A comparative analysis of the medicine use in HIV-exposed uninfected infants compared to HIV-unexposed uninfected infants in the first year: A secondary analysis of a mother-infant cohort study in Cape Town, South Africa.

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PREAMBLE

Declaration

I, Hilkka M'lunga, hereby declare that the work on which this dissertation/thesis is based on my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

In the case of multi-authored published or unpublished papers I will be the lead author and my contribution as agreed to by the relevant co-authors will be outlined in each publication. In addition, I have detailed contributions in the preface to this thesis and in the introduction to each chapter.

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Abstract

Background: Despite several studies investigating medicine exposures in infants, the administration and monitoring of medications in infants who are HIV-exposed uninfected (HEU), a growing population, remains poorly studied. This study aimed to describe and compare medication consumption patterns, including immunization coverage, between infants who are HEU and HIV-unexposed uninfected (HUU) during their first year of life.

Methods: This was a secondary analysis of a birth cohort study of pregnant women living with and without HIV and their infants between 2017 and 2019 in Cape Town, South Africa. Interviewer-administered questionnaires captured sociodemographic factors, self-reported medication use, infant feeding practices, and vaccine use over four postnatal visits (<7 days, 10 weeks, 6 and 12 months). Data was manually classified and coded by a clinical pharmacist and student. Logistic regression models were employed to compare patterns of use among infants who are HEU and HUU, as well as to identify other maternal and infant factors associated with medication use and vaccine coverage.

Findings: A total of 772 mother-infant pairs were analyzed. Compared to infants who are HUU, HEU infants were preterm (64/393 vs. 39/379; $p = 0.02$), less often breastfed (314/393 vs. 322/379; $p < 0.001$), and weighed less (median, 3288g vs. 3405 g; $p = 0.03$). HEU infants were found to take at least one medication at a significantly higher rate 388/393 (98.7%) vs 345/379 (91.0%) than infants who are HUU ($p < 0.001$). HEU infants reported lower use of over-the-counter (OTC) medicine (69.2% vs. 80.2%; $p < 0.01$) and traditional, complementary, and alternative medicine (TCAM) (16.8% vs. 26.1%; $p < 0.001$) compared to HUU infants. Mothers of HEU infants were less likely to forget a medicine's name (29.3% vs. 36.9%, $p<0.001$) than HUU mothers. Prescription medicine use, excluding antiretroviral (ARV) prophylaxis medicines routinely administered to infants who are HEU at birth, was significantly higher among infants who are HEU compared to HUU (65.4%. vs. 23.0%; $p < 0.01$). Vaccine coverage showed no significant difference between infants who are HEU and HUU but steadily declined over the year (95.0% coverage with birth immunizations, vs 70.0% at 9 months) across the entire cohort. Only 293 infants (38.0%) had complete immunization coverage at 1 year. In the adjusted models, being a HEU infant was a protective factor against self-medication. (aOR 0.45; 95% CI 0.31 – 0.65; $p < 0.001$). Conversely, being breastfed (aOR 2.46; 95% CI 1.56 –3.83; $p < 0.001$) was a significant risk factor for self-medication infants. Prescription medicine use (excluding ARV prophylaxis medicines) was significantly associated with increased maternal age (aOR 1.06; 95% CI 1.03 – 1.08; $p < 0.001$) and infants who are HEU (aOR 6.52; 95% CI 4.66 – 9.21; $p < 0.001$). No significant associations were found between maternal and infant characteristics and full vaccine coverage.

Interpretation: The study revealed that infants who are HEU were more exposed to prescribed medicine (excluding ARV prophylaxis medicines) compared to their HUU counterparts, however, mothers of HUU infants, generally reported higher usage of both TCAM and OTC compared to HEU infants. The study also revealed drops in vaccine coverage rates among infants over the first year of life, indicating a gap in protection

against vaccine-preventable diseases. Further research is needed to study medication patterns in different settings. Medication literacy efforts need to be prioritized in pregnant women and mothers of newborns to support rational and safe medicine (including vaccine) usage and subsequently improve the health outcomes for all infants, irrespective of HIV status.

Keywords: HIV; Exposed Uninfected; Infant; Medicine pattern or exposure; vaccine coverage; South Africa

List of Abbreviations

ANC	Antenatal clinics
AOR	Adjusted odds ratio
ART	Antiretroviral therapy
ARV	Antiretroviral
ATC	Anatomical Therapeutic Chemical
AZT	Zidovudine
BCG	Bacillus Calmette- Guérin
CI	Confidence Intervals
C-section	Caesarean section
CTX	Cotrimoxazole
DTP – IPV- HiB – HepB	Diphtheria, Pertussis, Tetanus, Haemophilus influenzae type B, Hepatitis B
EPI	Expanded Programme Immunisation
GA	Gestational age
HEU	HIV-exposed and uninfected
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
HUU	HIV-unexposed and uninfected
IQR	Interquartile ranges
LBW	Low birth weight
MOU	Maternal-Obstetric Unit
MUAC	Mid-upper arm circumference.
MV	Measles.
NVD	Natural vaginal delivery
NVP	Nevirapine
OPV	Oral polio vaccine
OTC	Over-the-counter
PER	Pregnancy Exposure Register
PCR	Polymerase chain reaction
PCV	Pneumococcal conjugate vaccine
PMTCT	Prevention of mother-to-child transmissions
PWLO HIV	Pregnant women living without HIV
PWLHIV	Pregnant women living with HIV
RTHB	Road to Health Booklet
RV	Rotavirus
RX	Prescribed medicine
SDG	Sustainable Development Goals
TCAM	Traditional, Complementary, and Alternative medicine
TM	Traditional and Herbal medicine
UCT	University of Cape Town
UOR	Unadjusted odds ratio
VPD	Vaccine-preventable diseases
WHO	World Health Organization
WLOHIV	Women living without HIV
WLHIV	Women living with HIV

Table of Contents

List of Tables

A. Protocol

B. Manuscript

List of Figures

A. Protocol

B. Manuscript

C. Appendices

A. **PROTOCOL**

1. **Synopsis**

HIV-exposed uninfected (HEU) children account for around 30% of the paediatric population in Southern African countries, with 25% living in South Africa. The implementation of lifelong antiretroviral therapy (ART) for all women living with HIV (WLHIV) not only reduces vertical HIV transmission but also improves maternal health. Consequently, this has led to an increased usage of ART among pregnant and postpartum women, resulting in marked reductions in new paediatric HIV infections. Nonetheless, this progress brings to light a new concern – HEU infants, who are at a higher risk for infections and adverse drug reactions, with vulnerabilities to infectious diseases in infancy surpassing those of their HIV- unexposed uninfected (HUU) counterparts.

The existing body of literature suggests that infant medicine use is scarce, particularly in developing countries. While some studies have investigated medicine exposures in infants, there is a lack of research on the administration and monitoring of medications in HEU infants. The SMARTT study, which monitored the effects of ART on children who are HEU found adverse effects of maternal ART on birth outcomes. Given the widespread use of medication in pregnant and breastfeeding women and their infants, it is imperative to include these populations in pharmacovigilance activities to mitigate medication-related risks. Nevertheless, limited efforts have been made to establish pharmacovigilance systems for this vulnerable population in high HIV-burden countries highlighting the importance of assessing medicine exposure and other treatment combinations for infants by HIV exposure. Moreover, the impact of maternal HIV status on child vaccination status, particularly among HEU children, is a critical consideration in vaccine coverage assessments. These children face a disproportionately higher risk of being under-immunized compared to infants of women living without HIV, with studies indicating a 30-70% chance of being incompletely immunized. While progress has been made in improving vaccination rates in South Africa, more research is needed to understand and address the differences in vaccine coverage among vulnerable populations, regardless of their HIV exposure status.

The primary aim of this study is to examine and compare the consumption of medications between HEU and HUU infants during their first year of life. This secondary analysis forms part of the B-positive study at the Maternal-Obstetric Unit (MOU) at Gugulethu Community Health Care Centre, Western Cape Town, South Africa. The B-positive cohort study was a prospective observational study whose main aim was to "comprehensively monitor the effectiveness, impact, and risks of the WHO Option B+ prevention of mother-to-child transmission (PMTCT) of HIV strategy at a population level in the entire Western Cape Province". It involved three linked sentinel site activities under a single study team which established a cohort of 900 pregnant women – 450 women living with HIV (WLHIV) and 450 women without HIV – who were closely followed antenatally and up to 12 months postnatally. This cohort of mother-infant pairs is the focus of this analysis based on data derived from interviewer-administered questionnaires of mothers regarding infant medication administration postnatally. The study was conducted between January 2017 and July 2018 at a large primary-level antenatal and obstetric unit in Gugulethu. Gugulethu is characterized by high levels of

poverty, risk factors for poor child health, and antenatal seroprevalence of 30%. Despite the high disease prevalence, the obstetric primary healthcare facility not only provides free healthcare services but also offers universal ART to all pregnant women living with HIV, along with basic antenatal and postnatal care. Moreover, the local clinics offer child healthcare including vaccinations.

In the B-positive study, pregnant women attending their first antenatal care visit were recruited by the study staff and provided with an informed consent form in either English or isiXhosa, the latter being the most preferred language in Gugulethu and Western Cape. Interested women were screened and enrolled in the study if they met the eligibility criteria which included a confirmed routine HIV test, were above 18 years old, living with and living without HIV, and planned to reside in Cape Town for at least one year postpartum with their live infants who were either HIV exposed or unexposed. For each participant, data for the study was collected through a well-designed questionnaire that covered sociodemographic factors, medication use, side effects, and infant feeding practices. Follow-up was conducted through face-to-face and telephonic interviews at various intervals during the antenatal and postpartum periods, up to 12 months after childbirth. The data obtained from the B-positive study will be analyzed using univariate, bivariate, and multivariate statistical analyses.

The current research involves analyzing data already collected as part of the B – positive study. The risk to the study participants is minimal due to the potential loss of confidentiality. No extra information will be gathered from the participants. Furthermore, this analysis will only use anonymized datasets, as each participant is assigned a distinct identifier that will be used throughout the study. This approach ensures that no personal identifiers are included in any of the collected data, thereby protecting privacy. Participants in the study will have no direct benefits, but the knowledge gained is expected to improve our understanding of how medication use affects these populations, which could inform future research and interventions aimed at improving healthcare for infants in the Western Cape, particularly those who are HEU. Furthermore, the findings will potentially contribute to scientific knowledge on this topic, which will be used to inform policy and clinical decision-making and potentially reduce unnecessary medication use in this vulnerable population.

2. **Introduction**

2.1 **Background**

The HIV pandemic remains a major threat to global health, with an estimated 39 million people living with the virus globally [1]. Antiretroviral therapy (ART) has not only been important in managing HIV infection but has also proven to be effective in reducing the risk of vertical transmission of HIV from mother to child [2-19]. In 2018, the global population of children who are HIV-exposed and uninfected (HEU) was estimated to be around 14.8 million [5-7]. In Sub-Saharan Africa, it is reported that South Africa, Uganda, Mozambique, Tanzania, and Nigeria collectively account for 50% of all children who are HEU, with South Africa being home to 25% of the world's HEU children [3, 5, 7]. Given this perspective, the additional adverse health consequences linked to HEU children can significantly influence the region and South Africa's capacity to achieve the Sustainable Development Goals (SDGs), specifically SDG- 3 good health and well-being [6, 15, 26].

South Africa has a high antenatal HIV prevalence of < 29%, with over 95% of pregnant women living with HIV receiving ART [4-9, 17]. As a result, approximately 30% of infants born in South Africa are vertically exposed to HIV, leading to significant in-utero exposure to both HIV and multiple antiretroviral (ARVS) drugs [4, 7, 19]. This exposure carries potential long-term consequences for child health, including higher morbidity and mortality rates [5-7, 10-12, 16, 19, 23, 26]. While ART plays a critical role in reducing vertical transmission rates, this is not without adverse effects and potential risks associated with the use of these medications during pregnancy [6, 8, 14]. Adverse effects associated with maternal ART may include anaemia, hepatic, liver, and mitochondrial changes [6, 19]. Moreover, research suggests a potential link between prenatal exposure to ART and adverse perinatal outcomes such as preterm birth, neonatal mortality, low birth weight, and viral resistance [3, 14-16, 19]. While the recent focus is on evaluating birth outcomes and teratogenicity of in-utero ARV exposure [16, 26], it should be emphasized that most current treatments generally have a favourable risk-benefit profile in pregnancy [26, 41]. Nonetheless, there is still limited understanding of the long-term safety implications of in-utero ARVs and combination ART [15, 26]. The SMARTT study, which monitors the effects of ART on HEU children, finds little adverse effects of maternal ART on birth outcomes. However, specific ARV medications such as atazanavir, tenofovir, and dolutegravir may have an impact on language acquisition, bone mineral content and neural tube defects, respectively [7, 20]. Furthermore, data on adverse birth outcomes linked to ARV use often emerge from developed countries or are hindered by small sample sizes [6, 10, 13, 15, 18, 23, 38].

While some studies investigate medicine exposures in infants, there is a lack of research on the administration and monitoring of medications in HEU infants [39, 42-44]. However, a study conducted in Malawi finds that 80% of HEU infants are frequently prescribed antibacterial drugs, with the most prescriptions (67%) being for respiratory indications [36]. Furthermore, research suggests that cotrimoxazole (CTX) preventive therapy can

reduce antibacterial drug prescriptions for HEU infants, but routine CTX prophylaxis is associated with increased antibiotic resistance [31, 36]. Moreover, HEU infants born to mothers with low CD4 cell counts have a greater risk of requiring respiratory medications due to their increased susceptibility to infections, particularly pneumonia and sepsis [6]. However, limited efforts have been made to establish pharmacovigilance systems for this vulnerable population in high HIV- burden countries, highlighting the importance of assessing medicine exposure and other treatment combinations for infants by HIV exposure [8, 21, 28, 40].

The National Expanded Program for Immunization (EPI) is one of the most cost-effective interventions in preventing vaccine-preventable diseases (VPD) [33, 46 - 47]. Vaccination plays an important role, particularly for HEU infants who have compromised immune systems and are more susceptible to various infectious diseases. Despite its significance, global immunization coverage remains stagnated below 90%, resulting in most infants being incompletely vaccinated and unvaccinated [45]. Poor vaccination coverage increases the susceptibility of HEU children to VPD, thereby increasing both morbidity and mortality risks compared to HUU infants [30]. Research shows that infants born to WLHIV have a 30-70% likelihood of incomplete immunization, which correlates with increased rates of early-life infectious diseases and elevated mortality rates [30]. Moreover, research shows that HEU infants had lower vaccination rates than HUU infants for pneumococcal disease and rotavirus vaccines, primarily due to limited healthcare access [22, 37]. Given their heightened susceptibility to infectious morbidity, ensuring timely vaccination with higher coverage among HEU children becomes imperative in South Africa.

Building upon the existing limited knowledge, this study seeks to analyze medication usage patterns including immunization coverage among a cohort of infants who are HEU and compare them with HUU infants during their first year of life in a peri-urban township in Cape Town, South Africa. The primary objective is to examine and compare the consumption of medications between these two groups of infants. Furthermore, the study will assess the vaccination status of both HEU and HUU infants and identify maternal factors (e.g., maternal education status, maternal age, etc.) and infant factors (birth weight, gestational age at birth, hospitalization) that contribute to increased medication usage in both groups.

2.2 **Study rationale**

Infants who are HEU are at increased risk of poor health outcomes due to their exposure to HIV, comorbid conditions, and medications to treat these conditions in utero. This creates a need for further research to investigate the potential differences in postnatal medication exposure (including immunizations) between HEU and HUU infants. Such research will identify opportunities to improve rational prescribing and use of medicines and reduce the risk of medicine-related harm while optimizing the care of both HEU and HUU infants in South Africa. Moreover, by comparing HEU and HUU infants, the research will identify potential disparities in health outcomes and healthcare practices among minors, shedding light on health inequities. This

knowledge will enable targeted interventions to improve the well-being of vulnerable populations. Furthermore, by examining medication usage patterns and vaccination coverage, the research can uncover disparities in healthcare access and delivery, leading to interventions that address these gaps and promote equitable health outcomes.

3. **Study Aims and Objectives**

3.1 **Specific aims**

Primary aim: To investigate the patterns of medication usage among HEU infants during their first year of life in a peri-urban township of Cape Town, South Africa, and to identify any significant variations in medication consumption within this cohort.

Secondary aim: To explore potential associations between maternal demographic factors (such as age and socioeconomic status) and infant-specific factors (including birth weight, preterm birth, feeding choices, and thriving) with medication utilization, including vaccination, among both HEU and HIV-unexposed uninfected (HUU) infants during their initial year of life in the specified Cape Town community.

3.2 **Objectives**

We plan to achieve this aim by accomplishing the following objectives:

1. Describe medicine use (e.g., prevalence, type of medicine in terms of ATC level 2 code and whether Rx, OTC or TCAM; number of medicines used) and adherence and coverage of recommended immunizations in HEU and HUU infants from the B-positive Cohort during the first year of life as reported by the mother.
2. To assess the association between maternal HIV status and pattern of medicine use in infants during the first year of life as reported by the mother.
3. To identify maternal (i.e., socioeconomic status (SES), age and feeding practices) and infant (i.e., infectious-related hospitalization, low birth weight (LBW), preterm) risk factors that are associated with medicine use in HEU and HUU infants during their first year of life.
4. To compare the vaccination status (adherence and coverage) for routine childhood immunizations of HEU and HUU infants during their first year of life.

3.3 **Hypothesis**

Hypothesis: There is no significant difference in medicine use and vaccine coverage in HEU and HUU infants seeking care at Gugulethu Community Health Clinic in Western Cape South Africa in their first year of life.

