------------	-----------

Thank you!

3. QUESTIONNAIRES AND DATA ABSTRACTION FORMS

B-POS: AUDIT & DUDIT
Xhosa-English Version 2.1, 15 May 2018

AUDIT & DUDIT A1

PWID: _____ - _____

MATERNAL HISTORY OF SUBSTANCE USE

This CRF applies to **ALL** enrolled BPOS participants
To be completed at **ALL** Study visits

Visit Date									Visit Code	
D	D	M	M	M	Y	Y	Y	Y	A	1

A: AUDIT (Alcohol Use Disorders Identification Test)

Ngoku sizokubiza eminye imibuzo malunga nokusebenzisa kwakho utywala njengoko uye wafumanisa ukuba ukhulelwe. Nceda ukhethe impendulo echanekileyo ngokubiyela ibhokisi efanelekileyo. Nceda uqale umbuzo ngamnye ngo "Njengoko uye wafumanisa ukuba ukhulelwe"

Now we are going to ask you some questions about your use of alcohol beverages *since you found out you were pregnant*. Please choose the correct answer by circling in the appropriate box. Please start each question with "Since you found out you were pregnant"

	0	1	2	3	4
1. Ubusela kangakanani utywala? <i>How often do you have a drink containing alcohol? Uba u'Gqithela ku Q3 If '0' SKIP to 3</i>	Zange Never	Kanye ngenyanga nangaphantsi Once a month or less often	Kabini ukuya kwisine ngenyanga 2-4 times a month	Kabini ukuya kwisithathu ngeveki 2-3 times a week	Kane nangaphezulu evekini 4 times or more a week
2. Zingaphi iglasi zotywala oziselayo ngemini? <i>How many drinks containing alcohol do you have on a typical day when you are drinking?</i>	Kanye okanye kabini 1 or 2	Kathathu okanye kane 3 or 4	Kahlanu okanye kathandathu 5 or 6	Kasixhenxe okanye kalithoba 7 or 9	Kalishumi nangaphezulu 10 or more
3. Kukangakanani usela iglasi ezintandathu nangaphezulu ngexesha elinye? <i>How often do you have six or more drinks on one occasion?</i>	Zange Never	Ngaphantsi kwenyanga Less than monthly	Ngenyanga Monthly	Ngeveki Weekly	Ngosuku okanye phantse yonke imihla Daily or almost daily
4. Kukangakanani kulonyaka uphelileyo ufumanisa ukuba awukwazi ukuyeka ukusela xa sele uqalile? <i>How many times have you needed a drink in the morning to get yourself going after a heavy drinking session?</i>	Zange Never	Ngaphantsi kwenyanga Less than monthly	Ngenyanga Monthly	Ngeveki Weekly	Ngosuku okanye phantse yonke imihla Daily or almost daily
5. Kukangakanani ungaphumeleli ukwenza into ebekumele ukuba uyayenza awakwazi ngenxa yokuba ubusela? <i>How often have you failed to do what was normally expected of you because of drinking?</i>	Zange Never	Ngaphantsi kwenyanga Less than monthly	Ngenyanga Monthly	Ngeveki Weekly	Ngosuku okanye phantse yonke imihla Daily or almost daily

Page 1 of 4

Initials of interviewer: _____

	0	1	2	3	4
6. Kukangaphi ufuna "ukuqabula" ekuseni kuba ufuna ukuqala usuku lwakho kakhuhle emva kokuba ubusele utywala kakhulu? <i>How many times have you needed a drink in the morning to get yourself going after a heavy drinking session?</i>	Zange Never	Ngaphantsi kwenyanga Less than monthly	Ngenyanga Monthly	Ngeveki Weekly	Ngosuku okanye phantse yonke imihla Daily or almost daily
7. Kukangakanani uzifumanisa unesazela okanye uzisola emva kokuba usele? <i>How often have you had a feeling of guilt or remorse after drinking?</i>	Zange Never	Ngaphantsi kwenyanga Less than monthly	Ngenyanga Monthly	Ngeveki Weekly	Ngosuku okanye phantse yonke imihla Daily or almost daily
8. Kukangakanani ungayikhumbuli into eyenzekileyo kubusuku obudlulileyo ngenxa yokuba ubusela? <i>How often have you been unable to remember what happened the night before because you had been drinking?</i>	Zange Never	Ngaphantsi kwenyanga Less than monthly	Ngenyanga Monthly	Ngeveki Weekly	Ngosuku okanye phantse yonke imihla Daily or almost daily
9. Ukhe wonzakala okanye omnye umntu wonzakala ngenxa yokuba ubusele? <i>Have you or anyone else been injured as a result of your drinking?</i>	Hayi No	Ewe, kodwa hayi kulonyaka uphelileyo Yes, but not in the past year	Ewe, kulonyaka uphelileyo Yes, during the past year		
10. Sikhona isizalwana okanye umhlobo wakho, ugqirha okanye omnye umsebenzi wezempilo othe waxhalaba ngendlela osela ngayo waza wakucebisa ukuba uthobe isantya? <i>Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?</i>	Hayi No	Ewe, kodwa hayi kulonyaka uphelileyo Yes, but not in the past year	Ewe, kulonyaka uphelileyo Yes, during the past year		
Record total of specific items here					

Page 2 of 4

PWID: _____

B: DUDIT (Drug Use Disorders Identification Test)

Ngoku sizokubuzisa eminye imibuzo malunga nokusebenzisa kwakho iziyobisi njengoko uye wafumanisa ukuba ukhulelwe. Nceda ukhethe impendulo echanekileyo ngokubiyela kwibhokisi efanelekileyo. Nceda uqale umbuzo ngamnye ngo "Njengoko uye wafumanisa ukuba ukhulelwe"

We are now going to ask you some questions about your use of drugs since you found out you were pregnant. Please choose the correct answer by crossing with an "X" in the appropriate box. Please start each question with "Since you found out you were pregnant"

	0	1	2	3	4
1. Uzisebenzisa kangakanani ezinye iziyobisi ngaphandle kotywala? <i>How often do you use drugs other than alcohol?</i>	Zange Never	Kanye ngenyanga nangaphantsi Once a month or less often	Kabini ukuya kwisine ngenyanga 2-4 times a month	Kabini ukuya kwisithathu ngeveki 2-3 times a week	Kane ngeveki okanye ngaphezu koko 4 times a week or more often
2. Usebenzisa ngaphezu kohlobo olunye lweziyobisi ngexesha elinye? <i>Do you use more than one type of drug on the same occasion?</i>	Zange Never	Kanye ngenyanga nangaphantsi Once a month or less often	Kabini ukuya kwisine ngenyanga 2-4 times a month	Kabini ukuya kwisithathu ngeveki 2-3 times a week	Kane ngeveki okanye ngaphezu koko 4 times a week or more often
3. Mangaphi amaxesha owathathayo ngosuku xa usebenzisa iziyobisi? <i>How many times do you take drugs on a typical day when you use drugs?</i>	Awekho 0	Kanye okanye kabini 1-2	Kathathu okanye kane ngeveki 3-4 a month	Kahlanu okanye kathandathu 5-6 a week	Kasixhenxe nangaphezulu 7 or more
4. Kukangakanani uphantsi kwempembelelo yeziyobisi ngokugqithisileyo? <i>How often are you influenced heavily by drugs?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
5. Ukhe waziva urhalela iziyobisi kakhulu kangangokuba awakwazi ukuzinqanda? <i>Have you felt that your longing for drugs was so strong that you could not resist it?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
6. Ibikhe yenzeka into yokuba ungakwazi ukuyeka iziyobisi xa sele uqalile ukuzisebenzisa? <i>Has it happened that you have not been able to stop taking drugs once you started?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
7. Ukhe wasebenzisa iziyobisi waze awayenza into ebekufaneleke ukuba uyayenza? <i>Have you taken drugs and then neglected to do something you should have done?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day