4. **Methodology**

This study will conduct a secondary analysis of data obtained from infants born to women who participated in the primary B-positive cohort study at the Maternal-Obstetric Unit (MOU) at Gugulethu Community Health Care Centre, Western Cape Town, South Africa (HREC approval number: REF Number 749/2015). The design and methods of the B-positive study have been previously described elsewhere [28], but in brief, its main aim was to "comprehensively monitor the effectiveness, impact, and risks of the WHO Option B+ prevention of mother-to-child transmission (PMTCT) of HIV strategy at a population level in the entire Western Cape Province". It involved three linked cohorts: 1) a cohort of approximately 900 pregnant women – about 450 women living with HIV (WLHIV) and 450 women without HIV – who were enrolled at a single primary health facility and were then closely followed antenatally and up to 12 months postnatally. 2) At the same sentinel site, a pregnancy exposure registry enrolled all pregnant women at the same facility from their initial antenatal visit until delivery. 3) A provincial maternal data cascade was developed that identified, through a series of electronic evidence (e.g. presence of a rhesus test, a syphilis test, admission into a labour/delivery ward) all pregnant women in the province. The first cohort of mother-infant pairs is the focus of this analysis based on data derived from semi-structured interviews of mothers regarding infant medication administration postnatally.

4.1 **Study design**

The study will be a retrospective cohort study design.

4.2 **Study setting**

The B-positive study was an observational prospective cohort study that enrolled pregnant women, attending antenatal care at a primary maternity healthcare facility in Gugulethu, a peri-urban township in Cape Town, South Africa. Gugulethu is marked by high levels of poverty, unemployment, and an HIV antenatal prevalence of 30% [28]. Despite the high prevalence of disease in the area, the GMOU primary healthcare facility provides free healthcare services to all residents. For pregnant women living with HIV (WLHIV), the facility offers universal ART and basic antenatal and postnatal care. As part of the facility's standard of care, women on ART are required to bring their infants to the clinic within one month of delivery. Moreover, the local clinics offer child health care including vaccinations (Table 1) [33].

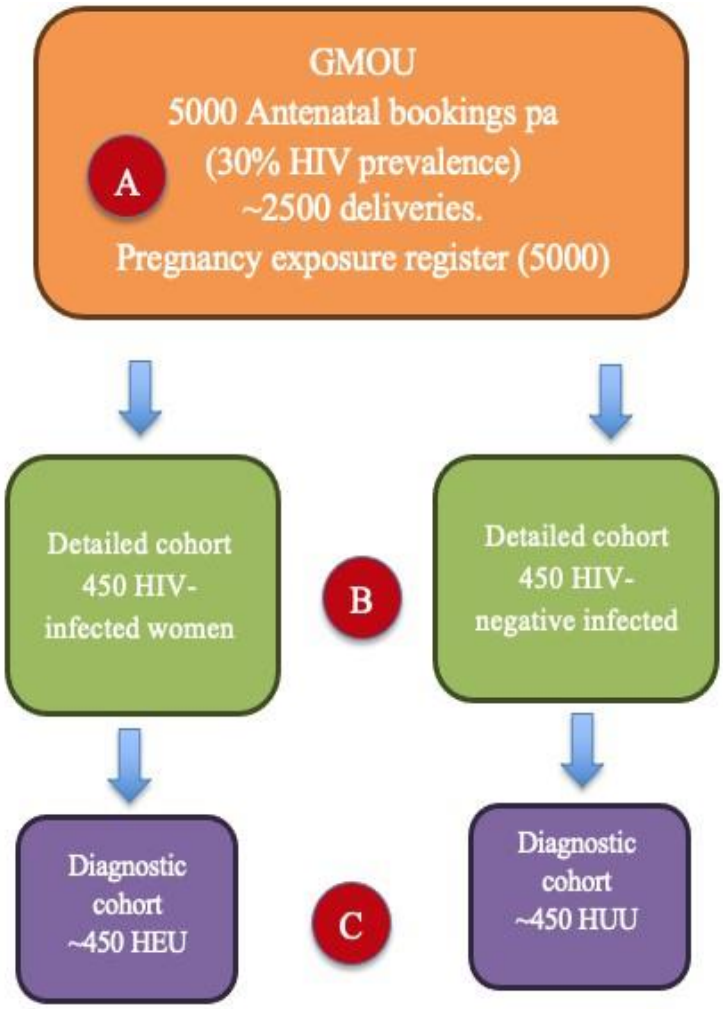

Figure 1. *Schematic outline of sentinel site cohorts. A: Pregnancy Exposure Register (GMOU) B: Detailed cohort of 900 women booking at GMOU for antenatal care (450 HIV-infected and 450 HIV-uninfected; C: infants of the 900 women participating in B, regardless of site of delivery (~450 HIV-exposed and ~450 HIV unexposed).*

Table 1. *Schedule for childhood/special immunization.*

AGE → VACCINE	**BIRTH**	**6 WEEKS**	**10 WEEKS**	**14 WEEKS**	**6 MONTHS**	**9 MONTHS**
BCG						
OPV						
RV						
DTP – IPV- HiB – HepB						
PCV						
MEASLES						

BCG - Bacillus Calmette- Guérin; OPV – Oral polio vaccine; RV – Rotavirus vaccine; DTP – IPV- HiB – HepB – Hepatitis B, Diphtheria, Pertussis, Tetanus, Haemophilus influenzae type B; PCV – Pneumococcal Conjugate vaccine.

4.3 **Study population**

Consecutive pregnant women aged ≥ 18 years old, with and without HIV, were screened and recruited at their first antenatal care visit (ANC). Eligible women were enrolled in the study between January 2017 and July 2018. Women were considered eligible to participate in the study if they had a confirmed maternal HIV test, provided informed consent, and intended to live in Cape Town for at least one year postpartum with their uninfected or HIV-negative infants.

Inclusion criteria: a) pregnant WLHIV or not who have provided written informed consent, which included permission to view their and their infants' medical records, b) infants must be liveborn and HEU or HUU at birth.

Exclusion criteria: a) not provided written informed consent, b) infants diagnosed with HIV at birth or during the 1st year of life, and c) women with unknown pregnancy outcome and pregnancy loss including miscarriage, termination of pregnancy, and stillbirth.

4.4 **Sampling**

After accounting for potential attrition, the study had an effective sample size of 450 mother-infant pairs in each group.

5. **Research Procedures and Data Collection Methods**

5.1 **Data collection**

Data were collected from three sources: (1) interviews, (2) clinical assessments, and (3) information abstracted from clinical record reviews of hospital admissions. Mothers were interviewed at enrollment and then twice during their pregnancy depending on how early they presented for antenatal care. Mother-infant pairs were also evaluated by the study teams at birth and postpartum (refer to Table 2) A well-designed questionnaire collected data on sociodemographic factors, medication use, indication of use, side effects experienced, and infant feeding practices. The research team reviewed the questionnaire for appropriateness and language before administering it to study participants during these follow-up periods (refer to Appendix 2). Follow-up activities were conducted through both face-to-face and telephonic interviews, spaced at various intervals during the antenatal and postpartum periods, and continued up to 12 months after childbirth. These interviews, conducted in the predominant local language isiXhosa, served to collect essential information on maternal and infant health, ensuring ongoing communication and engagement with the participants throughout the study duration.

The antenatal and postnatal data endpoints that were collected at specific follow-up visits with both maternal and infant are reflected in Table 2. The measures of interest for this study include maternal demographics, infant feeding practices, intercurrent clinical care of the infant, and questionnaires related to the infants' medication history, including immunization status (refer to Appendix 2). The study staff recorded all infant medication use reported by the mother, whether prescribed or provided by clinic and hospital staff (doctors and nurses), medications obtained from pharmacies, as well as those from traditional healers, spiritual healers, friends, or family members.

***Table 2**. Schedule of outcome measures used in the B-positive during study visits of interest to the proposed study.*

Questionnaires	**ANC visit 13**	**7 days pp**	**6 weeks pp**	**3 months pp**	**6 months pp**	**12 months pp**
Maternal						
Demographic information	**x**					
Clinical history	**x**					
Patient medication use	**x**					
Inter-current clinical care of mother	**x**					
Disclosure (HIV+ only)	**x**					
ART adherence and ART acceptability (HIV+ only)	**x**					
Infant						
Infant anthropometry (weight, length, head circumference, MUAC)		**x**	**x**	**x**	**x**	**x**
Inter-current clinical care of infant (incl medication use and EPI)		**x**	**x**	**x**	**x**	**x**
Infant feeding		**x**	**x**	**x**	**x**	**x**

Pp – postpartum; ANC – Antenatal care; MUAC – Mid-Upper Arm Circumference; EPI – Expanded Programme for Immunization.

6. **Data Safety and Monitoring**

6.1 **Data management and Data analysis**

All self-reported medication use will be coded by generic name and classified according to the World Health Organization's Anatomical Therapeutic Chemical Classification System (ATC) [34]. The ATC classification system has five levels of coding, describing organ system, therapeutic, pharmacological, and chemical properties [34]. For this analysis, all medications will be classified up to the second level ATC coding system. Additionally, medications will be categorized as prescription (RX), over-the-counter (OTC), or traditional and complementary medicine (TCAM). This coding process will be performed by the master's student and checked by the primary supervisor, who is a qualified pharmacist. Medicines that are classified as Schedule 3 and above will be classified as prescription medicines. Immunization exposures will be assessed separately, with coverage defined per antigen as the proportion of infants who obtained the full recommended schedule of the individual vaccine antigens (e.g., the proportion of infants who received all DTP vaccines, etc.). Complete adherence to the immunization schedule will be defined as the proportion of infants who received all recommended vaccinations during their first year of life, while incomplete adherence will be defined as infants who missed at least one recommended vaccine during their first year of life. Infants who received < 50% of their recommended immunizations will be categorized as poorly adherent infants.

The study used Research Electronic Data Capture (REDCap), a secure web-based application, for data collection. Statistical analysis will be performed using R version 3.6.0 (2019-04-26). The collected data will be analyzed using univariate, bivariate, and multivariate statistical methods. Univariate analysis will describe the data distribution using descriptive statistics, including measures such as median, interquartile ranges (IQR), mean, and 95% confidence intervals for continuous variables. The baseline characteristics will be stratified by the infants who are HEU and HUU. Categorical variables will be described using frequency and percentages. To assess statistical significance, the student t-test or nonparametric Mann-Whitney U test will be applied for continuous outcomes, while the chi-squared statistic or Fisher exact test will be used for proportional differences in categorical outcomes. Multiple logistic regression analysis will be conducted for statistically significant outcomes, accounting for potential confounding variables and determining the relationship between dependent and independent variables. A significance level of < 0.05 was chosen for all statistical analyses, and the inclusion of 1 in the 95% confidence interval will indicate insignificance.

Table 3*.The 1st level ATC codes (the main anatomical groups) as described by the WHO (1996) [28]:*

1st level ATC classification system
A: *Alimentary tract and metabolism*
B: *Blood and blood forming organs*
C: *Cardiovascular system*
D: *Dermatologicals*
G: *Genito urinary system and sex hormones*
H: *Systemic hormonal preparations, excluding sex hormones*
J: *Anti-infectives for systemic use*
L: *Antineoplastic and immunomodulating agents*
M: *Musculo-skeletal system*
N: *Nervous system*
P: *Antiparasitic system*
R: *Respiratory system*
S: *Sensory organs*
V: *Various*

Exposure measure:

- Maternal HIV status (infant exposed vs. unexposed).
- Other potential risk factors for medicine use in infants in the first year of life (i.e., maternal age, SES, feeding practices, and infant hospitalization).

Outcome measure:

The following outcomes will be assessed:

- The proportion of infants who received co-trimoxazole (CTX) prophylaxis, Nevirapine (NVP) with or without Zidovudine (AZT) prophylaxis.
- The proportion of infants exposed to at least one medicine (including RX, OTC, and TCAM) during the first year of life.
- The percentage of vaccination coverage and adherence to the national recommended vaccination schedule in terms of completeness will be compared between HEU and HUU infant cohorts.
- Risk factors for infection-related hospitalization for more than 24 hours over the first year of life for the proportion of infants.

Table 4. *Variables list used in the HIV+ cohort and HIV- cohort study of pregnant women attending an antenatal care facility in Gugulethu (Cape Town) for HEU and HUU infants.*

Variables	**Data Type**
Sex *n* (%) • **Female** • **Male**	Categorical – binary
Birth weight (grams) *n* (%) • **Low weight** • **Normal weight** • **Macrosomia**	Categorical – ordinal
Gestational age (weeks) • **Pre-term <37 weeks** • **Term >= 37 weeks**	Categorical – binary
Place of Delivery *n* (%) • **Groote Schuur Hospital** • **Gugulethu MOU** • **Mowbray Maternity Hospital** • **Other**	Categorical – nominal
Breast-feeding *n* (%) • **Yes** • **No**	Categorical – binary
Hospital admissions *n* (%) • **Yes** • **No**	Categorical – binary
Head Circumference (cm) median [IQR]	Numerical (continuous)
Length (cm) median [IQR]	Numerical (continuous)

Table 5. *The main variables used in the HIV+ cohort and HIV- cohort study of pregnant women attending an antenatal care facility in Gugulethu (Cape Town).*

Variables	Data Type
Age (years) median [IQR]	Numerical (discrete)
Education status *n* (%) • **Primary** • **Secondary** • **Post- Secondary**	Categorical - ordinal
Employment status *n* (%) • **Employed** • **Unemployed**	Categorical - binary
Household crowding *n* (%) • **1** • **1-3** • **>3**	Categorical – ordinal
Household Income status (ZAR) *n* (%) • **< R5000** • **>R5000** • **Not reported**	Categorical – ordinal
Number of children *n* (%) • **1** • **1-3** • **>3**	Categorical – ordinal
Housing *n* (%) • **Formal house** • **Informal house**	Categorical – binary
TB status *n* (%) • **Before pregnancy** • **During pregnancy**	Categorical – binary
Gravidity *n* (%) • **<1** • **1-3** • **>3**	Categorical – ordinal
Toilet *n* (%) • **Yes** • **No**	Categorical – binary
Running water *n* (%) • **Yes** • **No**	Categorical – binary
Electricity • **Yes** • **No**	Categorical – binary
Parity *n* (%) • **<1** • **1-3** • **>3**	Categorical – ordinal
Mode of delivery • **Natural vaginal delivery** • **Emergency caesarean section** • **Elective caesarean section**	Categorical – nominal

6.2 **Potential strengths and limitations**

The proposed analysis has several strengths. Firstly, it addresses a crucial research gap by providing a detailed account of medicine use in both HEU and HUU infants, an area that had been overlooked in previous studies. This will also be the first study of its kind in South Africa to assess medicine use in infants who are HEU and HUU. Nevertheless, it is not without limitations. Firstly, there may be selection bias due to the focus on a single Obstetrics Unit in Cape Town, which could limit the generalizability of the results to other populations. Additionally, data constraints from the study and relying solely on self-reported medication usage without clinical record confirmation may introduce potential reporting biases and missingness in the data. Moreover, the possibility of loss to follow-up could lead to confounding effects. It will be important to interpret the findings cautiously to ensure accurate conclusions.

7. **Ethical Considerations**

This study uses data from the B-positive study. Ethical approval for the B-positive study including the informed consent procedure was approved by the University of Cape Town (UCT) Health Science Faculty's Human Research and Ethics Committee (UCT-HREC), REF Number 749/2015). The study protocol, informed consent forms, the relevant data collection tools, and any other requested information have therefore already been approved by UCT-HREC). This study will request additional ethical approval from the UCT-HREC to conduct a specific secondary analysis as described above.

7.1 **Risks and benefits**

The main risk associated with this protocol is confidentiality being compromised during data processing and analysis. However, this analysis will only use anonymized datasets, as each participant is assigned a distinct identifier that will be used throughout the study. This approach ensures that no personal identifiers are included in any of the collected data, thereby protecting privacy.

Although there are no direct benefits to the participants of this study, the knowledge gained will improve our understanding of how medication use affects these populations. This knowledge will inform future research and serve as valuable guidance for public health interventions aimed at improving healthcare for infants in the Western Cape, particularly those who are HEU. Moreover, the study findings will potentially contribute to scientific knowledge on this topic, which will be used to inform policy and practice, clinical decision-making, and potentially reduce unnecessary medication use in this vulnerable population. Additionally, the findings will serve as a resource for counselling mothers living with HIV on the risks and benefits of medication and vaccination in HEU infants. Overall, the benefits of the study outweigh the potential risks.

7.2 **Informed consent**

Data for this study were derived from questionnaires administered to the mothers and clinical service data routinely collected. Trained interviewers used a standardized script in the participants' home language, isiXhosa, to obtain informed consent. For the follow-up of HEU and HUU subsets, which involved minimal additional data collection on immunizations, growth, and intercurrent illness, consent was obtained from the children's mothers at delivery or within the first postnatal review at the GMOU, usually between 3 to 7 days postpartum. Participation was voluntary and participants could withdraw at any time. Women participating in the B-positive study were given the option to provide written consent for their involvement in the study and were assured that their decision would not impact the care they received at healthcare facilities. All participants provided informed consent for the B-positive study as required by (HREC REF 749/2015). For this analysis, no additional data and informed consent will be obtained from the participants.

7.3 **Reimbursement**

The B-positive study did not offer compensation or reimbursement to participants from the Pregnancy Exposure Register (PER) and Birth Defects Surveillance (BDS). In contrast, participants from the sentinel cohort were reimbursed R100 per study visit to cover travel and opportunity costs. This reimbursement was approved by the HREC for non-invasive studies and provided in the form of cash or grocery vouchers, based on the research team's experience.

7.4 **Privacy and Confidentiality**

For the B-positive prospective study, participants were informed that their information would remain strictly confidential. As part of the study, participants' names were not written on their study forms or linked to any information or lab samples that were collected. Unique PIDs were used on the database to minimize the risk of confidentiality throughout this study. All staff involved in the data collection and data management process received specific training concerning confidentiality and were required to sign a confidentiality agreement form. Hard copy participant-related information was stored in locked filing cabinets for the B-positive study, electronic records were made password-protected, and files were encrypted. The anonymized datasets were kept in a password-protected computer in a locked office. To ensure the confidentiality and privacy of participants in this secondary analysis, a confidentiality agreement was signed by the master's student, and this sub-analysis will follow security measures like those implemented in the B-positive study.

7.5 **Dissemination of Results**

The research findings of this study will be submitted as partial fulfilment of the requirement for the Master of Public Health in Epidemiology and Biostatistics degree. In addition, the results will be reported in a manuscript that will be submitted to a peer-reviewed journal for publication.

8. **Budget**

As this is a student research project, there is no funding for this protocol.

9. **Gantt**

Table 6. *Time schedule for the proposed dissertation.*

Month	October 2023	November 2023	December 2024	January – February 2024	March – April 2024	May – June 2024	July 2024	August 2024
Ethical approval								
Data management								
Data analysis								
Results								
Discussion								
Final write-up of minor dissertation								
Submission of minor dissertation								

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B. **MANUSCRIPT**

A comparative analysis of medicine use in HIV-exposed uninfected infants compared to HIV unexposed uninfected infants in their first year of life: A secondary analysis of a mother-infant cohort study in Cape Town, South Africa.

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[1]This manuscript adheres to the requirements outlined in the Authors' guidelines for the Maternal and Child Health Journal. An extract of these guidelines is provided in the appendix section of this mini dissertation.

ABSTRACT

Background: Despite several studies investigating medicine exposures in infants, the administration and monitoring of medications in infants who are HIV-exposed uninfected (HEU), a growing population, remains poorly studied. This study aimed to describe and compare medication consumption patterns, including immunization coverage, between infants who are HEU and HIV-unexposed uninfected (HUU) during their first year of life.

Methods: This was a secondary analysis of a birth cohort study of pregnant women living with and without HIV and their infants between 2017 and 2019 in Cape Town, South Africa. Interviewer-administered questionnaires captured sociodemographic factors, self-reported medication use, infant feeding practices, and vaccine use over four postnatal visits (<7 days, 10 weeks, 6 and 12 months). Data was manually classified and coded by a clinical pharmacist and student. Logistic regression models were employed to compare medicine use patterns among infants who are HEU and HUU infants and to identify other maternal and infant factors associated with medication use and vaccine coverage.

Findings: A total of 772 mother-infant pairs were analyzed. Compared to infants who are HUU, HEU infants were preterm (64/393 vs. 39/379; $p = 0.02$), less often breastfed (314/393 vs. 322/379; $p < 0.001$), and weighed less (median, 3288g vs. 3405 g; $p = 0.03$). HEU infants were found to take at least one medication at a significantly higher rate 388/393 (98.7%) vs 345/379 (91.0%) than infants who are HUU ($p < 0.001$). Mothers of HEU infants reported lower use of over-the-counter (OTC) medicine (69.2% vs. 80.2%; $p < 0.01$) and traditional, complementary, and alternative medicine (TCAM) (16.8% vs. 26.1%; $p < 0.001$) compared to mothers of HUU infants. Mothers of HEU infants were less likely to forget a medicine's name (29.3% vs. 36.9%, p<0.001) than HUU mothers. Prescription medicine use, excluding antiretroviral (ARV) prophylaxis medicines routinely administered to infants who are HEU at birth, was significantly higher among infants who are HEU compared to HUU (65.4%. vs. 23.0%; $p < 0.01$). Vaccine coverage showed no significant difference between infants who are HEU and HUU but steadily declined over the year (95.0% coverage with birth immunizations, vs 70.0% at 9 months) across the entire cohort. Only 293 infants (38.0%) had complete immunization coverage at 1 year. In the adjusted models, being a HEU infant was a protective factor against self-medication. (aOR 0.45; 95% CI 0.31 – 0.65; $p < 0.001$). Conversely, being breastfed (aOR 2.46; 95% CI 1.56 –3.83; $p < 0.001$) was a significant risk factor for self-medication infants. Prescription medicine use (excluding ARV prophylaxis medicines) was significantly associated with increased maternal age (aOR 1.06; 95% CI 1.03 – 1.08; $p < 0.001$) and infants who are HEU (aOR 6.52; 95% CI 4.66 – 9.21; $p < 0.001$). No significant associations were found between maternal and infant characteristics and full vaccine coverage.

Interpretation: The study revealed that infants who are HEU were more exposed to prescribed medicine (excluding ARV prophylaxis medicines) compared to their HUU counterparts. However, mothers of HUU infants, generally reported higher usage of both TCAM and OTC compared to HEU infants.

The study also revealed drops in vaccine coverage rates among infants over the first year of life indicating a gap in protection against vaccine-preventable diseases. Further research is needed to study medication patterns in different settings. Education literacy efforts need to be prioritized in pregnant women and mothers of newborns to support rational and safe medicine (including vaccine) usage and subsequently improve the health outcomes for all infants, irrespective of HIV status.

Keywords: HIV; Exposed Uninfected; Infant; Medicine pattern or exposure; vaccine coverage; South Africa

1. Introduction

1.1 Background

The HIV/AIDS epidemic continues to pose a burning threat to global health, with an estimated 39 million people living with the virus universally [1]. Antiretroviral therapy (ART) has been a turning point in treating HIV infection and has also had a prevailing impact on slowing down the rate of vertical transmission of the virus from HIV-infected mothers to their children [2, 4-19, 21-27]. In 2021, approximately 15.9 million children globally were estimated to be HIV-exposed and uninfected (HEU) [4]. The Global South, specifically in sub-Saharan Africa, accounts for at least 60% of all HEU children. Moreover, an estimated one million new HEU children are born annually (Figure 1) [5, 6, 8, 16, 18, 27]. South Africa has the largest population of HEU children, representing more than 25% of the world's HEU children [4, 5]. Given this perspective, the additional adverse health consequences linked to HEU children could significantly influence the region and South Africa's capacity to achieve the Sustainable Development Goals (SDGs), specifically SDG- 3, which promotes Good Health and Well-being [3, 6, 30].

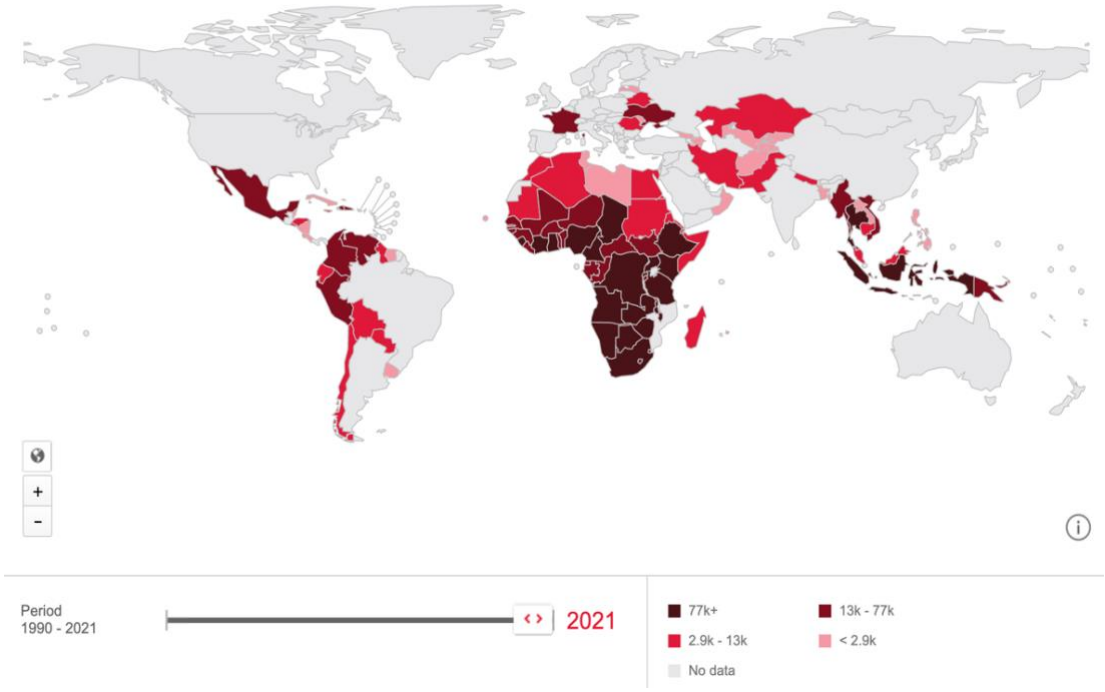

Figure 1. *The global number of HIV-exposed uninfected children (HEU children), 2021. Source UNAIDS data 2021.*

Over the past decade, in South Africa, the antenatal HIV prevalence declined from 30.0% to 27.5% [2] with over 95% of pregnant women living with HIV (PWLHIV) and breastfeeding women receiving lifelong ART (WHO Option B+) regardless of CD4 cell count or clinical stage of the disease [4-10, 11, 18-19, 33]. This universal adoption of lifelong ART for all PWLHIV not only enhanced maternal health but also significantly reduced new paediatric HIV infections, reinforcing the symbiotic relationship between ART implementation for treatment and prevention [7, 9-10, 13, 15, 27, 33]. Nonetheless, this progress brought to light a new concern—HEU infants also antiretrovirals (ARV) – exposed have a mortality rate approximately twice that of infants who are HIV unexposed uninfected (HUU) [4, 5, 7, 13, 19, 22].

Several studies have reported infants who are HEU to be at a greater risk of experiencing adverse health outcomes, such as a higher risk of hospitalization for infection, and vulnerabilities to infectious diseases in infancy surpassing those of their HUU counterparts, with in-utero ARV exposure potentially contributing to this disparity [5, 13, 22, 26, 32, 34]. For example, the SMARTT study, which monitored the effects of ART on children who are HEU, and the PROMISE study, which monitors the efficacy and safety of ARV regimens for the prevention of vertical HIV transmission, both found adverse effects of maternal ART on birth outcomes [7, 35]. Moreover, ARV drugs such as atazanavir, tenofovir, and dolutegravir may have an impact on language acquisition, bone mineral content, and neural tube defect risk, respectively [7, 24]. This widespread use of medicines in pregnant and breastfeeding women and their infants necessitates the inclusion of these populations in pharmacovigilance activities to protect them from medication risks [9, 8, 21, 28, 35]. However, limited efforts have been made to establish pharmacovigilance systems for this vulnerable population in high HIV- burden countries, highlighting the importance of assessing medicine exposure and other treatment combinations for infants by HIV exposure [6, 8 - 10, 28 - 29, 35].

Medication exposure in infants is a critical concern due to the differences in drug pharmacokinetics and pharmacodynamics between children and adults. These differences increase their risk of certain serious adverse effects, such as Reye's syndrome with aspirin, as well as susceptibility to drug interactions and complications from misuse or delayed diagnosis of underlying conditions [30, 29, 40, 41, 43, 44, 47, 48]. While studies on infant medicine use are scarce, particularly in developing countries, existing evidence suggests high medication use among infants, which tends to decrease as they grow older [37-38, 40, 43, 45]. This is concerning because infants commonly receive off-label or unlicensed medications, often at dosages extrapolated from older children or adults, further raising the risk of serious adverse effects [40, 48].

The use of medicine in children including prescribed and OTC medicines has been studied previously. A study conducted in three countries (UK, Italy, and Netherlands) in 2008 on drug use in children aged 0-14 years revealed that prescription use was highest for children aged under 2 [40]. Similarly, Headley *et al.* found that 75% of the study children (aged 0-7.5 years old) were exposed to some form of medicine before two months of age [38]. Studies in sub-Saharan Africa have also highlighted the high prevalence of medication use in infants. A 2020 study in the Democratic Republic of Congo reported that 95.8% of mothers practiced self-medication on their children with antimalarials (91.6%) and antipyretics/analgesics (41.3%) being the most

common medication used [50]. In South Africa, a study found 79.3% of paediatric patients aged 0-1 years old in public hospitals were exposed to many off-label and unlicensed medicines, averaging three medicines prescribed per infant in the study [48]. Another study conducted in KwaZulu-Natal revealed that a high prevalence of 97% of mothers or caregivers were found to have given their infants non-prescribed medicine in their first three months of life [49]. Furthermore, Koopmans *et al.* reported infants in the paediatric ward (51.1%) and paediatric intensive care unit (53.7%) were prescribed more than 1 antimicrobial drug [39]. Despite these studies, the administration and monitoring of medications in infants who are HEU, a growing population, remains poorly studied.

The use of traditional, complementary, and alternative medicine (TCAM) adds another layer of complexity to the health landscape of infants who are HEU. According to WHO, TCAM refers to "any diagnosis, treatment, and prevention that are used alongside standard medical treatment (complementary) or instead of it (alternative)" [55]. The WHO estimates that 80% of people in developing countries, including about 58.2% of people in Africa use TCAM, particularly traditional medicine, as their primary healthcare choice [55, 57, 59]. The use of TM is deeply connected to cultural beliefs and practices. For example, Xhosas in Transkei believe that TM is an integral part of their culture and to abandon TM would be akin to abandoning the Xhosa culture [60]. Mothers or caregivers were found to use TM to "strengthen the womb against witchcraft or sorcery" and improve the well-being of the baby [49, 56, 60]. Other reasons for the high prevalence of TCAM use include dissatisfaction with conventional healthcare, such as the unavailability of medicines and negative attitudes from healthcare providers, and low cost associated with the use of TM treatment or products [54, 55, 57, 60]. However, their safety and efficacy remain poorly understood [56-58].

In 1974, the World Health Organization (WHO) introduced the Expanded Programme on Immunization (EPI), marking a pivotal moment in global public health by advocating for routine childhood vaccination [69, 76]. Fifty years on, this initiative transformed global public healthcare delivery, making immunization one of the most cost-effective interventions in preventing infectious diseases and averting between three and four million deaths annually [63, 67, 69-70, 73-74, 76-77]. However, despite these successes, there remains a concerning gap in childhood vaccination coverage, particularly in low- and middle-income countries where logistical support, socioeconomic, and cultural barriers hinder access to basic vaccines through routine immunization services [66, 74, 76-77, 79]. This gap leaves millions of children vulnerable to vaccine-preventable diseases (VPD), highlighting the urgent need for targeted interventions to bridge these disparities [69, 77].

TABLE 1: SA IMMUNISATION SCHEDULE

Age	Antigens
Birth	OPV 0, BCG
6 weeks	OPV 1, DTaP-IPV-Hib-HBV 1, , RV 1, PCV 1
10 weeks	DTaP-IPV-Hib-HBV 2,
14 weeks	DTaP-IPV-Hib-HBV 3, , RV 2, PCV 2
6 months	Measles 1
9 months	PCV3
12 months	Measles 2
18 months	DTaP-IPV-Hib-HBV 3, PCV3
6 years	Td
12 years	Td
Grade 4 girls, aged 9 years and older	HPV

Figure 2. *The public sector routine immunization schedule (2020). Source Health Department of the Republic of South Africa.*

In Africa, particularly in South Africa, vaccine coverage has shown improvements over time, with the EPI programme in South Africa (EPI-SA) playing a significant role in improving vaccine coverage in children in their first year of life [74]. Currently, the EPI-SA offers eleven essential antigens free of charge at all government healthcare facilities, ensuring widespread access to immunization services across the country (Figure 2) [63, 66]. These efforts have led to the eradication of life-threatening and disabling VPD and have averted an estimated 2.5 million deaths annually [66]. Despite these achievements, South Africa still faces challenges, such as suboptimal coverage rates resulting in outbreaks of measles, rubella, and pertussis [66, 75]. Additionally, missed opportunities for vaccination (MOV) – "any health service contact by eligible individuals that does not result in receiving necessary vaccine doses" – further exacerbates under-immunization, and suboptimal coverage in South Africa [63, 76]. The vaccine coverage rate for fully vaccinated under 1-year-olds was 76.9% in 2017/2018, a 6% increase from the previous period [63]. This represents progress and highlights the need for continued efforts to reach higher coverage levels nationwide.

Furthermore, the impact of maternal HIV status on child vaccination status, particularly among HEU children, is a critical consideration in vaccine coverage assessments [67, 70]. These children face a disproportionately higher risk of being under-immunized compared to infants of women living without HIV, with studies indicating a 30-70% chance of being incompletely immunized [62, 64, 67, 73]. This disparity is concerning, as infants who are HEU are more susceptible to infection by various VPDs with low vaccination coverage contributing to their increased burden of infectious diseases in early life [61, 65, 67, 70]. In addition, while several studies have assessed vaccination coverage among children, they did not compare vaccine coverage

between infants who are HEU and those who are HUU [68, 69, 71, 63]. While progress has been made in improving vaccination rates in South Africa, more research is needed to understand and address the differences in vaccine coverage among vulnerable populations, including but not limited to HIV exposure status.

Thus, this study sought to address this information gap by analyzing medication usage patterns including vaccination coverage among a cohort of infants who are HEU and comparing them with HUU infants during their first year of life in a peri-urban township in Cape Town, South Africa. The primary objective was to examine and compare the consumption of medications between these two groups of infants. Furthermore, given the importance of vaccination for children who are HEU and the data suggesting that they are at a higher risk of under-vaccination, we sought to assess the vaccination status of both infants who are HEU and HUU and identify maternal factors (e.g., maternal education status, maternal age) and infant factors (birth weight, gestational age at birth, hospitalization) that contribute to patterns of medication usage in both groups.

2. **Methodology**

2.1 **Study design and setting**

This was a secondary analysis of data obtained from infants born to women who participated in the primary B-positive birth cohort study at the Maternal-Obstetric Unit (MOU) at Gugulethu Community Health Care Centre, Western Cape Town, South Africa. The design and methods of the B-positive study have been previously described elsewhere [28], but briefly, the overarching purpose of the B-positive study was to "comprehensively monitor the effectiveness, impact, and risks of the WHO Option B+ prevention of mother-to-child transmission (PMTCT) of HIV strategy at a population level in the entire Western Cape Province." It involved three linked cohorts: 1) a cohort of approximately 900 pregnant women – about 450 women living with HIV (WLHIV) and 450 women without HIV – who were enrolled at a single primary health facility and were then closely followed antenatally and up to 12 months postnatally. 2) At the same sentinel site, a pregnancy exposure registry enrolled all pregnant women at the same facility from their initial antenatal visit until delivery. 3) A provincial maternal data cascade was developed that identified, through a series of electronic evidence (e.g., presence of a rhesus test, a syphilis test, admission into a labour/delivery ward), all pregnant women in the province. This cohort of mother-infant pairs was the focus of this analysis based on data derived from interviewer-administered questionnaires of mothers around infant medication administration postnatally and vaccine coverage.