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Initials of interviewer: _____

	0	1	2	3	4
8. Kukangakanani ufuna ukusebenzisa iziyobisi ekuseni emva kokuba ubuzisebenzise kakhulu kusuku oludlulileyo? <i>How often have you needed to take a drug in the morning after heavy drug use the day before?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
9. Kukangakanani uzisola okanye unesazela ngenxa yokuba ubusebenzise iziyobisi? <i>How often have you had guilt feelings or a bad conscience because you used drugs?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
10. Ukhe wonzakala okanye konzakala omnye umntu (ngokwasengqondweni okanye ngokwasemzimbeni) ngenxa yokuba ubusebenzise iziyobisi? <i>Have you or anyone else been hurt (mentally or physically) because you used drugs?</i>	Hayi No	Ewe, kodwa hayi kulonyaka uphelileyo Yes, but not in the past year	Ewe, kulonyaka uphelileyo Yes, in the past year		
11. Ingaba isizalwana okanye umhlobo, ugqirha okanye unesi, okanye omnye umntu baxhalabile ngokusebenzisa kwakho iziyobisi okanye bathi kuwe kufuneka uyeke ukusebenzisa iziyobisi? <i>Has a relative or a friend, doctor or a nurse, or anyone else, been worried about your drug use or said to you that you should stop using drugs?</i>	Hayi No	Ewe, kodwa hayi kulonyaka uphelileyo Yes, but not over the past year	Ewe, kulonyaka uphelileyo Yes, in the past year		
Total score:					

Signed Interviewer completing CRF: _____ Date: ____ / ____ / ____
DD MMM YYYY

Signed QC Officer: _____ Date: ____ / ____ / ____
DD MMM YYYY

Signed Study Coordinator: _____ Date: ____ / ____ / ____
DD MMM YYYY

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MATERNITY CASE RECORD ABSTRACTION FORM[illegible]

Year	Gestation	Delivery	Weight	Sex	Outcome	Complications

THIS Pregnancy Healthy: ☐ YES ☐ NO If <u>NO</u> tick all options that apply	☐ Hypertension ☐ Epilepsy ☐ Cardiac ☐ TB ☐ Other: _____ Further details if any of the above selected: _____
	Any Medications: <i>please specify</i> _____
	Previous Pregnancies ☐ Family History
☐ Twins ☐ Diabetes ☐ TB ☐ Congenital ☐ Other: _____ Further details if any of the above selected: _____ _____	

PWID: _____ - ____

Details of Booking Examination

Date	____ / ____ / ____ DD MMM YYYY	BP	____ / ____ Systolic Diastolic	HB	____ g/dl
Height: ____ cm	Weight: ____ kg		MUAC: ____ cm		
SFH: ____ cm					

RPR Result	Neg	Pos	Titre if pos: ____	Rhesus: ____	ABO Bloodgroup: ____
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1st HIV Test	____ / ____ / ____ DD MMM YYYY	RESULT			2nd HIV Test	____ / ____ / ____ DD MMM YYYY	RESULT			
		POS	NEG	Decline			POS	NEG	Decline	
On ART	Y	N	Initiation Date	____ / ____ / ____ DD MMM YYYY	Regimen					

EDD Estimation

Date of assessment #1	____ / ____ / ____	# 1: Type	Date / LNMP	SFH	USS
Gestational Age (weeks):		EDD: ____ / ____ / ____ DD MMM YYYY			
Date of assessment #2	____ / ____ / ____	#2: Type	Date / LNMP	SFH	USS
Gestational Age (weeks):		EDD: ____ / ____ / ____ DD MMM YYYY			
Date of assessment #3	____ / ____ / ____	#3: Type	Date / LNMP	SFH	USS
Gestational Age (weeks):		EDD: ____ / ____ / ____ DD MMM YYYY			

Additional Notes:

Signed by Abstractor: _____

PWID: _____ - _____

ODA

OBSTETRICS ABSTRACTION FORM

**This form applies to ALL enrolled BPOS Participants
Complete after delivery**

Date of Data Abstraction:	____ / ____ / ____ DD MM YYYY	Initials of Data Abstractor:	
Participant Full Name:			Participant Date of Birth: ____ / ____ / ____ DD MM YYYY
Participant National ID		Provincial Folder Number: specify 3 letter facility prefix: GUP or other	G U P _____
Source Document	☐ Maternity Case Record ☐ Delivery Register ☐ PMTCT Register (incl DISA/Trakcare) ☐ Other, Please Specify: _____		

MOTHERS DETAILS

Name of clinic		GA at 1st visit		Booking Date	____ / ____ / ____ DD MM YYYY
Hb		Rhesus	Pos Neg	Syphilis	Pos Neg
HIV results	Pos Neg	HIV retest	Pos Neg	ART	Y N
Regimen			☐ NR	ART Start Date	____ / ____ / ____ DD MM YYYY
Estimated Gestational Age	Weeks: _____ If weeks not recorded: ☐ Term ☐ Preterm		Gestational Age estimated by	☐ Dates ☐ Palpitation ☐ SFH ☐ Ultrasound Scan ☐ Not Reported	

LABOUR DETAILS

Delivery Date	____ / ____ / ____ DD MM YYYY	Delivery time	____ : ____
Fetal Heart	Present Absent uncertain	Fetal Distress	Y N NR
Place of Delivery	☐ GMOU ☐ MMH ☐ GSH ☐ Other, Specify: _____	Delivery Method <i>Please tick all methods used during this delivery</i>	☐ NVD ☐ C/S ☐ Induction of labour ☐ Vacuum ☐ Forceps ☐ BBA

If C/S, Primary indication	☐ Fetal distress ☐ Obstructed labour ☐ Twins/Triples ☐ Pre-eclampsia / eclampsia ☐ APH ☐ Previous C/S ☐ Other, specify: _____	If by C/S, was it performed after membrane rupture?	☐ Yes, Duration: ____ Mins ☐ No ☐ NR
-----------------------------------	---	--	---

Please tick all major medical and/or obstetric conditions the mother experienced during pregnancy and/or during delivery.	☐ Chorio amnionitis	☐ Sepsis	☐ UTI / Pyelonephritis
	☐ IUGR	☐ Hypertension	☐ Pre-eclampsia/ eclampsia
☐ Diabetes mellitus	☐ Preterm labour	☐ APH	
☐ PPH	☐ Prolonged ROM	☐ Prolonged labour	
☐ Cervical tear	☐ Perineal tear	☐ Episiotomy	
☐ Other, Specify: _____			