The study took place at the Gugulethu Maternal-Obstetric Unit (GMOU) which is a midwife-run public sector healthcare facility that serves a population of about 350,000 with integrated ARVs services and midwives prescribing and dispensing medication including ART [27, 28]. The Gugulethu community is a peri-urban township marked by high levels of poverty, unemployment, an antenatal seroprevalence of 30% and prevalent child health risks such as HIV [9, 19]. Despite the existence of a working GMOU, the perinatal death rate in

this township is 15.6 per 1,000 inhabitants [27]. As part of the standard of care at GMOU, women on ART were required to attend the clinic with their infants within one month of delivery. Local clinics also provide paediatric care services including vaccinations such as Bacille Calmette-Guerin (birth); rotavirus (6 and 14 weeks); and pneumococcal conjugate vaccines (6, 10, and 14 weeks); monthly well baby checks, including growth monitoring, HIV-infection status updates, deworming from the age of six months, and vitamin A supplementation [28]. Clinic and hospital findings are recorded in the infant's "Road to Health" booklet (RTHB), which serves as a patient-held health record.

2.2 **Study procedures**

Consecutive pregnant women above 18 years with and without HIV, were screened and recruited at their first ANC. Eligible participants were enrolled in the study between January 2017 to July 2018. Women were eligible to participate in the study if they had a confirmed maternal HIV test and if they planned to reside in Cape Town for at least one year postpartum with their infants. All eligible infants were enrolled from birth if the caregiver or mother provided written consent and intended to stay in Cape Town with the infant during the study period. Infants who are HEU were identified based on maternal HIV test results and HIV deoxyribonucleic (DNA) Polymerase Chain Reaction (PCR) test, taken at birth and 6 to 10 weeks according to national guidelines [27]. Our analysis included liveborn singleton and twin infants who were HIV-negative at 2 weeks of age and had negative PCR results at any point time during the 12-month follow-up period. Only infants with recorded medication exposure – encompassing at least one type of medication, including RX, OTC, and TCAM – and vaccination coverage (according to the national recommended vaccination schedule) during the first year of life were included. Infants were excluded if they had neither medication exposure nor vaccine recorded. Figure 3 gives a diagrammatic description of how the final sample was derived.

2.3 **Sample size**

This was a secondary analysis, and the sample size was determined based on the primary objectives of the study, not on the objective of assessing medication and vaccine exposure in infants.

2.4 **Data collection and measures**

All in-person interviews were conducted in the mothers' preferred language either English or isiXhosa during regularly scheduled antenatal or postnatal clinic appointments by trained study staff. Furthermore, brief phone interviews were conducted to gather basic information on mother and infant health and maintain ongoing communication with the participants. Study staff were trained to collect data using a validated interviewer-administered questionnaire. Data was collected on basic sociodemographic information at baseline including maternal age, and maternal education status categorized into three levels (primary, completed some secondary,

and completed secondary), maternal income levels, working status (employed/unemployed), housing (formal/shack-informal), and basic amenities (toilet, running water and electricity).

Obstetric variables were also captured and included mode of delivery, parity defined as the number of previous births (0, 1-3 or ≥3 previous births), at a gestational age of 24 weeks or more – regardless of whether the infant was born alive or was stillborn, gravidity, number of children, and pregnancy outcomes. Other variables included TB during and before the pregnancy and the place of delivery. Infant characteristics collected at baseline included gender, feeding practices (breastfed or not), birth weight (low defined as weight at birth of < 2500 grams [9]) measured within 24h of birth by health facility nurses; gestational age (GA) was estimated at the first antenatal visit with ultrasound, last menstrual period, and symphysial-fundal height. Pre-term was defined at less than 37 weeks gestation. The infant's weight was measured in grams, accurate to the nearest 10g after removing clothing and diaper, while the recumbent length and head circumference were measured in centimetres, accurate to the nearest 0.5 cm, respectively. At each study visit, trained study staff took and averaged two measurements. All immunizations, infant medical events experienced, and medication use were also recorded. This resulted in a maximum of 5 study visits including baseline and follow-up (<7 days postpartum, 6 weeks, 3, 6, and 12 months), which were integrated with routine care at the nearest clinics, according to local standard of care.

2.5 **Outcomes**

The primary outcome of interest in this study was medication use, defined as the proportion of infants who received at least one type of medication during their first year of life. "At least one type of medication" encompassed any medication administered to infants from birth through the end of the follow-up period. This included prescribed medications — any medications prescribed by healthcare professionals, including ARV prophylaxis (Nevirapine (NVP) with or without zidovudine (AZT)) and co-trimoxazole (CTX) prophylaxis aimed at preventing HIV transmission — as well as non-prescribed medications, which included over-the-counter (OTC) medications and TCAM. It is important to note that vaccine exposures were excluded from this primary outcome measure and were considered a secondary outcome. This distinction allowed for a more focused analysis of the overall medication exposure among infants, independent of vaccination practices. Data on infant medication use were collected by study staff and encompassed all medications reported by the mother or caregiver. This included prescriptions or medications provided by clinic and hospital staff (such as doctors and nurses), as well as medications obtained from pharmacies or other retail sources, and those given by traditional healers, spiritual healers, friends, or family members.

Our secondary outcome of interest was vaccine coverage. We defined vaccine coverage according to the EPI-SA schedule as the proportion of infants who receive the full recommended schedule of individual vaccines at a certain age, regardless of the timing of the administration. In this study, infants who received all vaccine doses were considered fully vaccinated, while those who missed at least one vaccine dose were referred to as

incompletely vaccinated. Poorly vaccinated referred to infants who received less than 50% of any doses of the routine vaccine per EPI-SA recommendations.

2.6 **Data processing and analysis**

Data on self-reported medicine exposure were collected from the questionnaires administered by trained study staff at all study visits, manually cleaned, and coded into prescribed (RX) with ARV (RX - ARV) and RX without ARV (given that HEU infants were on NVP and AZT). All medicines reported were classified as either RX, OTC, or TCAM by a clinical pharmacist. All medications were evaluated to identify and list the active ingredient of each medication and coded using the WHO Anatomical Therapeutic Chemical (ATC) system [34]. The ATC level 1 and 2 categorizations were determined for each medicine except for non-medicinal product use (e.g., light therapy, green soap, baby powder), which was classified as "not a medication" and TCAM. Additionally, names of medications that were ambiguous or not identified by the participant were categorized as "medication unknown." Each medicine was only counted as one exposure per infant, regardless of how many times it was reported during their first year of life. When assessing for duplicate information in the medicine dataset, a total of 80 rows of participant data were duplicated, and all rows were removed from the dataset.

2.7 **Statistical analysis**

The collected data were cleaned and coded, using an Excel spreadsheet from Microsoft, and all statistical analysis was performed using R version 3.6.0 (2020-04-26) [78]. Descriptive statistics were performed to summarize the sociodemographics of the mothers stratified by HIV status, as well as the characteristics of infants who are HEU versus HUU. Categorical variables were described using frequency and percentages, whereas continuous variables were described using median, and interquartile ranges (IQR). Mann-Whitney U test was applied for continuous variables to assess the difference in distribution, while the chi-squared test or Fisher's exact test was used to compare the association between categorical variables. The dataset contained missing values for self-reported breastfeeding, head circumference, length, birth weight, and vaccine coverage (secondary outcome). A conditional multiple imputation method was employed for vaccine coverage to address missing data for the outcome and self-reported breastfeeding as a predictor variable. This method replaced the missing values with estimated values based on the observed data [79]. The imputation was performed multiple times, creating several complete datasets with different imputed values for the missing data [79]. After analyzing these complete datasets, the one that closely matched the distribution of the variables in the original dataset was selected and analyzed [79]. This approach was flexible and could handle both continuous and categorical variables. It also accommodated missing data that was missing at random, which meant that the probability of missing data depended on observed data but not on the missing data itself [79]. This was the case for the vaccine coverage and self-reported breastfeeding variable, where the data were

missing randomly. A significance level of 0.05 was used for all analyses to determine statistical significance. In addition, proportions were used to evaluate vaccine coverage, with vaccination age calculated as the number of days between birth and vaccination dates. Multivariable logistic regression models were used to assess the association between maternal and infant characteristics and medicine use (Prescription without ARV – considering that most HEU infants were on ARV prophylaxis or non-prescription – including only TCAM and OTC), and full vaccine coverage for each vaccine (fully immunization versus incomplete immunization). Results were presented using adjusted odds ratio (aORs) and 95% confidence intervals (CI). Confounding variables such as maternal, household, and infant factors were assessed. Priority was given to controlling for previously reported contributing factors to medicine use and vaccination coverage and included preterm birth, maternal age, mode of delivery, number of children, household crowding, infant's gender, breastfeeding, maternal education, income, and housing (see Appendix E).

2.8 **Ethical consideration**

Ethical approval for the parent and sub-studies was approved by the University of Cape Town Human Research Ethics Committee (REF 541/2015, 749/2015, and 197/2020). All participants (mothers) provided informed consent at enrolment and their confidentiality was maintained, with data access restricted to the investigators. Mothers or caregivers gave consent at the first postnatal visit. This current study, a descriptive analysis of prospectively collected medication and vaccine coverage of infants who are HEU and HUU was approved by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee [HREC 724/2023, Appendix 1].

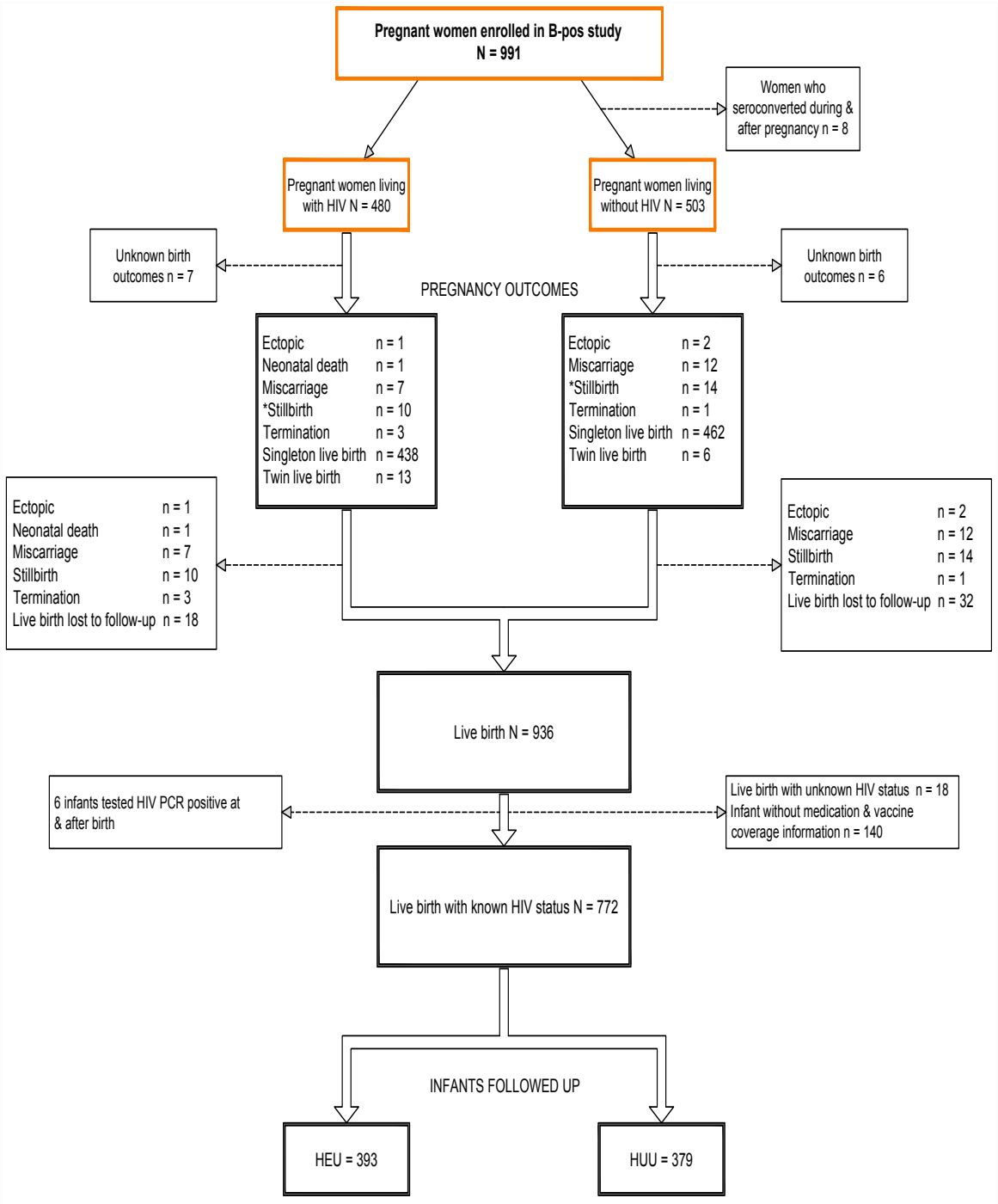

Figure 3. *The flow diagram of participants included in the study (N=772). *Stillbirth were twins born with no signs of life at least 20 weeks gestation. Only twins with medication exposures and RTHB were included in the study.*

3. **Results**

3.1 **Demographic characteristics of the study population**

The primary study sample included 991 pregnant women, 503 WLOHIV, and 480 WLHIV. Characteristics of excluded women are shown in Figure 3. Among the 936 live-born infants, 18 had unknown HIV status, 6 infants seroconverted (1 at birth and 5 after birth), and 140 infants with missing data on medication and vaccine coverage were excluded from the analysis. The final sample size included 772 mother-infant pairs, with 379 HUU and 393 HEU infants. Table 1 and Table 2 show the infant and maternal characteristics, respectively.

Table 1 shows the characteristics of infants (HUU = 379; HEU = 393), born between February 2017 and January 2019 and followed up from birth until 12 months of age. There were no statistically significant differences in the distribution of sex at birth, with 50.4% females in HUU and 52.9% in HEU ($p = 0.53$). Preterm birth was more prevalent in the HEU infant cohort vs. HUU (16.3% vs. 10.3%, $p = 0.02$). The median birthweight and head circumference at birth were similarly smaller in infants who are HEU (Table 1). HUU infants were more likely to be breastfed compared to infants who are HEU (85.0% vs. 79.9%; $p < 0.001$).

Table 2 shows that among the 772 mothers of the infants included in this analysis, the median age at baseline was 35 (IQR [23, 52]) and statistically different across the groups ($p < 0.001$), with WLOHIV being younger at 33 (IQR [23, 52]) than WLHIV at 37 (IQR [24, 50]). WLOHIV tended to be more socioeconomically stable in terms of housing, employment ($p = 0.04$), income ($p = 0.02$), and education ($p = 0.05$). Overall, gravidity among the mothers showed statistically significant differences ($p < 0.001$), with most mothers (n = 454, 58.8%) being pregnant and having experienced one or more pregnancies at baseline. WLOHIV were more likely to be primiparous (n = 241, 63.6%) compared to WLHIV (n = 196, 49.9%). Similarly, WLHIV had more children compared to WLOHIV (65.2% vs 53.2%; $p < 0.001$; Table 2), although the number of people per household was similar for both groups (Table 2).

Table 1: Clinical and demographic characteristics of infants who are HEU and HUU at their first postnatal visits in B-positive cohort study 2017-2018 Cape Town, South Africa.

Birth and Infant characteristics	**HUU = 379[1]**	**HEU = 393[1]**	**N = 772[1]**	***P*-value**
Sex				0.53
Female	191 (50.4%)	208 (52.9%)	399 (51.7%)	
Male	188 (49.6%)	185 (47.1%)	373 (48.3%)	
Birth weight (grams)				0.28
Low Weight < 2500g	38 (10%)	54 (13.7%)	92 (11.9%)	
Normal Weight	325 (85.8%)	323 (82.2%)	648 (83.9%)	
Macrosomia > 4500g	16 (4.2%)	16 (4.1%)	32 (4.1%)	
Birth weight (grams)	3405 [3042, 3800]	3288 [2910, 3666]	3315 [3000, 3730]	**0.03***
Missing	53 (14.0%)	53 (13.5%)	106 (13.7%)	
Length at birth (cm) [IQR]	50.1 [48.5, 52]	50 [48, 52]	50 [48, 52]	0.12
Missing	54 (14.2%)	53 (13.5%)	107 (13.9%)	
Head circumference at birth (cm) [IQR]	36 [34.2, 37]	35 [34, 36.5]	35.5 [34, 36.1]	**<0.01***
Missing	54 (14.2%)	53 (13.5%)	107 (13.9%)	
Gestational age				**0.02***
Preterm <37 weeks	39 (10.3%)	64 (16.3%)	103 (13.3%)	
Term >37 weeks	340 (89.7%)	329 (83.7%)	669 (86.7%)	
Place of delivery				0.42
Groote Schuur Hospital	30 (7.9%)	45 (11.5%)	75 (9.7%)	
Gugulethu MOU	136 (35.9%)	138 (35.1%)	274 (35.5%)	
Mowbray Maternity Hospital	191 (50.4%)	189 (48.1%)	380 (49.2%)	
Other	22 (5.8%)	21 (5.3%)	43 (5.6%)	
Self-reported Breastfeeding				**<0.001***
Yes	322 (85.0%)	314 (79.9%)	636 (82.4%)	
No	2 (0.5%)	21 (5.3%)	23 (3.0%)	
Missing	55 (14.5%)	58 (14.8%)	113 (14.6%)	

1 Statistics presented: Frequency (%) for categorical variables and median (IQR) for continuous variables.

IQR – interquartile range; N – total number of infants; HEU – HIV-exposed uninfected; HUU – HIV-unexposed uninfected; MOU – Maternity of Unit

*Significant at *p-value* ≤0.05

Table 2: Maternal socio-demographic profile by HIV infection in B-positive cohort study 2017-2018 Cape Town, South Africa.

Maternal characteristics	Mothers of HUU N = 379[1]	Mothers of HEU N = 393[1]	Overall N = 772[1]	*P*-value
Age in years [IQR]	33 [23, 52]	38 [24, 50]	35 [23, 52]	**<0.001***
Education				**<0.05***
Primary school	11 (2.9%)	20 (5.1%)	31 (4.0%)	
Secondary school	355 (93.7%)	370 (94.1%)	725 (93.9%)	
Post - secondary	12 (3.2%)	4 (1.0%)	16 (2.1%)	
Employment				**0.04***
Employed	112 (29.6%)	145 (36.9%)	257 (33.3%)	
Unemployed	267 (70.4%)	248 (63.1%)	515 (66.7%)	
Income status				**0.02***
<R5 000 per month	90 (23.7%)	127 (32.3%)	217 (28.1%)	
>R5 000 per month	21 (5.5%)	15 (3.8%)	36 (4.7%)	
No income reported	268 (70.7%)	251 (63.9%)	519 (67.2%)	
Housing				0.21
Formal housing	187 (49.3%)	171 (43.5%)	358 (46.4%)	
Shack/informal	192 (50.7%)	222 (56.5%)	414 (53.6%)	
Running water				0.18
No	196 (51.7%)	223 (56.7%)	419 (54.3%)	
Yes	183 (48.3%)	170 (43.3%)	353 (45.7%)	
Toilet				0.15
No	251 (66.2%)	280 (71.2%)	531 (68.8%)	
Yes	128 (33.8%)	113 (28.8%)	241 (31.2%)	
Electricity				0.47
No	10 (2.6%)	15 (3.8%)	25 (3.2%)	
Yes	369 (97.4%)	378 (96.2%)	747 (96.8%)	
Household crowding				0.51
0	9 (2.4%)	15 (3.8%)	24 (3.1%)	
1-3	152 (40.1%)	154 (39.2%)	306 (39.6%)	
>=3	218 (57.5%)	224 (57.0%)	442 (57.3%)	
Gravidity				**<0.001***
0	108 (28.5%)	55 (14.0%)	163 (21.1%)	
1-3	208 (54.9%)	246 (62.6%)	454 (58.8%)	
>=3	63 (16.6%)	92 (23.4%)	155 (20.1%)	
Parity				**<0.001***
0	241 (63.6%)	196 (49.9%)	437 (56.6%)	
1-3	129 (34.0%)	178 (45.3%)	307 (39.8%)	
>=3	9 (2.4%)	19 (4.8%)	28 (3.6%)	
Number of children				**<0.001***
0	247 (65.2%)	209 (53.2%)	456 (59.1%)	
1-3	124 (32.7%)	170 (43.3%)	294 (38.1%)	
>=3	8 (2.1%)	14 (3.6%)	22 (2.8%)	
TB status during pregnancy				0.25
No	379 (100%)	390 (99.2%)	769 (99.6%)	
Yes	0 (0%)	3 (0.8%)	3 (0.4%)	
Mode of delivery				0.76
Emergency Caesarean	83 (21.9%)	76 (19.3%)	159 (20.6%)	
NVD	245 (64.6%)	261 (66.4%)	506 (65.5%)	
Scheduled Caesarean	51 (13.5%)	56 (14.2%)	107 (13.9%)	
Single/Multiple birth				0.62
Single Birth	374 (98.7%)	385 (98.0%)	759 (98.3%)	
Twin	5 (1.3%)	8 (2.0%)	13 (1.7%)	

1 Statistics presented: Frequency (%) for categorical variables and median (IQR) for continuous variables.

IQR – interquartile range; N – numbers; HEU – HIV-exposed uninfected; HUU – HIV-unexposed uninfected.

*Significant at $p \leq 0.05$

3.2 **Prevalence and type of medicines used for infants during the study period.**

Table 3: The proportion of infants who are HEU and HUU taking at least one type of medicine in the first year of life.

Type of medication used	**HUU N = 379[1]**	**HEU N = 393[1]**	**Overall N = 772[1]**	***P*-value**
Prescription Medicine (including ARVs)	88 (23.2%)	385 (98.0%)	473 (61.3%)	**<0.01***
Prescription Medicine (excluding ARVs)	87 (23.0%)	257 (65.4%)	344 (44.6%)	**<0.01***
OTC	304 (80.2%)	272 (69.2%)	576 (74.6%)	**<0.01***
TCAM	99 (26.1%)	66 (16.8%)	165 (21.4%)	**<0.001***
Medication unknown	140 (36.9%)	115 (29.3%)	255 (33.0%)	**<0.001**
No. of reported medicines in the first year of life				**<0.001***
None	34 (9.0%)	5 (1.3%)	39 (5.1%)	
One	95 (25.1%)	28 (7.1%)	123 (16.0%)	
Two - three	145 (38.3%)	100 (25.4%)	245 (32.0%)	
>= Four	105 (28.0%)	260 (66.2%)	365 (47.3%)	
Median number of medicines reported during first year of life [IQR]	2 [1, 4]	5 [3, 7]	3 [3, 7]	**<0.001***

1 Statistics presented: Frequency (%) for categorical variables and median (IQR) for continuous variables.

ARVs – Antiretrovirals; OTC - Over-the-counter; TCAM - Traditional, Contemporary and Alternative Medicine; IQR – interquartile range; N – numbers; HEU – HIV-exposed uninfected; HUU – HIV-unexposed uninfected.

*Significant at $p \leq 0.05$.

In ***Table 3***, we can see that 74.6% of infants were on OTC medications, making it the most commonly used type of medication during the first year of life. In contrast, TCAM treatments were the least commonly used, with only 21.4% of infants reported by mothers. Prescription medications, including ARVs, were reported for 61.3% of infants, while 44.6% received prescriptions excluding ARVs. Interestingly, a small proportion of infants (5.1%) were not reported using any medication within the first year. The median number of medications reported for infants who are HEU was greater than for infants who are HUU (median of 5 (IQR: 3, 7) vs. median of 2 (IQR: 1, 4); $p < 0.001$). Additionally, medicine use was much higher in the HEU group with 66.2% of HEU infants administered four or more medicines in the first year of life compared to 28% in the HUU cohort ($p < 0.001$). HUU infants were more likely to be on OTC (80.2% vs. 69.2%; $p < 0.01$) and TCAM usage (26.1% vs. 16.8%; $p < 0.001$), as well as the use of unidentified medication (36.9% vs. 29.3%; $p < 0.001$) compared to HEU infants.

Table 4: Self-reported medicine use by ATC Level 1 and 2 classifications between infants who are HEU and HUU in the first year of life.

ATC code	Med class	HUU N = 379[1]	HEU N = 393[1]	Overall N = 772[1]	*P*-value
A	**Gastrointestinal preparations**				
A02	Antacid	35 (10.1%)	31 (8.0%)	66 (9.0%)	0.40
A06	Laxatives	-	2 (0.5%)	2 (0.3%)	0.50
A07	Antidiarrheals	26 (7.5%)	14 (3.6%)	40 (5.5%)	**<0.05***
A11	Vitamins	23 (6.7%)	27 (7.0%)	50 (6.8%)	0.99
A12	Mineral supplements	13 (3.8%)	11 (2.8%)	24 (3.3%)	0.62
B	**Blood and blood forming organs**				
B03	Antianemia	4 (1.2%)	2 (0.5%)	6 (0.8%)	0.43
D	**Dermatologicals**				
D01	Tropical antifungals	3 (0.9%)	1 (0.3%)	4 (0.5%)	0.35
D02	Emollients and protectants	48 (13.9%)	37 (9.5%)	85 (12.0%)	0.10
D04	Antipruritic	3 (0.9%)	-	3 (0.4%)	0.10
D07	Corticosteroids, dermatological preparations	3 (0.9%)	5 (1.3%)	8 (1.1%)	0.73
D08	Antiseptic and disinfectants	214 (62.0%)	195 (50.3%)	409 (55.8%)	**<0.001***
D11	Other dermatological preparations	-	2 (0.5%)	2 (0.3%)	0.50
G	**Genito-urinary system and sex hormones**				
G01	Gynecological anti-infective and antiseptics	1 (0.3%)	-	1 (0.1%)	0.50
J	**Anti-infectives for systemic use**				
J01	Antibacterial for systemic use	80 (23.2%)	257 (66.2%)	337 (46.0%)	**<0.001***
J04	Antimycobacterial	-	1 (0.3%)	1 (0.1%)	**<0.05***
J05	Antivirals for systemic use	1 (0.3%)	373 (96.1%)	374 (51.0%)	**<0.001***
M	**Musculo-skeletal system**				
M01	Anti-inflammatory and antirheumatic products	-	2 (0.5%)	2 (0.3%)	0.50
N	**Nervous system**				
N02	Analgesics including paracetamol and aspirin	133 (38.6%)	100 (25.8%)	233 (31.8%)	**<0.001***
N05	Psycholeptics	21 (6.1%)	15 (3.9%)	36 (4.9%)	0.22
P	**Antiparasitics, insecticides and repellents**				
P02	Anthelmintic	-	1 (0.3%)	1 (0.1%)	0.99
P03	Ectoparasticides	-	3 (0.8%)	3 (0.4%)	0.25
R	**Respiratory system**				
R01	Nasal preparations	10 (2.9%)	9 (2.3%)	19 (2.6%)	0.80
R03	Drugs for obstructive airways disease	3 (0.9%)	4 (1.0%)	7 (1.0%)	0.99

Table 4 *(continued)*.

ATC code	Med class	HUU N = 379[1]	HEU N = 393[1]	Overall N = 772[1]	*P*-value
R	**Respiratory system**				
R05	Cough and cold preparations	35 (10.1%)	35 (9.0%)	70 (9.5%)	0.70
R06	Antihistamines	16 (4.6%)	15 (3.9%)	31 (4.2%)	0.73
S	**Sensory organs**				
S01	Eye preparation NOS	2 (0.6%)	-	2 (0.3%)	0.22
V	**Various**				
V03	Medical gases	5 (1.4%)	6 (1.5%)	11 (1.5%)	0.99
00	Medicine unknown	153 (44.3%)	120 (30.9%)	273 (37.2%)	**<0.001***

1 Statistics presented: Frequency (%) for categorical variables and median (IQR) for continuous variables.

N – numbers; HEU – HIV-exposed uninfected; HUU – HIV-unexposed uninfected; NOS – Not otherwise specified.

*Significant at $p \leq 0.05$.

Overall, antiseptics were the most frequently reported medication accounting for 55.8%, followed by antivirals at 51%, and antibacterials at 46% of the medication profile across the cohort (Table 4). Infants who are HEU were significantly more likely to receive antivirals (96.1% vs 0.3%; p <0.001) and antibiotics (66.2% vs 23.3%). In contrast, infants who are HUU were more likely to receive analgesics (e.g., paracetamol and aspirin) (38.6% vs 25.2%; p <0.001) and medicines that mothers could not identify (medication unknown) (44.3% vs 30.9%; p <0.001). Furthermore, among the 257 HEU infants on antibacterial for systemic use, 234 infants (91.1%; 234/257) received CTX prophylaxis, while 23 infants (9%; 23/257) were treated with other antimicrobials instead of CTX prophylaxis. For the 373 infants who are HEU on antivirals for systemic use, 296 infants (79.4%; 296/373) were administered NVP, 12 infants (3.2%; 12/373) received AZT, and 65 infants (17.4%; 65/373) were treated with both AZT and NVP. Medication classes such as antacids, vitamins and multivitamins, emollients, and cough and cold preparations showed relatively minor differences between the two infant groups, with no significant disparities observed (Table 4).

Table 5: TCAMs reportedly used between infants who are HEU and HUU in their first year of life.

TCAM	HUU N = 379[1]	HEU N = 393[1]	Overall N = 772[1]	P-value
Gripe water	34 (9.0%)	29 (7.4%)	63 (8.2%)	0.31
Herman drops	20 (5.3%)	14 (3.6%)	34 (4.4%)	0.22
Medication unknown (for Umoya)	7 (1.8%)	5 (1.3%)	12 (1.6%)	0.60
Umthombothi	3 (0.8%)	2 (0.5%)	5 (0.6%)	0.70
Castor oil ointment	2 (0.5%)	1 (0.3%)	3 (0.4%)	0.60
Entressdrupples H.M.	2 (0.5%)	1 (0.3%)	3 (0.4%)	0.60
Clement drops NOS	1 (0.3%)	1 (0.3%)	2 (0.3%)	0.99
Lennons	2 (0.5%)	-	2 (0.3%)	0.22
Qhuma	2 (0.5 %)	-	2 (0.3%)	0.22
Saccheroi Syrup	1 (0.3%)	1 (0.3%)	2 (0.3%)	0.99
Colic NOS	1 (0.3%)	-	1 (0.1%)	0.50
Glycerine and borax	-	1 (0.3%)	1 (0.1%)	0.99
Imbiza Colic NOS	1 (0.3%)	-	1 (0.1%)	0.50
Borsdruppels	1 (0.3%)	-	1 (0.1%)	0.50
Muthi wenyoni antacid	1 (0.3%)	-	1 (0.1%)	0.50

1 Statistics presented: Frequency (%) for categorical variables and median (IQR) for continuous variables.

TCAM - Traditional, Contemporary, and Alternative Medicine; N – numbers; HEU – HIV-exposed uninfected; HUU – HIV-unexposed uninfected; NOS – Not otherwise specified.

*Significant at $p \leq 0.05$.

Table 5. presents the types and frequency of reported TCAM used. Overall, mothers of HEU and HUU infants reported a 6.5% (n = 50) use of TCAM, with a higher overall prevalence of reported use among HUU infants compared to HEU infants (8.7% vs. 4.3%, $p < 0.01$) during the follow-up period. There was no statistically significant difference in the use of different types of TCAM products across the 2 groups of infants. Gripe water, an herbal supplement commonly used to relieve colic and teething pains was the most reported product at 8.2% (n = 63). A traditional Dutch remedy colloquially called "Herman drops" (Haarlemensis drops) indicated to relieve symptoms of kidney and bladder complaints was also notably used at 4.4 % (n = 34) followed by the Oral Rehydration Solution (homemade) at 4.3% (n = 34).

3.3 **Immunization profile.**

Table 6: Vaccination coverage from birth to 9 months of age between infants who HEU and HUU in Cape Town.

Time points	Vaccines	HUU N = 379[1]	HEU N = 393[1]	Overall N = 772[1]
Birth	BCG (%)	360 (95.0%)	373 (95.0%)	733(95.0%)
	OPV0 (%)	366 (97.0%)	379 (96.4%)	745 (96.5%)
6 weeks	RV1 (%)	348 (92.0%)	351 (89.3%)	699 (90.5%)
	OPV1 (%)	347 (92.0%)	351 (89.3%)	698 (90.4%)
	DTP – IPV- HiB – HepB (1) (%)	348 (92.0%)	351 (89.3%)	699 (90.5%)
	PCV1 (%)	348 (92.0%)	351 (89.3%)	699 (90.5%)
10 weeks	DTP – IPV- HiB – HepB (2) (%)	335 (88.4%)	340 (87.0%)	675 (87.4%)
14 weeks	RV2 (%)	324 (85.5%)	326 (83.0%)	650 (84.2%)
	DTP – IPV- HiB – HepB (3) (%)	324 (85.5%)	326 (83.0%)	650 (84.2%)
	PCV2 (%)	324 (85.5%)	321 (82.0%)	645 (83.5%)
9 months	MV1 (%)	311 (82.1%)	311 (79.1%)	622 (80.6%)
	PCV3 (%)	271 (72.0%)	269 (68.4%)	540 (70.0%)

1 Statistics presented: Frequency (%) for categorical variables and median (IQR) for continuous variables.

BCG - Bacillus Calmette- Guérin; OPV0 – birth dose Oral polio vaccine; RV1 – 1st dose Rotavirus; OPV1 – 1st dose Oral polio vaccine; DTP – IPV- HiB – HepB (1) – 1st dose Hepatitis B, Diphtheria, Pertussis, Tetanus, Haemophilus influenzae type B; PCV1 – 1st dose Pneumococcal Conjugate vaccine; DTP – IPV- HiB – HepB (2) – 2nd dose Hepatitis B, Diphtheria, Pertussis, Tetanus, Haemophilus influenzae type B; RV2 – 2nd dose Rotavirus; DTP – IPV- HiB – HepB (3) – 3rd dose Hepatitis B, Diphtheria, Pertussis, Tetanus, Haemophilus influenzae type B; PCV2 – 2nd dose Pneumococcal Conjugate; MV1 – 1st dose Measles; PC3 – 3rd dose Pneumococcal Conjugate; MV2 – 2nd dose Measles.

Table 6. shows an overview of vaccine coverage for the 772 infants included in the analysis. At birth, both infant groups presented uniformly high coverage rates for BCG and OPV0 vaccines (95.0% and 96.5%), with a few cases of unknown BCG and OPV0 vaccination status (n = 39 and n = 27) respectively. By 6 weeks, a slight decline in vaccination rates was observed, with RV1, OPV1, DTP – IPV- HiB – HepB (1), and PCV1 vaccines showing a 92.0% coverage in infants who are HUU infants versus 89.3%, a slightly lower coverage in infants who are HEU, with 73 cases of unreported vaccination status for all four vaccines. At 10 weeks, the DTP – IPV- HiB – HepB (2) coverage rate was 88.4% in infants who are HUU and 87.0% in infants who are HEU. Similarly, at 14 weeks, the coverage for RV2, DTP – IPV- HiB – HepB (3), and PCV2 dropped to 85.5% in infants who are HUU and to 83.0% in infants who are HEU. The coverage for MV1 and PCV3 at 9 months, showed a more pronounced decrease, with rates of 82.1% for MV1 in infants who are HUU, 79.1% for infants who are HEU, and 72.0% for PCV3 in infants who are HUU, 68.4% for infants who are HEU.