INFANT DETAILS

Infant DOB	____ / ____ / ____ DD MMM YYYY	Infant DOB for Twin B	____ / ____ / ____ DD MMM YYYY
Gender	☐ Male ☐ Female	Gender Twin B	☐ Male ☐ Female
Outcome	☐ Alive ☐ Stillborn ☐ NND	Outcome Twin B	☐ Alive ☐ Stillborn ☐ NND
Resuscitation	☐ Yes ☐ No	Resuscitation Twin B	☐ Yes ☐ No
Birthweight	_____ g	Birthweight Twin B	_____ g
Head circumference	_____ cm	Head circumference Twin B	_____ cm
Length	_____ cm	Length Twin B	_____ cm
APGAR Score	1 min: _____ 5 min: _____	APGAR Score Twin B	1 min: _____ 5 min: _____
Congenital Abnormalities?	☐ Yes ☐ No ☐ NR Specify: _____	Congenital Abnormalities Twin B	☐ Yes ☐ No ☐ NR Specify: _____
Polio Vaccine?	☐ Yes ☐ No ☐ NR	Polio Vaccine Twin B	☐ Yes ☐ No ☐ NR
BCG Vaccine?	☐ Yes ☐ No ☐ NR	BCG Vaccine Twin B	☐ Yes ☐ No ☐ NR
NVP at birth?	☐ Yes ☐ No ☐ NR	Twin B NVP at birth?	☐ Yes ☐ No ☐ NR
Feeding Option	☐ Breast ☐ Formula		

DISCHARGE SUMMARY

Family planning choice	☐ Oral contraceptive ☐ Implant	☐ Injectable ☐ Tubal ligation	☐ IUD ☐ Other: _____
Date of discharge	____ / ____ / ____ DD MMM YYYY		

PWID: _____

MATERNAL HISTORY OF SUBSTANCE USE
This CRF applies to **ALL** enrolled BPOS participants
To be completed at **ALL** Study visits

Visit Date								
D	D	M	M	M	Y	Y	Y	Y

Visit Code	
A	1

A: AUDIT (Alcohol Use Disorders Identification Test)

Ngoku sizokubiza eminye imibuzo malunga nokusebenzisa kwakho utywala njengoko uye wafumanisa ukuba ukhulelwe. Nceda ukhethe impendulo echanekileyo ngokubiyela ibhokisi efanelekileyo. Nceda uqale umbuzo ngamnye ngo "Njengoko uye wafumanisa ukuba ukhulelwe"

Now we are going to ask you some questions about your use of alcohol beverages since you found out you were pregnant. Please choose the correct answer by circling in the appropriate box. Please start each question with "Since you found out you were pregnant"

	0	1	2	3	4
1. Ubusela kangakanani utywala? <i>How often do you have a drink containing alcohol?</i> Uba u'0' Gqithela ku Q3 <i>If '0' SKIP to 3</i>	Zange <i>Never</i>	Kanye ngenyanga nangaphantsi <i>Once a month or less often</i>	Kabini ukuya kwisine ngenyanga <i>2-4 times a month</i>	Kabini ukuya kwisithathu ngeveki <i>2-3 times a week</i>	Kane nangaphezulu evekini <i>4 times or more a week</i>
2. Zingaphi iglasi zotywala oziselayo ngemini? <i>How many drinks containing alcohol do you have on a typical day when you are drinking?</i>	Kanye okanye kabini <i>1 or 2</i>	Kathathu okanye kane <i>3 or 4</i>	Kahlanu okanye kathandathu <i>5 or 6</i>	Kasixhenxe okanye kalithoba <i>7 or 9</i>	Kalishumi nangaphezulu <i>10 or more</i>
3. Kukangakanani usela iglasi ezintandathu nangaphezulu ngexesha elinye? <i>How often do you have six or more drinks on one occasion?</i>	Zange <i>Never</i>	Ngaphantsi kwenyanga <i>Less than monthly</i>	Ngenyanga <i>Monthly</i>	Ngeveki <i>Weekly</i>	Ngosuku okanye phantse yonke imihla <i>Daily or almost daily</i>
4. Kukangakanani kulonyaka uphelileyo ufumanisa ukuba awukwazi ukuyeka ukusela xa sele uqalile? <i>How often during the last year have you found that you were not able to stop drinking once you had started?</i>	Zange <i>Never</i>	Ngaphantsi kwenyanga <i>Less than monthly</i>	Ngenyanga <i>Monthly</i>	Ngeveki <i>Weekly</i>	Ngosuku okanye phantse yonke imihla <i>Daily or almost daily</i>
5. Kukangakanani ungaphumeleli ukwenza into ebekumele ukuba uyayenza awakwazi ngenxa yokuba ubusela? <i>How often have you failed to do what was normally expected of you because of drinking?</i>	Zange <i>Never</i>	Ngaphantsi kwenyanga <i>Less than monthly</i>	Ngenyanga <i>Monthly</i>	Ngeveki <i>Weekly</i>	Ngosuku okanye phantse yonke imihla <i>Daily or almost daily</i>

Page 1 of 4

Initials of interviewer: _____

	0	1	2	3	4
6. Kukangaphi ufuna "ukuqabula" ekuseni kuba ufuna ukuqala usuku lwakho kakhuhle emva kokuba ubusele utywala kakhulu? <i>How many times have you needed a drink in the morning to get yourself going after a heavy drinking session?</i>	Zange <i>Never</i>	Ngaphantsi kwenyanga <i>Less than monthly</i>	Ngenyanga <i>Monthly</i>	Ngeveki <i>Weekly</i>	Ngosuku okanye phantse yonke imihla <i>Daily or almost daily</i>
7. Kukangakanani uzifumanisa unesazela okanye uzisola emva kokuba usele? <i>How often have you had a feeling of guilt or remorse after drinking?</i>	Zange <i>Never</i>	Ngaphantsi kwenyanga <i>Less than monthly</i>	Ngenyanga <i>Monthly</i>	Ngeveki <i>Weekly</i>	Ngosuku okanye phantse yonke imihla <i>Daily or almost daily</i>
8. Kukangakanani ungayikhumbuli into eyenzekileyo kubusuku obudlulileyo ngenxa yokuba ubusela? <i>How often have you been unable to remember what happened the night before because you had been drinking?</i>	Zange <i>Never</i>	Ngaphantsi kwenyanga <i>Less than monthly</i>	Ngenyanga <i>Monthly</i>	Ngeveki <i>Weekly</i>	Ngosuku okanye phantse yonke imihla <i>Daily or almost daily</i>
9. Ukhe wonzakala okanye omnye umntu wonzakala ngenxa yokuba ubusele? <i>Have you or anyone else been injured as a result of your drinking?</i>	Hayi <i>No</i>	Ewe, kodwa hayi kulonyaka uphelileyo <i>Yes, but not in the past year</i>	Ewe, kulonyaka uphelileyo <i>Yes, during the past year</i>		
10. Sikhona isizalwana okanye umhlobo wakho, ugqirha okanye omnye umsebenzi wezempi othe waxhalaba ngendlela osela ngayo waza wakucebisa ukuba uthobe isantya? <i>Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?</i>	Hayi <i>No</i>	Ewe, kodwa hayi kulonyaka uphelileyo <i>Yes, but not in the past year</i>	Ewe, kulonyaka uphelileyo <i>Yes, during the past year</i>		
Record total of specific items here					

Page 2 of 4

Initials of interviewer: _____

PWID: _____

B: DUDIT (Drug Use Disorders Identification Test)

Ngoku sizokubiza eminye imibuzo malunga nokusebenzisa kwakho iziyobisi njengoko uye wafumanisa ukuba ukhulelwe. Nceda ukhethe impendulo echanekileyo ngokubiyela kwibhokisi efanelekileyo. Nceda uqale umbuzo ngamnye ngo " Njengoko uye wafumanisa ukuba ukhulelwe"

We are now going to ask you some questions about your use of drugs since you found out you were pregnant. Please choose the correct answer by crossing with an "X" in the appropriate box. Please start each question with "Since you found out you were pregnant"

	0	1	2	3	4
1. Uzisebenzisa kangakanani ezinye iziyobisi ngaphandle kotywala? <i>How often do you use drugs other than alcohol?</i>	Zange Never	Kanye ngenyanga nangaphantsi Once a month or less often	Kabini ukuya kwisine ngenyanga 2-4 times a month	Kabini ukuya kwisithathu ngeveki 2-3 times a week	Kane ngeveki okanye ngaphezu koko 4 times a week or more often
2. Usebenzisa ngaphezu kohlobo olunye lweziyobisi ngexesha elinye? <i>Do you use more than one type of drug on the same occasion?</i>	Zange Never	Kanye ngenyanga nangaphantsi Once a month or less often	Kabini ukuya kwisine ngenyanga 2-4 times a month	Kabini ukuya kwisithathu ngeveki 2-3 times a week	Kane ngeveki okanye ngaphezu koko 4 times a week or more often
3. Mangaphi amaxesha owathathayo ngosuku xa usebenzisa iziyobisi? <i>How many times do you take drugs on a typical day when you use drugs?</i>	Awekho 0	Kanye okanye kabini 1-2	Kathathu okanye kane ngeveki 3-4 a month	Kahlanu okanye kathandathu 5-6 a week	Kasixhenxe nangaphezulu 7 or more
4. Kukangakanani uphantsi kwempembelelo yeziyobisi ngokugqithisileyo? <i>How often are you influenced heavily by drugs?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
5. Ukhe waziva urhalela iziyobisi kakhulu kangangokuba awakwazi ukuzinqanda? <i>Have you felt that your longing for drugs was so strong that you could not resist it?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
6. Ibikhe yenzeka into yokuba ungakwazi ukuyeka iziyobisi xa sele uqalile ukuzisebenzisa? <i>Has it happened that you have not been able to stop taking drugs once you started?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
7. Ukhe wasebenzisa iziyobisi waze awayenza into ebekufaneleke ukuba uyayenza? <i>Have you taken drugs and then neglected to do something you should have done?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day

Page 3 of 4

Initials of interviewer: _____

	0	1	2	3	4
8. Kukangakanani ufuna ukusebenzisa iziyobisi ekuseni emva kokuba ubuzisebenzise kakhulu kusuku oludlulileyo? <i>How often have you needed to take a drug in the morning after heavy drug use the day before?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
9. Kukangakanani uzisola okanye unesazela ngenxa yokuba ubusebenzise iziyobisi? <i>How often have you had guilt feelings or a bad conscience because you used drugs?</i>	Zange Never	Ngaphantsi kwenyanga Less often than a month	Ngenyanga zonke Every month	Qho ngeveki Every week	Ngosuku okanye phantse yonke imihla Daily or almost every day
10. Ukhe wonzakala okanye konzakala omnye umntu (ngokwasengqondweni okanye ngokwasemzimbeni) ngenxa yokuba ubusebenzise iziyobisi? <i>Have you or anyone else been hurt (mentally or physically) because you used drugs?</i>	Hayi No	Ewe, kodwa hayi kulonyaka uphelileyo Yes, but not in the past year	Ewe, kulonyaka uphelileyo Yes, in the past year		
11. Ingaba isizalwana okanye umhlobo, ugqirha okanye unesi, okanye omnye umntu baxhalabile ngokusebenzisa kwakho iziyobisi okanye bathi kuwe kufuneka uyeke ukusebenzisa iziyobisi? <i>Has a relative or a friend, doctor or a nurse, or anyone else, been worried about your drug use or said to you that you should stop using drugs?</i>	Hayi No	Ewe, kodwa hayi kulonyaka uphelileyo Yes, but not over the past year	Ewe, kulonyaka uphelileyo Yes, in the past year		
Total score:					

Signed Interviewer completing CRF: _____ Date: ____/____/____
DD MM YYYY

Signed QC Officer: _____ Date: ____/____/____
DD MM YYYY

Signed Study Coordinator: _____ Date: ____/____/____
DD MM YYYY

Page 4 of 4

Initials of interviewer: _____

PWID: _____ - _____

MATERNAL DEMOGRAPHICS & CLINICAL HISTORY

This CRF applies to ALL enrolled BPOS participants

Visit Date									
D	D	M	M	M	Y	Y	Y	Y	

Visit Code	
A	1

A: SOCIODEMOGRAPHIC INFORMATION

1. Uzelwe Nini? <i>What is your date of birth?</i>	____ / ____ / ____ DD MMM YYYY
2. Uthetha oluphi ulwimi ekhaya? <i>What language do you speak at home?</i>	☐ isiXhosa ☐ isiZulu ☐ isiBhulu <i>Afrikaans</i> ☐ isiNgesi <i>English</i> ☐ Olunye <i>Other</i> Cacisa <i>Specify</i> : _____
3. Leliphi elona banga liphezulu oliphumeleleyo? <i>What is the highest level of schooling/education that you have completed?</i>	☐ Inqanaba: _____ <i>Grade</i> Okanye or ☐ Ibanga: _____ <i>Standard</i> ☐ Imfundo ephezulu: cacisa _____ <i>Postsecondary, specify</i> ☐ Akukho nenye <i>None</i>
4. Ingaba uyasebenza na ngoku kwaye/okanye uyafunda? <i>Are you currently working and/or studying?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
5. Ukuba nguEwe, yeyiphi kwezi zilandelayo eyichaza ngcono into oyenzayo? <i>If yes, which one of the following best describes what you do?</i> Khethe ibenye kuphela <i>Choose ONE only</i>	☐ Uphangela isigxina <i>Employed full-time</i> ☐ Uphangela manqapha-nqapha <i>Employed part-time</i> ☐ Umsebenzi onjengokuthengisa endlini okanye esitalatweni. <i>Informal job/hawker</i> ☐ Uhamba isikolo/ngumfundi <i>Attending school/learner</i> ☐ Uhamba isikolo eYunivesithi/Kholeji <i>Attending tertiary education (University/College)</i>
6. Ingaba ukhona umvuzo owufumanayo? <i>Do you earn an income?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>