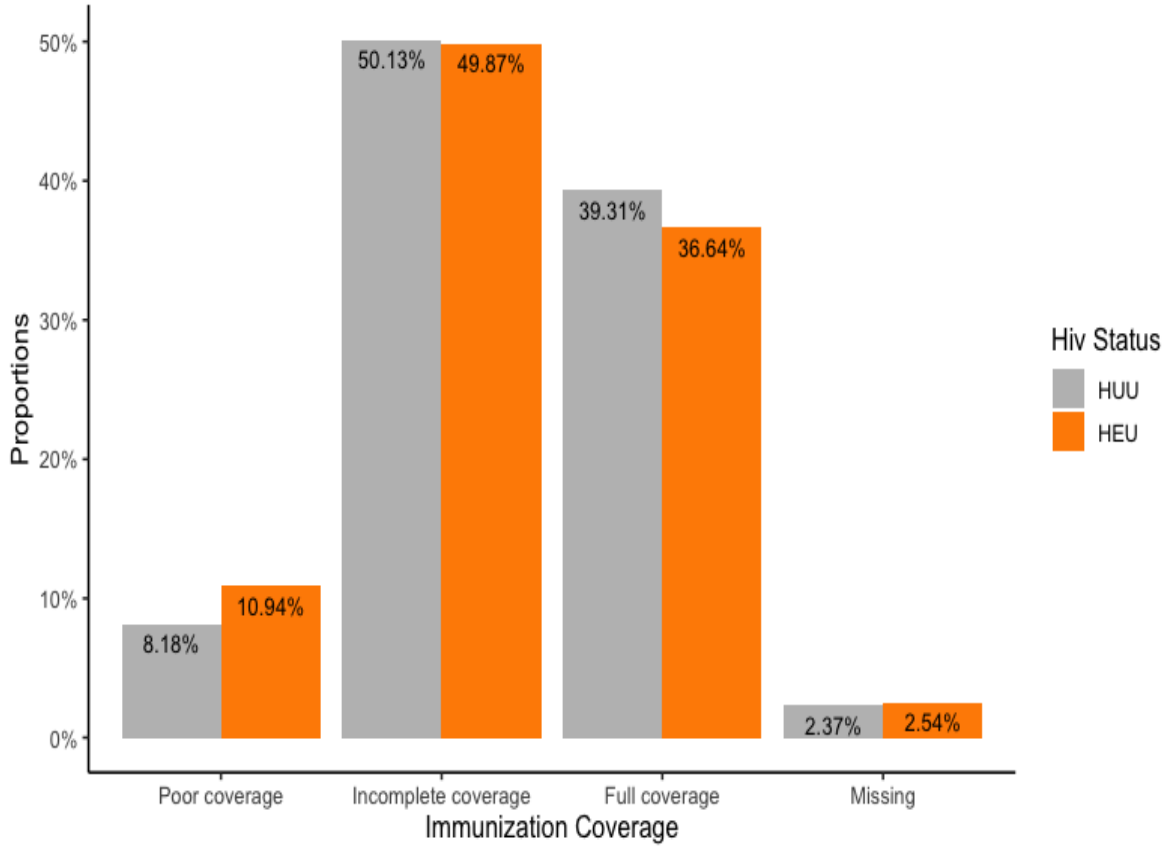

Figure 4. *Presents the vaccine coverage of infants who are HUU and HEU in their first year of life in Cape Town (N = 772)*[2].

Vaccine coverage did not significantly differ between infants who are HUU and infants who are HEU groups (p = 0.40) with between 36-39% of the cohort being fully vaccinated and only a small proportion of infants with missing immunization history (2.37% in the HUU group and 2.54% in the HEU group) See Figure.4.

[2] Full coverage refers to infants who received all the vaccines, incomplete coverage refers to infants who missed at least one vaccine dose and poor coverage refers to infants who received less than 50% of any doses of the routine vaccine per EPI-SA recommendations before 12 months of age. Missing refers to infants who had no vaccine information during the study period.

3.4 **Logistic Regression Analysis**

Table 7: Results of logistic regression model assessing the association between maternal and infant characteristics and non-prescription medicine (including TCAM and OTC).

Characteristic	Unadjusted OR [95% CI]	P-value	†Adjusted OR [95% CI]	P-value
HIV Status				
HUU	Ref		Ref	
HEU	0.45 [0.31– 0.65]	**<0.001***	0.45 [0.30 – 0.67]	**<0.001***
Maternal age (years)	0.98 [0.95 – 1.01]	0.19	0.99 [0.96 – 1.03]	0.84
Infant Sex				
Female	Ref		Ref	
Male	0.86 [0.60 – 1.22]	0.39	0.84 [0.58 – 1.21]	0.36
Gestational age				
Term	Ref		Ref	
Pre-term	1.15 [0.69 – 2.01]	0.61	1.61 [0.92 – 2.96]	0.11
Working status				
Employed	Ref		Ref	
Unemployed	0.92 [0.63 - 1.33]	0.67	0.81 [0.10 - 5.03]	0.84
Income status				
> R5000 per month	Ref		Ref	
< R5000 per month	0.63 [0.21 - 1.60]	0.37	0.63 [0.20 – 1.65]	0.38
No income reported	0.61 [0.21 - 1.49]	0.32	0.71 [0.09 - 6.73]	0.75
Maternal education				
Primary	Ref		Ref	
Secondary	2.26 [1.02- 4.74]	**0.04***	2.13 [0.93 – 4.69]	0.06
Post - secondary	1.65 [0.45 - 7.02]	0.47	0.99 [0.25 - 4.50]	0.99
Housing				
Formal house	Ref		Ref	
Shack/informal	0.91 [0.64 - 1.30]	0.62	0.92 [0.62 – 1.37]	0.69
Household crowding[a]				
0	Ref		Ref	
1 - 3	2.28 [0.89 – 5.47]	0.07	2.05 [0.74 – 5.29]	0.15
>= 3	1.85 [0.73 – 4.34]	0.17	1.52 [0.55 – 3.92]	0.39
Mode of delivery				
Emergency c-section	Ref		Ref	
NVD	1.09 [0.70 – 1.68]	0.70	1.30 [0.80 – 2.08]	0.27
Elective c-section	1.26 [0.68 – 2.39]	0.47	1.51 [0.79 – 2.96]	0.22
Self -reported Breastfeeding				
No	Ref		Ref	
Yes	2.31 [1.51 – 3.51]	**<0.001***	2.46 [1.56 – 3.83]	**<0.001***

CI – Confidence interval; OR – Odds Ratio; HEU – HIV-exposed-uninfected; HUU – HIV-unexposed-uninfected; NVD – Natural vaginal delivery; C-section – Caesarean section.

a The numbers represent the number of people residing within the household.

†Adjusted variables for the multivariable analysis.

*Significant at $p \leq 0.05$.

As can be seen from the table (above), the association between various maternal, infant, and socio-economic characteristics with OTC and TCAM medicine use was analyzed using logistic regression, with results reported as unadjusted and adjusted odds ratios (ORs) with 95% CI. In the unadjusted model, logistic regression analysis revealed statistically significant associations between HIV status, maternal education, and self-reported breastfeeding practices with OTC and TCAM while other factors showed no statistically significant impact. Infants who are HEU were reported to be significantly less likely to use OTC and TCAM medicine compared to infants who were HUU, with an unadjusted odds ratio (uOR) of 0.45 (95% CI 0.31– 0.65; *p-value* < 0.001). This trend persisted in the adjusted model, with an aOR of 0.45 (95% CI 0.30 – 0.67; $p < 0.001$). Infants whose mothers had attended secondary schooling (uOR 2.26, 95% CI 1.02 – 4.74; $p = 0.04$) were statistically associated with reporting OTC and TCAM medicine use compared to those whose mothers had attended primary school in the unadjusted model, which was not observed in the adjusted model (Table 7). Infants who were breastfed had statistically significantly higher odds of OTC and TCAM medicine use (uOR 2.31, 95% CI 1.51 – 3.51; $p < 0.001$) compared to those who were not breastfed. Similarly, with the adjusted model, infants who were breastfed compared to infants who were not breastfed had 2.46 times the odds of OTC and TCAM medication use, this difference was statistically significant (95% CI 1.56 – 3.83; $p < 0.001$) (Table 7).

Table 8. Results of logistic regression model assessing the association between maternal and infant characteristics and non-ARV prescription medicine.

Characteristic	Unadjusted OR [95% CI]	P-value	†Adjusted OR. [95% CI]	P-value
HIV Status				
HUU	Ref		Ref	
HEU	6.34 [4.64 – 8.74]	**<0.001***	6.52 [4.66 – 9.21]	**<0.001***
Maternal age (years)	1.06 [1.03 – 1.08]	**<0.001***	1.02 [0.99 – 1.05]	0.14
Infant Sex				
Female	Ref		Ref	
Male	0.94 [0.71 – 1.25]	0.67	0.89 [0.65 – 1.24]	0.51
Gestational age				
Term	Ref		Ref	
Pre-term	1.05 [0.69 – 1.59]	0.81	0.75 [0.46 – 1.21]	0.24
Working status				
Employed	Ref		Ref	
Unemployed	0.88 [0.65 – 1.19]	0.40	1.37 [0.27 – 6.79]	0.70
Income status				
> R5000 per month	Ref		Ref	
< R5000 per month	1.45 [0.71 – 3.03]	0.32	1.31 [0.58 – 3.03]	0.52
No income reported	1.21 [0.61 – 2.47]	0.59	0.96 [0.17 – 5.81]	0.97
Maternal education				
Primary	Ref		Ref	
Secondary	0.85 [0.42 – 1.78]	0.67	1.04 [0.45 – 2.36]	0.93
Post - secondary	0.64 [1.17 – 2.16]	0.48	1.40 [0.32 – 5.68]	0.65
Housing				
Formal house	Ref		Ref	
Shack/informal dwelling	0.74 [0.55 – 0.98]	**0.04***	0.58 [0.41 – 0.82]	**<0.001***
Household crowding[a]				
0	Ref		Ref	
1 – 3	0.72 [0.31 – 1.68]	0.44	0.74 [0.28 – 1.89]	0.52
>= 3	0.85 [0.37 – 1.97]	0.71	0.79 [0.30 – 2.03]	0.62
Mode of delivery				
Emergency c-section	Ref		Ref	
NVD	1.08 [0.75– 1.55]	0.68	0.95 [0.63 – 1.45]	0.82
Elective c-section	0.99 [0.61 – 1.63]	0.99	0.87 [0.49 – 1.51]	0.61
Self -reported Breastfeeding				
No	Ref		Ref	
Yes	0.86 [0.59 – 1.27]	0.45	0.94 [0.61 – 1.46]	0.80

CI – Confidence interval; OR – Odds Ratio; HEU – HIV-exposed-uninfected; HUU – HIV-unexposed-uninfected; NVD – Natural vaginal delivery; C-section – Caesarean section.

a The numbers represent the number of people residing within the household.

†Adjusted variables for the multivariable analysis.

*Significant at $p \leq 0.05$.

Table 8. shows the same analyses using prescription without ARVs as the outcome. In the unadjusted model, logistic results showed significant associations between HIV status, housing, and maternal age with non–ARV prescriptions, while other factors demonstrated no statistically significant impact. HEU infants were 6.34 times more likely to be on a non–ARV prescription compared to HUU infants in the unadjusted model (95% CI 4.64 – 8.74; p <0.001). In the adjusted model, HEU infants had 6.52 (95% CI 4.46 – 9.21; p <0.001) times the odds of being on non–ARV prescription medicine compared to HUU infants holding all other variables constant (Table 8). In addition, the unadjusted model also indicated an association between maternal age and non–ARV prescription medicine use (uOR for a one-year increase in age, 1.06; 95% CI: 1.03 – 1.08; p < 0.001), which was not observed in the adjusted model (Table 8). Mothers of infants who lived in informal dwellings were 0.74 times more likely to be associated with non–ARV prescription medicine compared to mothers of infants who resided in formal dwellings in the unadjusted model (95% CI 0.55 – 0.98; p = 0.04). While in the adjusted model, mothers of infants who resided in informal dwellings compared to mothers of infants who resided in formal dwellings had 0.58 times the odds of reporting non-prescription medicine exposure, this difference was statistically significant (95% CI 0.41 – 0.82; p < 0.001) (Table 8).

Table 9. Results of logistic regression models assessing the association between maternal and infant characteristics and full immunization for all routine vaccinations.

Characteristic	Unadjusted OR [95% CI]	P-value	†Adjusted OR [95% CI]	P-value
HIV Status				
HUU	Ref		Ref	
HEU	0.89 [0.67 – 1.19]	0.44	0.87 [0.64 – 1.18]	0.38
Maternal age (years)	1.00 [0.98 – 1.03]	0.77	1.01 [0.98 – 1.04]	0.47
Infant Sex				
Male	Ref		Ref	
Female	1.26 [0.94 – 1.69]	0.12	1.27 [0.95 – 1.71]	0.11
Working status				
Employed	Ref		Ref	
Unemployed	1.04 [0.76 – 1.42]	0.81	0.49 [0.10 – 2.06]	0.34
Income status				
> R5000 per month	Ref		Ref	
< R5000 per month	1.03 [0.50 – 2.20]	0.93	1.13 [0.54 – 2.46]	0.74
No income reported	1.11 [0.56 – 2.30]	0.77	2.41 [0.49 – 13.65]	0.29
Maternal education				
Primary	Ref		Ref	
Secondary	1.12 [0.54 – 2.45]	0.77	1.09 [0.51 – 2.43]	0.83
Post - secondary	1.09 [0.30 – 3.79]	0.89	1.05 [0.28 – 3.79]	0.94
Housing				
Formal house	Ref		Ref	
Shack/informal dwelling	0.84 [0.62 – 1.12]	0.23	0.86 [0.63 – 1.19]	0.37
Number of children				
0	Ref		Ref	
1 - 3	1.05 [0.77 – 1.41]	0.77	0.98 [0.69 – 1.41]	0.91
>= 3	0.77 [0.29 – 1.87]	0.58	0.67 [0.23 – 1.76]	0.43
Household crowding[a]				
0	Ref		Ref	
1 - 3	1.76 [0.71 – 4.96]	0.25	1.63 [0.65 – 4.70]	0.33
>= 3	1.95 [0.80 – 5.46]	0.17	1.73 [0.68 – 5.05]	0.27
Self -reported Breastfeeding				
No	Ref		Ref	
Yes	0.97 [0.66 – 1.44]	0.90	0.97 [0.66 – 1.45]	0.88

CI – Confidence interval; OR – Odds Ratio; HEU – HIV-exposed-uninfected; HUU – HIV-unexposed-uninfected.

a The numbers represent the number of people residing within the household.

†Adjusted variables for the multivariable analysis.

*Significant at $p \leq 0.05$.

Table 9. shows the results from both the unadjusted and adjusted models, indicating no significant associations between maternal and infant characteristics and full vaccination coverage. Although, infant sex, maternal education, and income status, household crowding had the strongest effect on vaccine coverage (Table 9). Female infants compared to male infants were 1.27 times the odds of being fully immunized in their first year of life in the adjusted model (95% CI 0.95 – 1.71). After adjusting for other factors, infants whose mothers had only a secondary level of education and higher (post-secondary) level of education were 1.12 (95% CI 0.54 – 2.45) and 1.09 (95% CI 0.54 – 2.46) times the odds of being fully immunized compared to those whose mothers had only primary level of education. Similarly, infants whose mothers had no income and those earning less than R5000 were 2.41(95% CI 0.49–13.65) and 1.13 (95% CI 0.54 – 2.46) times the odds of being fully immunized than those whose mothers earned more than R5000. Furthermore, households with 3 occupants and those with more than 3 occupants were 1.63 (95% CI 0.65 – 4.70) and 1.73 (95% CI 0.68 – 5.05) times the odds of having fully immunized infants compared to households with just one occupant, after adjusting for other factors.

4. **Discussion**

4.1 **Patterns of medication use among infants who are HEU and HUU**

This study was the first to describe and compare medication consumption patterns, including vaccine coverage, among infants who are HEU and HUU during their first year of life in South Africa. It also explored potential associations between maternal demographic factors and infant-specific factors with medication utilization, including vaccination coverage, among both HEU and HUU infants. In this analysis, four main findings emerged. First, frequent use of medicine was commonplace among infants who are HEU and HUU in this cohort with a median of 5 medicines in their first year of life and with 66.2% receiving 4 or more medications. Second, infants who are HEU are known to have higher infectious morbidity and mortality compared to infants who are HUU, and this was reflected in the higher rate of use of medicines, including ARV prophylaxis drugs and antibiotics used to treat and prevent infectious diseases. Third, mothers of HUU infants were more likely to report OTC and TCAM use in their infants than their HEU counterparts and were more likely to report the use of medicines that they could not identify compared to mothers of HEU infants. Lastly, vaccine coverage was similar between the two groups, but this population had an alarming drop in vaccination coverage over the year that needs further investigation and response.

Some of these findings resonated well with previous research findings [5, 13, 22, 24, 28, 31, 41], suggesting that infants who are HEU may have had higher rates of medical conditions, particularly infectious diseases, thus requiring medication that reflected the unique healthcare requirements associated with infants exposed to HIV in utero. Consistent with this, our findings aligned with other studies and revealed a median of 3 medicines prescribed per infant (5 medicines HEU vs. 2 medicines HUU) [40, 48]. However, this was higher than the rates seen in a few high-income countries, indicating that paediatric patients in low- and middle-income countries (LMICs) may have been exposed to a high number of medicines, which could have led to an increased risk of adverse drug reactions (ADR), drug interactions, and medication errors [29, 44, 47-48, 54]. Infants who are HEU have increased hospitalization, morbidity, and mortality risk compared to HUU infants, and this was more pronounced in LMICs [15, 18, 26, 33]. A study by Anderson *et al*. using the same cohort data and focusing on infectious-caused hospitalization found that HEU infants had twice the risk of all-cause and infectious–cause hospitalization compared to HUU infants [18]. This heightened risk of hospitalization likely contributed to the higher medication use in HEU infants, as mothers may not have been privy to all medications prescribed to their infants during hospitalization.