→ Gqithela ku Q8
SKIP to Q8

→ Gqithela ku Q8
SKIP to Q8

7. Ingaba ungakanani umvuzo owufumanayo ngenyanga? <i>How much income do you earn per month?</i>	☐ Ngaphantsi kwe waka lerandi ngenyanga <i>Less than R1 000 per month</i> ☐ Iwaka ukuya kumawaka amahlanu erandi ngenyanga <i>R1 000 to R5 000 per month</i> ☐ Amawaka amahlanu ukuya kumawaka alishumi erandi ngenyanga <i>R5 000 to R10 000 per month</i> ☐ Amawaka alishumi ukuya kumawaka alishumi elinesihlanu erandi ngenyanga <i>R10 000 to R15 000 per month</i> ☐ Ngaphezu kwamawaka alishumi elinesihlanu erandi ngenyanga. <i>More than R15 000 per month</i>
8. Ingaba lukhona naluphi na uhlobo lwesibonelelo sika rhulumente olufumanayo? <i>Do you currently receive any social assistance in the form of government grants?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Gqithela ku Q11 SKIP to Q11
9. Loluphi uhlobo lwesibonelelo sika rhulumente olufumanayo ? <i>Which type of government grant do you receive?</i>	☐ Isibonelelo sabantwana <i>Children's grant</i> ☐ Isibonelelo sokukhubazeka <i>Disability grant</i> ☐ Isibonelelo sokukhathalela <i>Care Dependency grant</i> ☐ Okunye , nceda cacisa: _____ <i>Other, please specify</i>
10. Ufumana izibonelelo ezingaphi kwezi zikhankanywe ngasentla (Q9)? Nceda ucacise inani <i>How many of each of the grants mentioned above (Q9) do you receive?</i> Please specify number	☐ Isibonelelo sabantwana inani lezibonelelo ____ <i>Children's grant</i> <i># of grants</i> ☐ Isibonelelo sokukhubazeka inani lezibonelelo ____ <i>Disability grant</i> <i># of grants</i> ☐ Isibonelelo sokukhathalela inani lezibonelelo ____ <i>Care Dependency grant</i> <i># of grants</i> ☐ Ezinye, nceda cacisa inani lezibonelelo ____ <i>Other, please specify:</i> _____ <i># of grants</i>
11. Uhlala kwikhaya elinjani? <i>What kind of home do you live in?</i>	☐ Ityotyombe/ uhlaliso olungahlelwanga <i>Shack/informal dwelling</i> ☐ Indlu yesitena <i>Formal house</i> ☐ Ifleti/ indlu kamasipala <i>Flat/council home</i> ☐ Elinye, Cacisa: _____ <i>Other Specify:</i>

PWID: _____ - _____

12. Ingaba indlu yakho inazo ezi zinto zilandelayo: <i>Does your house have the following:</i> Phendula kuzo ZONKE <i>Respond to ALL</i>	a. Indlu yangasese engaphakathi <i>A toilet inside</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>	b. Amanzi empompo ngaphakathi endlini <i>Running water inside</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
	c. Umbane ngaphakathi endlini <i>Electricity inside</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>	d. Isikhenkcezisi <i>A refrigerator</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
	e. Umnxeba wasendlini <i>A landline telephone</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>	f. Umabonakude <i>A television</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
13. Oku kuquka nawe, bangaphi abantu (abadala nabantwana) abahlala endlini yakho. <i>Including yourself, how many people (adults and children) live in your house?</i>		Inani Labantu: _____ <i>Number of people</i>
14. Ukhulelwe kangaphi (kuquka noku kukhulelwa kwangoku)? <i>How many times have you been pregnant (including current pregnancy)?</i>		Inani lokukhulelwa: _____ <i>Number of pregnancies</i>
15. Bangaphi abantwana obazeleyo? <i>How many children have you given birth to?</i>		Inani labantwana: ☐ _____ ☐ Abekho <i>Number of children</i> <i>None</i> → Ukuba awunabo abantwana, Gqithela ku Q17 <i>If NONE, SKIP to Q17</i>
16. Bangaphi kwaba bantwana abaphilayo? <i>How many of these children are living?</i>		Inani labantwana: ☐ _____ ☐ Abekho <i>Number of children</i> <i>None</i>
B: MEDICAL HISTORY		
Ngoku sizokubuzwa imibuzo embalwa malunga nembali yempilo yakho kuquka isifo sephepha kunye nentsholongwane kagawulayo. <i>We are now going to ask you a few questions about your previous medical history including TB and HIV.</i>		
B1: TB HISTORY		
17. Koku kukhulelwa kwakho kwangoku, ingaba ugqirha okanye unesi wakhe wakuxelele ukuba une-TB? <i>During your current pregnancy, has a doctor or nurse told you that you have TB?</i>		☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Gqithela ku Q22 <i>SKIP to Q22</i>
18. Wafumanisa nini ukuba une TB? <i>When did you receive this TB diagnosis?</i>		_____ / _____ / _____ DD MMM YYYY
19. Wafumanisa phi ukuba une TB? <i>Where did you receive this TB diagnosis?</i>		Igama leklinikhi : _____ <i>Name of clinic</i>

20. Yayiphi emzimbeni wakho le TB (e.g, kwimiphunga, kwenye indawo)? <i>Where in your body was the TB (e.g., lungs, other location)?</i>	Indawo emzimbeni : _____ <i>Place in body</i>
21. Waye walufumana unyango lwe TB? <i>Did you receive treatment for TB?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
22. Ngaphandle koku kukhulelwa, ingaba ugqirha okanye unesi wakhe wakuxelela ukuba une-TB? <i>Other than during this pregnancy has a doctor or nurse ever told you that you have TB?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
23. Wafumanisa nini ukuba une TB eku Q22 (hayi koku kukhulelwa)? <i>When did you receive this TB diagnosis from Q22 (not during this pregnancy)?</i>	_____ / _____ / _____ DD MMM YYYY
24. Waye walufumana unyango lwe TB ngelaxesha yayifunyaniswa (Ku Q22)? <i>Did you receive treatment for TB when last diagnosed (From Q22)?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
25. Ngamaxesha amangaphi ewonke owathi wafumana ngawo unyango lweTB? <i>How many times in total have you been treated for TB?</i>	Inani lamaxesha: _____ <i>Number of times</i>
26. Walufumana phi unyango lwe TB (Ku Q22)? <i>Where did you receive your TB treatment (From Q22)?</i>	Igama lekliniki : _____ <i>Name of clinic</i>
27. Yaba lixesha elingakanani ufumana unyango lweTB ngexesha lokugqibela eyathi yafunyaniswa ngalo? <i>How long was your TB treatment the last time you were diagnosed?</i>	☐ inyanga ezintandathu 6 months ☐ inyanga ezisibhozo 8 months ☐ inyanga ezilithoba 9 months ☐ Iyaqhubeleka <i>On-going</i> ☐ Elinye, cacisa: _____ <i>Other, specify</i> ☐ Andazi <i>Don't know</i>
B2: HIV HISTORY	
28. Ingaba wakhe wayivavanyelwa intsholongwane kagawulayo? <i>Have you ever been tested for HIV?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i>
29. Ingaba uchaphazelekile na yintsholongwane ka gawulayo okanye hayi awuchaphazelekanga? <i>Are you HIV-negative or HIV-positive?</i>	☐ Andichaphazelekanga <i>Negative</i> ☐ Ndichaphazelekile <i>Positive</i> ☐ Andazi <i>Don't know</i>

PWID: _____ - _____

NB: Nceda gcwalisa yonke ifomu yentsholongwane ka gawulayo

Please complete HIV CRF for ALL PARTICIPANTS

Signed Interviewer completing CRF: _____

Date: _____ / _____ / _____
DD MMM YYYY

Signed QC Officer: _____

Date: _____ / _____ / _____
DD MMM YYYY

Signed Study Coordinator: _____

Date: _____ / _____ / _____
DD MMM YYYY

PWID: _____ - ____

MATERNAL HIV AND ART HISTORY

This CRF applies to ALL enrolled BPOS participants
To be completed at ALL Study visits

Visit Date								
D	D	M	M	M	Y	Y	Y	Y

Visit Code	
A	1

A: HIV HISTORY

Ngoku sizokubuza imibuzo embalwa ngembali yakho ye ntsholongwane ka gawulayo.
We are going to ask you a few questions about your HIV history.

Please specify data source:
Maternal Case Record or Self-report

☐ HIV-Negative

☐ HIV Positive

1. Ubuqala ukufumanisa ukuba unentsholongwane kagawulayo koku kukhulelwa okanye phambi koku kukhulelwa? <i>Did you first test HIV-positive in this pregnancy or before this pregnancy?</i>	☐ Koku kukhulelwa → Gcwalisa umhla ngezantsi kwaye ume apha!!! <i>In this pregnancy Complete date below and STOP here!!!</i> ☐ Phambi koku kukhulelwa <i>Before this pregnancy</i>
2. Kwakunini ukuqala kwakho ukufumanisa ukuba unentsholongwane kagawulayo? <i>When did you first test HIV-positive?</i>	____ / ____ / ____ DD MMM YYYY
3. Njengoko uthe wafumaneka unentsholongwane kagawulayo, ubukhe wakhulelwa? <i>Since you tested HIV positive, have you been pregnant?</i>	☐ Ewe Yes ☐ Hayi No → Gqithela ku Q5 <i>SKIP to Q5</i>
4. Ingaba wawanikwa na amayeza (iAZT kunye ne NVP) ngelaxesha wawusakhulelwe okanye xa wawubeleka? <i>Have you ever been given medication (AZT and NVP) while pregnant or at delivery?</i>	☐ Ewe Yes ☐ Hayi No
5. Ingaba wayisebenzisa na iART (yobom bonke)? <i>Have you ever taken triple drug antiretroviral therapy (lifelong ART)?</i>	☐ Ewe Yes ☐ Hayi No → Gqithela ku Q19 <i>SKIP to Q19</i>
6. Wawuyifumene phi iART ukugqibela kwakho? <i>Where did you receive ART the last time?</i>	Igama lekliniki: _____ <i>Name of clinic:</i>
7. Njengoko wathi waqala ukusebenzisa iART, wawukhe wayiyeka? <i>Since you first started taking ART, have you ever stopped?</i>	☐ Ewe Yes ☐ Hayi No → Gqithela ku Q12 <i>SKIP to Q12</i>

PWID: _____ - ____

8. Mangaphi amaxesha owawukhe wayiyeka waphinda wayiqalela iART? <i>How many times have you stopped and restarted ART?</i>	Inani lamaxesha: _____ <i>Number of times</i>
9. Waphinda wayiqalela nini iART ngexesha apho wawukhe wayiyeka? <i>When did you restart ART the last time you stopped?</i>	____ / ____ / ____ <i>DD MMM YYYY</i>
10. Usayisebenzisa iART? <i>Are you still taking ART?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Gqithela ku Q11 GO TO Q11
11. Wayeka nini ukusebenzisa iART? <i>When did you stop taking ART?</i>	____ / ____ / ____ <i>DD MMM YYYY</i> → Gqithela ku Q19 SKIP to Q19
12. Yintoni igama le ARVs ozisebenzisayo ngoku? <i>What are the names of the ARVs you are currently taking?</i>	☐ TDF-3TC-EFV ☐ TDF-3TC-NVP ☐ TDF-FTC-EFV (Tribuss/Odimune/Atripla) ☐ AZT-3TC-NVP ☐ AZT-3TC-EFV ☐ TDF-3TC-LPV/r ☐ AZT-3TC-LPV/r ☐ Other: _____
13. Uyithatha amaxesha amangaphi ngosuku iART? <i>How many times a day do you take your ART?</i>	Inani lamaxesha: _____ <i>Number of times</i>
14. Zingaphi ipilisi ozisebenzisayo ngexesha ngalinye? <i>How many pills do you take each time?</i>	Inani Iepilisi: _____ <i>Number of pills</i>
B: ADHERENCE	
Ngoku sizokubuza imibuzo embalwa malunga nokuncekelela kwakho unyango lwe ARV (ART). <i>We are going to ask you some questions about your adherence to ARV treatment (ART).</i>	
15. Kwezi ntsuku zingamashumi amathathu zidlulileyo, zintsuku ezingaphi owathi walibala ngazo ubuncinane bomlinganiselo omnye walo naliphi na iyeza lakho lentsholongwane ka gawulayo? <i>In the last 30 days, on how many days did you miss at least one dose of any of your HIV medicines?</i>	Inani lentsuku: _____ (0-30) <i>Number of days</i>
16. Kwezi ntsuku zingamashumi amathathu zidlulileyo, kukangakanani apho wathi wawasebenzisa ngendlela ekwakufaneleke uwasebenzise ngayo amayeza entsholongwane ka gawulayo? <i>In the last 30 days, how often did you take your HIV medicines in the way that you were supposed to?</i>	☐ Zange <i>Never</i> ☐ Ibingaxhaphakanga <i>Rarely</i> ☐ Ngamanye amaxesha <i>Sometimes</i> ☐ Ngesiqhelo <i>Usually</i> ☐ Phantse oko <i>Almost always</i> ☐ Oko <i>Always</i>

PWID: _ _ _ _ _ - _ _

17. Kwezi ntsuku zingamashumi amathathu zidlulileyo, wabamhle kangakanani umsebenzi owathi wawenza ngendlela ekwakufaneleke uwasebenzise ngayo amayeza entsholongwane ka gawulayo? <i>In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?</i>	☐ Kakubi kakhulu <i>Very poor</i> ☐ Kakubi <i>Poor</i> ☐ Phakathi <i>Fair</i> ☐ Kakuhle <i>Good</i> ☐ Kakuhle kakhulu <i>Very good</i> ☐ Kakuhle ngokugqithisileyo <i>Excellent</i>
18. Kunzima kangakanani kuwe ukusebenzisa amayeza entsholongwane kagawulayo ngendlela ekufaneleke uwasebenzise ngayo? <i>How hard is it for you to take HIV medicines in a way you are supposed to?</i>	☐ Kunzima ngokugqithisileyo <i>Extremely hard</i> ☐ Kunzima kakhulu <i>Very hard</i> ☐ Kunzima nje <i>Somewhat hard</i> ☐ Akunzimanga kakhulu <i>Not very hard</i> ☐ Akunzimanga konke-konke <i>Not hard at all</i>
C: DISCLOSURE Ngoku sizokubuza imibuzo ethile malunga nomntu (ukuba ukhona) othe wamxelela malunga nesimo sakho sentsholongwane kagawulayo. <i>We are going to ask you some questions about whom (if at all) you have disclosed to about your HIV status.</i>	
19. Ingaba ukhona na umntu owathi wamxelela ngesimo sakho sentsholongwane kagawulayo, ngaphandle kwengcaphephe zempilo? <i>Have you told anyone about your HIV status, other than health professionals?</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → PHELISA!!! END!!!
20. Ngawaphi kulamalungu osapho owathi wawaxelela ngesimo sakho sentsholongwane kagawulayo? Nceda phendula umbuzo ngamnye kule ilandelayo: <i>Which of these family members have you told about your HIV status? Please answer this question for each of the following:</i> Umzekelo: Ingaba wamxelele na u_____ ukuba wena unentsholongwane kagawulayo? <i>Example: Have you told your _____ that you are HIV-positive?</i>	
a. Umyeni <i>Husband</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamyeni) <i>No husband</i>
b. Umlingane/iqabane <i>Boyfriend/partner</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamlingane) <i>No boyfriend</i>
c. Umama <i>Mother</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamama) <i>No mother</i>
d. Utata <i>Father</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (andinatata) <i>No father</i>
e. Udade wenu <i>Sister</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (andina dadewethu) <i>No sister</i>
f. Umntakwenu <i>Brother</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamntakwethu) <i>No brother</i>
g. Umntwana oyintombi <i>Daughter</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamntwana oyintombi) <i>No daughter</i>
h. Unyana <i>Son</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinanyana) <i>No son</i>