In our study, the prevalence of prescribed medicine with and without ARVS was 61.3% and 44.6 %, respectively. The frequently used class of drugs as prescribed medicine was antivirals (51%) followed by antibiotics (46.0%). This finding was not surprising, considering that the ARV NVP was routinely prescribed with or without AZT to prevent vertical transmission of HIV in infants who are HEU. The difference in prescription medicine use persisted even after excluding ARVs (65.4% HEU vs. 23.0% HUU; p <0.01), with anti-infectives (ATC J) contributing to the increased use among HEU infants who are known to be more

susceptible to infections during infancy. Other studies reinforced this idea by revealing that anti-infectives for systemic use were the most frequently used medicine in children [37, 40, 48, 53]. Moreover, antibacterials were more frequently used in HEU populations than HUU infants (66.2% vs. 23.2%; p <0.001). This finding aligned with a study conducted in Malawi by Ewing *et al.* [41], which revealed that 80% of infants who are HEU received more than one prescription during their first year of life. This high rate of antibiotic use in infants who are HEU highlighted their complex medical needs, often requiring antibiotic treatment compared to their HUU peers [41, 51]. The most commonly used antibiotic in our study was CTX prophylaxis indicated for preventing opportunistic infections and severe bacterial infections, in infants who are HEU [36]. However, a recent review by Wedderburn *et al.* found no clinical benefit of CTX prophylaxis in these infants, except for malaria prevention, emphasizing the need to re-evaluate this treatment practice due to its contribution to increasing antibiotic resistance [36]. While early-life antibiotic use in infants provided immediate benefits, monitoring antibiotic prescriptions was crucial because of their potential risks, including microbiome disruption that resulted in longer-term adverse health effects in exposed infants and contributed to antimicrobial resistance (AMR) [39, 41, 48, 52-54].

Overall, prescription usage was high among the study's participants, and our analysis focused on self-reported medicine use. This approach likely underestimated prescription medicine use due to incomplete reporting by mothers or caregivers, particularly in cases where infants were hospitalized for care. This possibility was further supported by the fact that mothers or caregivers of infants were often only able to recall the names of some medicines during the follow-up visits. A study on the same cohort of mothers by Van der Hoven *et al.* found that self-reporting was a less useful data source than provincial electronic dispensing records for obtaining information on maternal prescription medicine use [28]. This would likely be the same when reporting the use of medicines in their infants.

As for non-prescription medicine, our study showed mothers or caregivers reported high rates of OTC use in their infants (74.6%), particularly in the HUU group compared to HEU. However, the rate of OTC use was higher than that reported in a study conducted in São Paulo (56.6%) and a study conducted in Turkey (63.5%) [47], but similar to that reported in a study conducted among infants before the age of 6 months in South Africa (75.4%) [44] and a 2020 study in the Democratic Republic of Congo (95.8%), which reported high rates of self-medication among mothers regarding their children [50]. Surprisingly, this high rate of OTC use among paediatric populations could be attributed to mothers and caregivers often playing an important role in self-medicating their infants [38, 43, 45, 50, 53]. Factors such as affordability compared to clinic and hospital visits, and lack of trust in the healthcare system contributed to mothers' and caregivers' reliance on OTC medications [38, 49-50, 53]. Moreover, the readily available OTC medications that did not require a doctor's prescription contributed to the widespread use of these medications, reinforcing the importance of public health interventions to rationalize this practice [43-44, 47-48]. These interventions should educate pregnant women, mothers and women of childbearing age on the rational and safe use of medicines.

In our study, the most commonly used OTC medications among HUU infants included analgesics such as paracetamol and aspirin (38.6%), emollients and protectants (13.9%), cough and cold medicines (10.1%) and antidiarrheals (7.5%). Our findings were consistent with Ahwinahwi *et al*., who reported paracetamol as the most frequently used medicine by mothers for their children (30.1%), followed by various other medications used for common paediatric illnesses [54].

Overall, TCAM use was relatively high, with only 21.4% (16.8% HEU vs. 26.1% HUU) of infants receiving such treatment. The most commonly used TCAM was gripe water (8.2%). Similar results were reported elsewhere in a study by Bland *et al.,* which found that the most common TCAM was gripe water mainly for 'colic' and/or 'wind' in a cohort of infants in their first 3 months of life in rural KwaZulu Natal [49]. Peltzer *et al*. also reported that gripe water was the most frequently used TCAM, followed by OTC, rooibos tea, galactagogue, and lastly, traditional and herbal medicine [56]. Interestingly, a higher prevalence of TCAM use was observed among infants who are HUU compared to infants who are HEU, which could be due to various reasons, including increased counselling to women living with HIV on ART on the importance of medication adherence, the risk of drug-drug interactions and potential adverse effects of medicines. It was also possible that the lower rate of reporting of OTC and TCAM was due to greater fears of the healthcare providers' disapproval of concurrent use of such treatments with ART [55-57]. This latter theory aligned with previous studies that reported a high prevalence of TCAM and OTC users not disclosing their use, citing concerns about negative attitudes from healthcare providers and fears of receiving substandard care as major contributing factors [35, 55-58]. While previous studies highlighted the prevalence of TCAM and OTC users not disclosing their use, the disparity in reported TCAM use between HEU and HUU infants warranted further investigation to determine whether it was due to actual differences in usage or if mothers of HEU infants were less likely to report TCAM use out of fear of reprimand. This reluctance could have stemmed from concerns regarding the concurrent use of ARVs by their infants or the fact that mothers of HEU infants, being more aware of ARV safety and potential drug interactions, exercised greater caution when administering TCAM to their infants.

The reported use of traditional medicines was extremely low; however, treatments like 'umoya' (spiritual air) and 'umthombothi' (inner bark or wood [60]) suggested some reliance on culturally specific practices rather than conventional medicine. This correlates with similar studies that found Africans, including South Africans, used traditional healing practices, primarily traditional medicine, using herbs as part of their primary healthcare [23, 55-60]. However, data on the safety, composition, dosage, efficacy, contraindications, interactions, and risks of TMs was lacking, particularly when acquired through informal healthcare sources [23, 56]. These findings shed light on the prevalence and types of traditional and home-based remedies within this population. Although most studies [55-56, 58-60] reported TM used by pregnant women, their findings identified differences in self-reported patterns of TM use in infants of PWLOHIV compared to PWLHIV, with higher usage observed among PWLOHIV.

In our study, almost all infants, except 39 (5.1%), were reported to have been exposed to at least one medicine during their first year of life. Interestingly, we found that infants who are HUU were more likely to be exposed to medications that could not be identified by their mothers or caregivers (36.9% vs. 29.3%; p <0.001) compared to their HEU counterparts. This difference in medication exposure recall between the two groups indicated the importance of addressing gaps in medication literacy and caution in medication use among mothers regardless of HIV status. Moreover, the combined findings of increased OTC use and the mothers' inability to recall the medicines they gave to their infants among HUU infants, compared to their HEU counterparts, suggested a different level of medication literacy and raised concerns about safe medication use among mothers living without HIV as well as mothers living with HIV. This supported the findings presented in *Table 7*, which showed a significant association between the level of maternal education and non-prescription (including OTC and TCAM) medicine usage for infants. More specifically, mothers with a secondary school education were more likely to self-medicate their infants compared to mothers with a tertiary education.

The study results revealed a significant difference in breastfeeding practices between the two groups (p < 0.001), which aligned with previous studies that found infants who are HEU and HUU have different infant feeding experiences [6, 8 - 9, 11, 17, 18,- 20]. With the introduction of universal ART, breastfeeding likely became ubiquitous, making it crucial to consider the potential transfer of medications to infants through breast milk. While there was extensive data on ARVs administered to lactating mothers that could be detected in breast milk, the full extent of transfer to the infant and its impact on their health was not well understood due to small limited studies [11, 21, 27]. However, for this analysis, we did not analyze medicine exposure through breast milk due to poor reporting and lack of information, highlighting the need for further research in this area.

We also observed an association between prescribed medicine without ARV in infants who are HEU, maternal age, and housing. Maternal age showed a positive association with prescription medicine use, which may be an artefact of older maternal age in PWLHIV compared to PWLOHIV. However, further investigation was required to fully understand whether maternal age increased the risk of prescription medicine use in infants in South Africa. Notably, infants living in informal housing were more likely to be exposed to prescription medicines compared to infants living in formal housing. The reasons for this were unclear, but it was plausible since housing served as a proxy for socioeconomic status, suggesting that poverty was a significant driver of poor infant health outcomes and reduced access to prescribed medications.

4.2 **Vaccine coverage among infants who are HEU and HUU**

Vaccine coverage among infants who were HEU and HUU in this study appeared to be suboptimal, particularly at 9 months and 12 months. Our findings showed that only 38% of all the infants received the complete complement of recommended vaccines in the first year of life which falls below the Western Cape (82.7 %)

and national estimates (76.9%) for under-1-year-olds for 2017/2018 [63]. These findings may be the result of cohort attrition rather than non-vaccination alone. We focused our analysis on vaccinations administered until 9 months, as it was possible that mother-infant pairs seen at 12 months had not yet gone for their 12-month vaccinations at the time of the study visit. The combination of losses to follow-up and non-vaccination at the time of the study visit may explain the vaccine coverage drop in vaccination coverage of both infants who are HEU and HUU at 12 months. However, this study found no meaningful differences in vaccination coverage at each of the visits between HEU and HUU infant cohorts. Our finding concurred with recent research that found irregularities in the 12 months of vaccine coverage, which may have been attributed to missing information on the vaccine coverage, such as lost-to-follow-up and/or incomplete vaccination for the infants or issues with vaccine retention or completion [66, 74].

Furthermore, the study revealed that the coverage of early vaccines administered closer to birth was high for both infant groups. These included BCG and OPV for which coverage was 95.0% [65-71, 73-74]. However, the coverage rates then dropped for subsequent vaccine doses; for example, at 14 weeks, 85.0 % of HUU and 83.0% of HEU infants received DTP – IPV- HiB – HepB (3), while at 9 months, the coverage rate for PCV3 further dropped to 70.0%. High vaccination coverage was particularly important among HEU infants as they are known to have a suboptimal response to vaccines, contributing to an increased infectious burden [61]. Unlike this study, a study conducted by Mast TC *et al*. found higher odds of incomplete vaccine among HEU infants compared to HUU infants [65, 68]. However, the proportion of unvaccinated infants in both groups, a concern in any EPI program, was low, with only 2.5% of infants not reporting any vaccine use (Figure 4). The findings in this study would need to be confirmed or refuted with a more robust study design involving a more representative sample and better recording of vaccination exposures.

Sociodemographic, obstetric, and infant factors were not predictors for vaccine coverage. Interestingly, our results did not align with several previous studies that reported risk factors that were previously associated with full vaccine coverage, including socioeconomic variables (maternal age and education), number of siblings, breastfeeding, and infant gender between infants who are HEU and HUU [65-71, 74]; this may be because our study was conducted at only one health facility, which could have limited the generalizability of the findings. However, our results were also consistent with the findings of other studies that reported that maternal age, educational attainment, employment, and other factors were not significantly associated with full vaccine coverage for any of the vaccines studied [67-68]. In contrast, some studies reported a positive association between maternal education, age, and childhood vaccination coverage [67, 69]. Our findings based on this small study suggested a divergence from this trend [68, 70, 74] and emphasized the need for further investigation to better understand the complex interactions of factors influencing vaccine coverage in different settings.

4.3 **Strengths and limitations of the study**

Although our study has many strengths, our results should be interpreted within the limitations of the study design. Infants who are HEU and HUU were enrolled simultaneously from the same community, enabling the comparison of shared socio-behavioural and economic traits between the two groups, as well as temporal assessments. The study and its data analysis approach made efforts to minimize confounding by referring to the literature to identify covariates potentially linked to both independent and dependent variables. However, our study had some limitations. The generalizability of medication usage and vaccination coverage is limited to settings with similar characteristics, thereby limiting broader applicability. There may have been recall bias between mothers of infants born HEU and HUU influenced by differences in medication literacy; mothers of infants born HEU may be more reluctant to report medication use in their infants or avoid non-essential medicine use, especially TCAM and OTC use, for fear of stigma or reprimand from health professionals or fear of unnecessarily exposing their child to medication-related harm. This recall bias may have attenuated the actual difference in medication use between the HEU and HUU infants. Reliance on self-reported data, particularly maternal recall of medication proportions, introduces potential reporting bias. Augmenting self-reports with other sources such as pharmacy records can enhance data accuracy. Another limitation may have been potential survivor bias, where infants lost to follow-up may have different medicine use patterns however, performing sensitivity analyses can help address the impact of this bias by including the infants who were lost to follow-up.

5. **Conclusion**

In conclusion, this study showed the importance of understanding differences in medication use and vaccine coverage among infants unexposed and exposed to HIV in utero and the need for tailored interventions to address their unique healthcare needs. Medication illiteracy and self-medication use appeared to be more prevalent among mothers of HUU infants, highlighting an important gap in health education in this mother-infant population. Addressing differences in medication use and vaccine coverage among HEU and HUU infants requires a multifaceted approach that considers socioeconomic status, healthcare access, maternal health, and cultural and health system factors, including pharmacovigilance surveillance systems. Our findings also reinforced the urgent need to explore medication use patterns, especially self-medication in infants who are HUU and the growing population of infants who are HEU in different settings, particularly in countries with high HIV prevalence such as South Africa. This will inform the development of targeted interventions and strategies aimed at preventing and minimizing the need for self-medication, which is a public health concern for both infants who are HEU and HUU.

6. **References**

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C. APPENDICES

Appendix A: Consent Forms

B-POSITIVE SENTINEL COHORT – INFANT DIAGNOSTIC COHORT INFORMATION AND INFORMED CONSENT

YOU ARE CURRENTLY ENROLLED IN THE B-POSITIVE COHORT STUDY. NOW THAT YOU HAVE DELIVERED YOUR BABY WE WOULD LIKE TO INVITE YOU AND YOUR BABY TO CONTINUE TO PARTICIPATE IN THE STUDY. THIS INFORMATION AND CONSENT FORM CONCERNS YOUR BABY'S ENROLMENT IN THE STUDY.

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 and their infants.

You are being asked to take part in this study because were enrolled in the earlier parts of this study and you have recently given birth. The purpose of this consent form is to give you information to help you decide if you and your baby want to continue in the next part of the study.

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

If you agree to take part, you will come in for at least **4 study visits**. These visits will take place today while you are in the clinic (after 7 days' post delivery), and then when your baby is about 6 weeks, 6 months and 12 months old. All of these study visits are separate from the usual clinic visits that you will have for your baby's health. Study visits can be arranged for dates and times that suit you. Each visit will take about 1 hour: 30 minutes. We may also speak to you over the phone in between these visits.

At these visits you will do the following:

- Answer questions about the use of any medicines and remedies
- Answer questions about your baby's health, feeding practices and infant health care
- Answer questions about any other health concerns
- Answer questions to assess whether you are stressed or unhappy (depressed)
- Discuss some aspects of your personal relationships
- Answer questions about the care you and your baby are receiving
- Have your baby's weight and height measured

Review of medical records

As part of this study, we will also be looking at and taking information from your medical, and laboratory records. We will also be looking at and taking information from the health care records of your baby (such as the Road to Health Card and details of any hospital visits). From these records, we are interested in learning

about the health care you receive as well as information about 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.

Other contact
As part of participating, we may ring you on your cellphone or send you reminder SMS's regarding your appointments. If we do this, we will not mention any aspect of your health or health care. We will simply refer to the "Appointment for you and your baby at the Gugulethu CHC".

Contact for future study
After the completion of the last study visit, we will speak to you again to see if 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 services of 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.

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.

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 or your baby receives at this or any other health facility.

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

Associate Professor Andrew Boulle
School of Public Health and Family Medicine
Faculty of Health Sciences
University of Cape Town
Tel 021 406-6715
Email: Andrew.Boulle@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 my baby's participation in this research study and know that I may withdraw at any time. My and my baby's 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 and my baby's medical records at this hospital or another hospital if necessary for this study. All 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 to be interviewed.

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!

B-POSITIVE SENTINEL COHORT – INFANT DIAGNOSTIC COHORT INFORMATION AND INFORMED CONSENT

NGOKU UBHALISILE KWI THE B-POSITIVE COHORT STUDY. NJENGOKO UMBELEKILE UMNTWANA WAKHO SIYAKUMEMA UKUBA WENA NOMNTWANA WAKHO NIQHUBELEKE NITHATHA INXAXHEBA KUPHANDO. OLU LWAZI KUNYE NE PHEPHA MVUME ZIQONDENE NOBHALISO LOMNTWANA WAKHO KUPHANDO

YINTONI INJONGO YOLUPHANDO?

Singabaphandi base Dyunivesithi yase Kapa kwaye siyakucela ukuba uthathe inxaxheba kuphando esiluqhuba e Gugulethu kwicala lokubelekisa - Midwife Obstetric Unit (MOU) kunye namaziko abo abathi bathumela kuwo. Injongo yoluphando kukuqonda nokuhlola impilo yamakhosikazi akhululelweyo nendlela abakhathaleleke ngayo kumaziko ezempilo ngexesha abakhulelewe ngalo kunye nasemva kokuba bebabelekile abantwana babo. Iquka impilo yengqondo neyomzimba kunye nawo nawaphi na amayeza kunye namachiza athe asetyenziswa ngexesha lokukhulelwa.

Siyayazi ukuba ibalulekile kwimpilo yabo kananjalo nakubantwana babo, lamakhosikazi akhulelweyo bafumana lonke ukhathalelo kunye nonyango abalufunayo ngexesha lokukhulelwa kwabo kunye nasemva kokuba bebelekile. Ulwazi olufundwe koluphando luyakusinceda ukuphuhlisa inkonzo zempilo zamakhosikazi akhulelweyo kunye nentsana zabo.

Uyacelwa ukuba uthathe inxaxheba koluphando kuba wabhalisa ngaphambili njengenxalenye yophando kwaye ubeleke kutshanje. Injongo yeliphepha-mvume kukunika ulwazi nokunceda ukuba uthathe isigqibo sokuba uyafuna na wena kunye nomntwana wakho niqhubeleke kwisigaba esizayo sophando.

KUMELE NDENZE NTONI UKUBA NDIYAVUMA UKUTHATHA INXAXHEBA?