PWID: _____ - ____

i. Umalume <i>Uncle</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamalume) <i>No uncle</i>
j. Umalumekazi/makazi/dadobawo <i>Aunt</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamalumekazi/makazi/dadobawo) <i>No aunt</i>
k. Umzala oyindoda <i>Male cousin</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamzala oyindoda) <i>No male cousin</i>
l. Umzala ongumfazi <i>Female cousin</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamzala ongumfazi) <i>No female cousin</i>
m. Amanye amalungu osapho angamadoda <i>Other male family member</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Awekho amalungu osapho angamadoda) <i>No other male family member</i>
n. Amanye amalungu osapho angomama <i>Other female family member</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Awekho amalungu osapho angomama) <i>No other female family member</i>
21. Ngaphandle kwalamalungu osapho adweliswe ngasentla, ngubani omnye umntu owathi wamxelela ngesimo sakho sentsholongwane kagawulayo? (funda kwaye uphendule konke) <i>Besides family members listed above, who else have you told about your HIV status? (read and answer for all)</i>	
a. Iqumrhu lenkxaso <i>Support group</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andilolungu laqumrhu lenkxaso) <i>Do not belong to a support group</i>
b. Iqabane owabelana nalo ngesondo ongahlali nawe <i>A sexual partner who does not live with you</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinaqabane endabelana nalo ngesondo) <i>Do not have a sexual partner</i>
c. Abahlobo <i>Friends</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinabahlobo) <i>Do not have friends</i>
d. Umphathi waseCaweni <i>Church minister</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamphathi waseCaweni) <i>Do not have a church minister</i>
e. Umthandazeli <i>Spiritual healer</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamthandazeli) <i>Do not have spiritual healer</i>
f. Umqeshi wangoku okanye owayesakuba ngumqeshi wakho <i>Current or former employer</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A (Andinamqeshi owayesaya kuba ngowam/umqeshi wangoku) <i>Do not have a former/current employer</i>
g. Ukuphumela elubala ekuhlaleni <i>Public disclosure/community</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A
h. Abanye, cacisa <i>Other, specify: _____</i>	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> ☐ N/A

Signed Interviewer completing CRF: _____

Date: ____ / ____ / ____

Signed QC Officer: _____

Date: ____ / ____ / ____

Signed Study Coordinator: _____

Date: ____ / ____ / ____

PWID: _____ - ____

MATERNAL MEDICATION USE AND SIDE EFFECT

This CRF applies to **ALL** enrolled BPOS Participants
To be completed at **ALL** Study visits

Visit Date								
D	D	M	M	M	Y	Y	Y	Y

Visit Code	
A	1

NCEDA UFUNDELE UMTATHI NXAXHEBA

Lemibuzo ilandelayo iyakubhekisa kuwo nawaphina na amayeza namachiza othe wawasebenzisa. Oku kuquka nawaphi na amayeza kunye/okanye amachiza aphuma kubasebenzi baseklinikhi nase sibhedlela (oogqirha namanesi), ekhemesti, kwivenkile zokutya, kumagqirha, kubathandazeli, abahlobo okanye amalungu osapho. Injongo yalemibuzo kukunceda ekwenzeni uluhlu lwento yonke obuyisebenzisa **kwezinyanga zilishumi elinesibini zidlulileyo**.

Olulwazi lubalulekile kuba sifuna ukuqonda ukuba amayeza kunye/okanye namachiza obuasebenzisa **kwezinyanga zilishumi elinesibini zidlulileyo** azakuzichaphazela na iziphumo zokukhulelwa kwakho.

Qaphela: Luninzi uphinda-phindo ukunceda wena ukuze ukhumbule onke amayeza othe wawasebenzisa! Sicela usinyamezele kwaye uzame ukuphendula yonke imibuzo kangangoko unako.

Uyakubuzwa uluhlu lwawo onke amayeza owasebenzisayo ngoku okanye obuwasebenzisa kwezinyanga zilishumi elinesibini zidlulileyo. Nceda uquke onke amayeza akhutshwa ngemvume kagqirha (ART, TB, Isifo seswekile njalo-njalo), namayeza angakhutshwa ngemvume ka gqirha (i.e amayeza okanye amachiza owathenga ekhawuntarini), amayeza ongezelelweyo (e.g Vitamins), namayeza esintu kunye/okanye amayeza alinywayo kunye namachiza.

PLEASE READ OUT TO PARTICIPANT

*The following questions will refer to any medicines and/or remedies you have been taking. This includes ANY medicines and/or remedies from the clinic and hospital staff (doctors and nurses), the chemist, grocery stores, traditional healers, spiritual healers, friends or family members. The aim of this questionnaire is to help make a list of all the things you have taken **in the last 12 months**.*

*This information is important because we need to understand how the medicines and/or remedies you have been taking **in the last 12 months**. to you will affect the outcome of your pregnancy.*

*Please note: There is a lot of repetition to help you remember all the medications you have taken!
Please bear with us and try to answer the questions as best you can.*

You will be asked to list all medications you are currently taking or have previously used in the last 12 months. Please include all prescription medicines (ART, TB, and Diabetes etc.), non-prescription medicines (i.e. over the counter medicines and remedies), complementary medicines (e.g. Vitamins), traditional and/or herbal medicines and remedies.

SPECIFIC CONDITIONS

We are going to ask you questions about your medical history.

In the last 12 months, have you been told by a doctor or a nurse that you have ANY of the following medical conditions?

PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 8, pg. 25) FOR EACH MEDICATION MENTIONED!!!

45

PWID: _ _ _ _ _ - _ _

7. Isifo sokuwa <i>Epilepsy</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Ukuba HAYI Gqithela ku Q8 <i>If NO Skip to Q8</i>	___ / ___ / ___ DD MMM YYYY	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> Cacisa: _____ <i>Specify medication</i>
8. Isifo samadlala <i>Thyroid disease</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Ukuba HAYI Gqithela ku Q9 <i>If NO Skip to Q9</i>	___ / ___ / ___ DD MMM YYYY	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> Cacisa: _____ <i>Specify medication</i>
9. Enye ingulo okanye imeko yengqondo nje "ngokucinga kakhulu", uxinizelelo, ukothuka, ixhala njalo-njalo. <i>Any psychological or mental conditions such as</i> <i>"thinking too much", depression, panic attacks, anxiety</i> <i>attacks etc."</i> NB: Efunyaniswe ngu gqirha okanye ngunesi <i>Diagnosed by a doctor or nurse</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Ukuba HAYI Gqithela ku Q10 <i>If NO Skip to Q10</i>	___ / ___ / ___ DD MMM YYYY	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> Cacisa: _____ <i>Specify medication</i>
10. Ezinye naziphi na imeko zesigulo <i>Any other medical conditions</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → Ukuba HAYI Gqithela ku Table2 <i>If NO Skip to Table2</i>	___ / ___ / ___ DD MMM YYYY	☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> Cacisa: _____ <i>Specify medication</i>

SPECIFIC MEDICATIONS					
Ngoku sizokubuza ukuba ubukhe wasebenzisa nayiphi na koluhlobo lwamayeza okanye amachiza <i>We are now going to ask you whether you have taken any of these specific medicines and/or remedies.</i>					
Kwezinyanga zilishumi elinesibini zidlulileyo, ubukhe wathatha okanye wasebenzisa nayiphi kwezi zilandelayo? Ukuba EWE, nceda CACISA? <i>In the past 12 months, have you taken or used any of the following? If YES, please SPECIFY?</i>					
PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 8, pg. 25) FOR EACH MEDICATION MENTIONED!!					
Uhlobo leyeza okanye Iechiza <i>Specific Medicine and/ or Remedy</i>	Phawula ZONKE ezifanelekileyo <i>Tick ALL that Apply</i>	Ulithatha kangakanani eliyeza, unyango okanye ichiza? <i>How often do you take this medicine, treatment or remedy?</i> 1 ☐ Yonke imihla <i>Everyday</i> 2 ☐ Amaxesha 1-2 ngeveki <i>1-2 times per week</i> 3 ☐ Amaxesha 2-3 ngeveki <i>2-3 times per week</i> 4 ☐ Ngaphezu kwamaxesha amathathu ngeveki <i>More than 3 times per week</i> 5 ☐ Kanye ngenyanga <i>Once per month</i> 6 ☐ Kabini nangaphezulu ngenyanga <i>Twice or more times per month</i> 7 ☐ Kanye kuphela <i>Once off only</i> 8 ☐ Enye, Cacisa <i>Other, Specify</i>	Waliqala nini ukuyoma nini eliyeza? Chaza Ixesha. Ukuba iyaqhubeleka yenza (X) <i>When did you start and stop using this medicine? State period. If on-going (X)</i>		
		Isihlandlo <i>Frequency</i>	Ukuqala <i>Start</i>	Uyokuma <i>Stop</i>	Iyaqhube <i>On-going</i>
1. Ukucwangcisa <i>Contraception/ Family planning</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → HAYI, Gqithela ku Q2 <i>If NO, Skip to Q2</i>	☐ Ipilisi <i>Pill</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Inaliti yenyanga ezimbini- <i>2-month injection</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Inaliti yenyanga ezintathu <i>3-month injection/Depo</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ IUD <i>Iluphu</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Upetsho lolusu <i>Skin patch</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Implanon	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Enye <i>Other</i> Cacisa: _____ <i>Specify</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i>	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐

Uhlobo leyeza okanye lechiza <i>Specific Medicine and/ or Remedy</i>	Phawula ZONKE ezifanelekileyo <i>Tick ALL that Apply</i>	Ulithatha kangakanani eliyeza, unyango okanye ichiza? <i>How often do you take this medicine, treatment or remedy?</i>	Waliqala nini ukuyoma nini eliyeza? Chaza Ixesha. Ukuba iyaqhubeleka yenza (X) <i>When did you start and stop using this medicine. State period. If on-going (X)</i>		
		Isihlandlo <i>Frequency</i>	Ukuqala <i>Start</i>	Uyokuma <i>Stop</i>	Iyaqhube <i>On-going</i>
2. Izakhamzimba <i>Vitamins</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → HAYI, Gqithela ku Q3 <i>If NO, Skip to Q3</i>	☐ Vitamin B12	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Vitamin C	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Vitamin D	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Vitamin B6	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Vitamin BCo	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Enye, other Cacisa: _____ <i>Specify</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
3. Amayeza ongezelelweyo nawokunyusa amajoni omzimba ase chemesti/evenkile ni yokutya <i>Supplements/ Immune boosters from chemist/pharmacy/grocery store</i> ☐ Ewe <i>Yes</i> ☐ Hayi <i>No</i> → HAYI, Gqithela ku Q4 <i>If NO, Skip to Q4</i>	☐ Folic acid	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Ferrous sulfate (Iron)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Magnesium silicate	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Calcium	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Multivitamin	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐
	☐ Enye <i>Other</i> Cacisa: _____ <i>Specify</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, <i>Specify:</i> _____	DD / MM / YYYY DD / MM / YYYY	DD / MM / YYYY DD / MM / YYYY	☐

Uhlobo lyeza okanye lechiza <i>Specific Medicine and/ or Remedy</i>	Phawula ZONKE ezifanelekileyo <i>Tick ALL that Apply</i>	Ulithatha kangakanani eliyeza, unyango okanye ichiza? <i>How often do you take this medicine, treatment or remedy?</i>	PWID: _____ <i>Waliqala nini ukuyoma nini eliyeza? Chaza ixesha. Ukuba iyaqhubeka yenza (X) When did you start and stop using this medicine? State period. If on-going (X)</i>			
			Ukuqala Start	Uyequmisa Stop	Iyaqhubeka On-going	
4. Iyeza lentlungu <i>Medicine for pain</i>	☐ Paracetamol (e.g. Panado)	1 ☐ Yonke imihla <i>Everyday</i> 2 ☐ Amaxesha 1-2 ngeveki <i>1-2 times per week</i> 3 ☐ Amaxesha 2-3 ngeveki <i>2-3 times per week</i> 4 ☐ Ngaphezu kwamaxesha amathathu ngeveki <i>More than 3 times per week</i> 5 ☐ Kanye ngenyanga <i>Once per month</i> 6 ☐ Kabini nangaphezulu ngenyanga <i>Twice or more times per month</i> 7 ☐ Kanye kuphela <i>Once off only</i> 8 ☐ Enye, Cacisa <i>Other, Specify</i>	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐
☐ Ewe Yes ☐ Hayi No	☐ Ibuprofen (e.g. Advil, Brufen, Nurofen)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐	
→ HAYI, Gqithela ku Q5 <i>If NO, Skip to Q5</i>	☐ Tramadol (e.g. Tramacet)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐	
	☐ Tramal, Codeine (e.g. in Stopayne)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐	
	☐ Aspirin (e.g. grandpa)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐	
	☐ Amitriptyline (e.g. Trepillane)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐	
	☐ Enye, Other Cacisa: _____ Specify: _____	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ Cacisa, Specify: _____	DD / MM / YYYY	DD / MM / YYYY	☐	

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BMC Pregnancy and Childbirth | Research article

Research article

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Conclusions

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Online document

Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999. [http://www.rsc.org/dose/title of subordinate document](http://www.rsc.org/dose/title%20of%20subordinate%20document). Accessed 15 Jan 1999.

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Supplementary material/private homepage

Doe J. Title of supplementary material. 2000. <http://www.privatehomepage.com>. Accessed 22 Feb 2000.

University site

Doe, J: Title of preprint. <http://www.uni-heidelberg.de/mydata.html> (1999). Accessed 25 Dec 1999.

FTP site

Doe, J: Trivial HTTP, RFC2169. <ftp://ftp.isi.edu/in-notes/rfc2169.txt> (1999). Accessed 12 Nov 1999.

Organization site

ISSN International Centre: The ISSN register. <http://www.issn.org> (2006). Accessed 20 Feb 2007.

Dataset with persistent identifier

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