Ukuba uyavuma ukuthatha inxaxheba, uyakuza ukuyokuma kwisine sotyelelo lophando. Elokuqala luyakuba namhlanje ngelixesha useklinikhi, kuphinde kubekho olunye xa umntwana wakho eneveki ezintandathu, inyanga ezintandathu kunye nenyanga ezilishumi elinesibini ubudala. Onke lamatyelelo ophando ohlukile kumatyelelo akho esiqhelo aseklinikhi ozakubanawo malunga nempilo yomntwana wakho. Amatyelelo ophando angahlengahlengiswa ngentsuku kunye namaxesha athandwa nguwe. Utyelelo ngalunye luyakuthatha malunga nemizuzu engamashumi amathathu ukuya kwimizuzu engamashumi amathandathu. Singathetha nawe emnxebeni phakathi nendawo kulamatyelelo.
Kulamatyelelo uyakwenza oku kulandelayo:

- Uyakuphendula imibuzo malunga nokusebenzisa nawaphi na amayeza kunye namachiza
- Uyakuphendula imibuzo malunga nempilo yomntwana wakho, iindlela omtyisa ngazo kunye nokhathalelo lwempilo yentsana.
- Uyakuphendula imibuzo malunga nayo nayiphi na eminye imiba yezempilo
- Uyakuphendula imibuzo ukuhlola ukuba awunaxinzelelo na okanye ukungonwabi
- Ingxoxo malunga nemibandela yobudlelwane bakho buqu
- Uyakuphendula imibuzo malunga nokhathalelo olufumanayo wena nomntwana wakho
- Kuyakuthathwa ubunzima nobude bomntwana wakho

Ukuhlolwa kwamarekhodi empilo
Njengenxalenye yophando, sizokujonga kwaye sizokuthatha ulwazi lwamayeza akho, kunye namarekhodi ase lebhu. Siyakujonga kwaye sizokuthatha ulwazi kumarekhodi okhathalelo lwempilo yomntwana wakho (njenge the Road to Health Card kunye nenkcukacha zalo naluphi na utyelelo lwasesibhedlela). Kulamarekhodi, sinomdla wokufunda malunga nokhathalelo lwempilo othe walufumana kunye nolwazi malunga nempilo yomntwana wakho. Yonke ingqokelela yolwazi esithe sayihlaziya kwaye sayiphononononga iyimfihlelo kwaye akukho magama abathathi nxaxheba ashicilelweyo kwimiqulu yophando.

Ulandelelo lotyelelo oluphosakeleyo
Uyakucelwa ukuba unikezele ngenkcukacha zakho ukuze sikwazi ukuqhagamshelena nawe ngexesha lophando. Abasebenzi bophando bayakuthetha nawe malunga nendlela engcono yokuqhagamshelana nawe. Kwisiganeko othe waphosa ngaso olunye utyelelo olucwangcisiweyo lophando, umsebenzi wophando uyakuqhagamshelana nawe khona ukuze afumane olunye usuku nexesha lokugqibezela utyelelo lwakho. Ukuba uthe waphinda-phinda uphosa utyelelo lwakho lophando okanye abasebenzi abakwazi ukuqhagamshelana nawe xa besebenzisa ulwazi othe wanikezela ngalo, kuyakubayimfuneko ukuba bakutyelele ekhaya khona ukuze batshintshe usuku oluphosileyo lophando.

Olunye uqhagamshelwano
Njengamthathi nxaxheba, singakutsalela umnxeba kumnxeba wakho ophathwayo okanye sikuthumelele uyalezo okukhumbuza ngedinga lakho. Ukuba senze oku, asiyi kuchaza nayo nayiphi kwimiba yempilo yakho okanye ukhathelelo lwempilo yakho. Siyakugqithisa nje kwi umyalezo we “Dinga lakho kunye nelomntwana wakho lase Gugulethu CHC”

Uqhagamshelwano lophando olulandelayo
Emva kokugqiba utyelelo lokugqibela kuphando, siyakuthetha nawe kwakhona sijonga ukuba ungavuya na ukuba ubeyinxalenye yophando lwexesha elizayo.

YEYIPHI IMINGCIPHEKO ELINDELEKILEYO?
Ungaziva ungakhululekanga kweminye imibuzo ebuzwa ngesiqu sakho. Ungala ukuphendula nayiphi na imibuzo ongafuniyo ukuyiphendula. Kukho umngcipheko ekwabelaneni ngolwazi lwakho buqu kunye nolwamayeza. Siyakulugcina ngenkathalo nangemfihlo kangangoko sinako ulwazi lwakho.

ZEZIPHI INZUZO EZILINDELEKILEYO?
Akukho nzuzo zibhekise ngqo kuwe xa uthatha inxaxheba koluphando. Ulwazi olufumaneke koluphando lunganceda ekuphuhliseni amaziko okukhathalelwa kwezempilo kumakhosikazi akhulelweyo nabantwana babo eKapa, kwiphondo lase Ntshona Koloni nase Mzantsi Afrika jikelele.

ZEZIPHI INDLELA ZOKUTHATHA INXAXHEBA?
Indlela yokuthatha inxaxheba koluphando kukuqhubeleka njengesiqhelo nokhathalelo lwempilo yakho. Ukuba ugqibe ekubeni ungathathi nxaxheba koluphando, ukhathalelo lwakho lwempilo lwesiqhelo alusayi kutshintsha nangayiphi na indlela.

KUTHIWANI NGEMFIHLELO?
Ukuba uyavuma ukuthatha inxaxheba, lonke ulwazi oluqokelelwe ngexesha lophando luyakugcinwa luyimfihlo. Igama lakho alisayi kubhalwa kwimpepha zophando kwaye aliyikusetyenziswa ngokunxulumene nalo naluphi na ulwazi okanye incindi eziqokelewa elebhu njengenxalenye yophando.

Zonke ingcombolo zophando ziyakugcinwa kwikhabhathi etshixwayo. Ngabasebenzi kunye nabantu ababandakanyekayo kwinkqubo yophendlo abayakufikelela kwezi ngcombolo. Bonke abasebenzi abayinxalenye kwingqokelela yolwazi kunye nabaphathi bayakufumana uqeqesho olukhethekileyo kwimfihlelo.

Kuzo zona ezinkqubo ukuba umsebenzi wophando uthe wafumanisa ukuba usemngciphekweni wokuzonzakalisa okanye omnye umntu okanye uhlukumezo lomntwana/okanye ukulahlwa kwakhe, umsebenzi wophando uyakwazisa abasemagunyeni.

IKHONA INTO ENDIZAKUYINIKWA NGOKUTHATHA KWAM INXAXHEBA?
Akukho ntlawulo yokuthatha inxaxheba. Ekupheleni kotyelelo ngalunye, uyakunikwa igrosari vawutsha exabisa iR100, iR20 yesithuthi, kunye nokutya nesiselo ngelixesha ukutyelelo.

INGABA KUKHO INDLEKO EZIKHOYO?
Akukho ndleko ngokuba koluphando.

NDINGALUSHIYA UPHANDO?
Unelungelo lokugqiba ekubeni ungayithathi inxaxheba koluphando, wale ukuphendula imibuzo, okanye urhoxe kuphando nanini na ngaphandle kwesohlwayo. Ayiyikuchaphazela ukhathalelo olufumanayo wena okanye umntwana wakho apha okanye nakwawaphi na amanye amaziko ezempilo.

UNAYO IMIBUZO ONAYO?
Ukuba kukho into engacacanga okanye ukuba ufuna ulwazi oluphangaleleyo, nceda ucele sikunike lona

Unayo imibuzo?

ULWAZI OLONGEZELELEKILEYO:
Ukuba unayo nayiphi na imibuzo okanye unengxaki ngelixesha uthathe inxaxheba koluphando, ungaqhagamshelana no:

Prof Landon Myer
School of Public Health and Family Medicine
Faculty of Health Sciences
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Tel: 021 406 6661
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Associate Professor Andrew Boulle
School of Public Health and Family Medicine
Faculty of Health Sciences
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Tel 021 406 6715
Email: Andrew.Boulle@uct.ac.za

Ukuba unayo nayiphi na imibuzo malunga namalungelo akho njengomthathi nxaxheba wophando, ungaqhagamshelana neli lungu lekomiti ye ethics lilandelayo:

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

IKHASI LOKUTYIKITYA

Umthathi nxaxheba makagcwalise (nceda phawula):

☐ Ndilufundile ulwazi lwalomqulu (okanye ndiyifundelwe). Ndiye ndayinikwa ikopi yesisivumelwano sokungenela uphando Ndiye ndakhuthazwa kwaye ndanikwa ithuba lokuba ndibuze imibuzo malunga nophando kwaye nokuthatha inxaxheba kwam kulo iye yaphendulwa. Ndivuma ngokukhululekileyo ukuba koluphando kwaye ndiyavuma ukuthatha inxaxheba ndisazi ukuba ndingarhoxa nangeliphi na ixesha. Mna nomntwana wam singene ngokuzithandela kuphando. Ndiyaqonda ukuba ndingenele okanye ndingangenelanga lonto ayizukuchaphazela inkonzo zokhathalelo lwempilo lwam lwanamhlanje, okanye nezexesha elizayo.

☐ Ndiyavuma ukuba iqela lophando lingafikelela kumarekhodi am ezempilo kwesi sibhedlela okanye kwesinye isibhedlela ukuba kuyimfuneko yoluphando. Ulwazi lwam luyakugcinwa luyimfihlo.

☐ Ndiyavuma ukunikezela ngenkcukacha zam eziyakugcinwa ziyimfihlo liqela lophando.

☐ Ndiyavuma ukuba nditsalelwe umnxeba ngelixesha lophando

Igama lomthathi nxaxheba (Nceda uprinte)	Isignitsha yomthathi nxaxheba	Umhla/Ixesha

Igama lomvavanyi (Nceda uprinte)	Isignitsha yomvavanyi	Umhla/Ixesha

Ukuba eliphepha-mvume lokuthatha inxaxheba liye lafundelwa umthathi nxaxheba ngenxa yokuba engakwazi ukulifunda okanye ukuba umthathi nxaxheba kufuneka anyathelise ubhontsi kwi gama lakhe, ingqina elingelolungu lophando okanye labaphandi malibekhona lizokusayina lengxelo ilandelayo:
Ndiyaqinisekisa ukuba ulwazi olukwisivumelwano sokungenela uphando kunye nayo yaluphi na olunye ulwazi olubhaliweyo lucaciswe ngokucacileyo kum, kwaye lwaqondwa, ngumthathi nxaxheba. Umthathi nxaxheba uye wavuma ngokukhululekileyo ukuba koluphando.

Igama le Ngqina (Nceda uprinte)	Isignitsha ye Ngqina	Umhla/Ixesha

Enkosi!

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 not 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 Boulle
School of Public Health and Family Medicine
Faculty of Health Sciences
University of Cape Town
Tel 021 406-6715
Email: Andrew.Boulle@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!

B POSITIVE SENTINEL COHORT – PREGNANT WOMEN
INFORMATION AND INFORMED CONSENT

YINTONI INJONGO YOLUPHANDO?

Singabaphandi base Dyunivesithi yase Kapa kwaye siyakucela ukuba uthathe inxaxheba kuphando esiluqhuba e Gugulethu kwicala lokubelekisa - Midwife Obstetric Unit (MOU) kunye namaziko abo abathi bathumele kuwo. Injongo yoluphando kukuqonda nokuhlola impilo yamakhosikazi akhululelweyo nendlela abakhathaleleke ngayo kumaziko ezempilo ngexesha abakhulelewe ngalo kunye nasemva kokuba bebabelekile abantwana babo. Iquka impilo yengqondo neyomzimba kunye nawo nawaphi na amayeza kunye namachiza athe asetyenziswa ngexesha lokukhulelwa.

Siyayazi ukuba ibalulekile kwimpilo yabo kananjalo nakubantwana babo, lamakhosikazi akhulelweyo afumana lonke ukhathalelo kunye nonyango abalufunayo ngexesha lokukhulelwa kwabo kunye nasemva kokuba bebelekile. Ulwazi olufundwe koluphando luyakusinceda ukuphuhlisa inkonzo zempilo zamakhosikazi akhulelweyo.

Uyacelwa ukuba uthathe inxaxheba koluphando kuba ukhulelwe kwaye ufumana ukhathalelo lokukhulelwa kwakho apha e Gugulethu MOU. Injongo yeliphepha-mvume kukunika ulwazi nokunceda ukuba uthathe isigqibo sokuba uyafuna na ukuthatha inxaxheba koluphando.

KUMELE NDENZE NTONI UKUBA NDIYAVUMA UKUTHATHA INXAXHEBA?

Ukuba uyavuma ukuthatha inxaxheba, uyakuza ukuyokuma kwisixhenxe sotyelelo lophando. Elokuqala luyakuba namhlanje ngelixesha useklinikhi, kuphinde kubekho malunga namabini phambi kokuba ubeleke kuxhomekeke ukuba ukhulelwe kangakanani na. Lamatyelelo ayakwenzeka emva kokuba uphuma kutyelelo lwakho lwesiqhelo lwe ANC eklinikhi. Emva kokuba ubelekile, utyelelo olulandelayo luyakwenzeka kwiveki enye emva kokuba umbelekile umntwana wakho kuphinde kwakhona kubekho olunye xa umntwana wakho eneveki ezintandathu, inyanga ezintandathu kunye nenyanga ezilishumi elinesibini ubudala. Lamatyelelo ophando ohlukile kumatyelelo akho esiqhelo aseklinikhi ozakubanawo malunga nokukhulelwa kwakho okanye awempilo yomntwana wakho kodwa singabeka ixesha lamatyelelo ophando ukuze abekho ngosuku olunye kunye nolo lokuza kwakho malunga nokukhulelwa kwakho kunye nolohlolo lomntwana wakho. Olutyelelo lokuqala lwanamhlanje luyakuthatha imizuzu engamashumi alithoba kwaye utyelelo ngalunye olulandelayo luyakuthatha malunga nemizuzu engamashumi amathathu ukuya kwimizuzu engamashumi amathandathu.

Kumatyelelo akhokhelwe ngelixesha ubukhulelwe, uyakwenza oku kulandelayo:

- Uyakuphendula imibuzo malunga nokukhulelwa kwakho kunye neminye imibandela/ngxaki ezinxulumene nokhathalelo lwezempilo.
- Uyakuphendula imibuzo malunga nayo nayiphi na enye inkxalabo okanye izigulo.
- Ingxoxo ngayo nayiphi na imeko yexesha elide yezempilo (ukuba ikhona njengangoku).
- Ingxoxo nangawaphi na amayeza kunye namachiza owasebenzisayo.
- Uyakuphendula imibuzo ukuhlola ukuba awunaxinzelelo na okanye ukungonwabi.
- Ingxoxo malunga nemibandela yobudlelwane bakho buqu.
- Uyakuphendula imibuzo malunga nokhathalelo olufumanayo.

Ukuba siyabona ukuba unengxaki enkulu sizokuthumela kumaziko akhethekileyo oncedo.

Iveki enye emva kokubeleka

Emva kweveki enye umbelekile umntwana wakho, uyakuza eklinikhi kutyelelo oluyakubandakanya oku: kulandelayo:

- Impinda yeminye yemibuzo eyayixoxiwe ngaphambili (ezempilo, amayeza, uxinzelelo)
- Imibuzo malunga nokubeleka kwakho, impilo yomntwana wakho kunye nokumtyisa.

Kwamanye amatyelelo emva kokuba umntwana wakho ezelwe (kwiveki ezintandathu, inyanga ezintandathu kunye nenyanga ezingamashumi amabini anesibini) uyakwenza oku kulandelayo:

- Uyakuphendula imibuzo malunga nempilo yakho yakutsha nje kunye nayiphi na inxalabo ngezempilo
- Uyakuphendula imibuzo malunga nempilo yomntwana wakho, indlela zokumtyisa kunye nogonyo.
- Inggxoxo ngengxaki ekusebenzise amayeza.
- Uyakuphendula imibuzo ukuhlola ukuba awunaxinzelelo okanye ukungonwabi na.
- Ingxoxo ngeminye yemibandela yobudlelwane bakho buqu.
- Uyakuphendula imibuzo malunga nokhathalelo olufumanayo.

Ukuhlolwa kwamarekhodi empilo
Njengenxalenye yophando, siyakujonga kwaye siyakuthatha ulwazi lokuhlukuhla kwakho, ukubeleka kwakho, amayeza, kunye namarekhodi ase lebhu. Siyakujonga kwaye siyakuthatha ulwazi kumarekhodi okhathalelo lwempilo yomntwana wakho emva kokuba ezelwe. Kulamarekhodi, sinomdla wokufunda malunga nokhathalelo othe walufumana xa ubukhulelwe, amayeza obuwasebenzisa kananjalo nolwazi malunga nokubeleka kwakho kunye nempilo yomntwana wakho. Yonke ingqokelela yolwazi esithe sayihlaziya kwaye sayiphonononga iyimfihlelo kwaye akukho magama abathathi nxaxheba ashicilelweyo kwimiqulu yophando.

Ulandelelo lotyelelo oluphosakeleyo
Uyakucelwa ukuba unikezele ngenkcukacha zakho ukuze sikwazi ukuqhagamshelena nawe ngexesha lophando. Abasebenzi bophando bayakuthetha nawe malunga nendlela engcono yokuqhagamshelana nawe. Kwisiganeko othe waphosa ngaso olunye utyelelo olucwangcisiweyo lophando, umsebenzi wophando uyakuqhagamshelana nawe khona ukuze afumane olunye usuku nexesha lokugqibezela utyelelo lwakho. Ukuba uthe waphinda-phinda uphosa utyelelo lwakho lophando okanye abasebenzi abakwazi ukuqhagamshelana nawe xa besebenzisa ulwazi othe wanikezela ngalo, kuyakubayimfuneko ukuba bakutyelele ekhaya khona ukuze batshintshe usuku oluphosileyo lophando.

Uqhagamshelwano lophando olulandelayo
Emva kokugqiba utyelelo lokuqala emva kokuba ubelekile, siyakuthetha nawe kwakhona siqinisekisa ukuba ukonwabele ukuba ubeyinxalenye yophando ngokubanzi.

YEYIPHI IMINGCIPHEKO ELINDELEKILEYO?
Ungaziva ungakhululekanga kweminye imibuzo ebuzwa ngesiqu sakho. Ungala ukuphendula nayiphi na imibuzo ongafuniyo ukuyiphendula. Kukho umngcipheko ekwabelaneni ngolwazi lwakho buqu kunye nolwamayeza. Siyakulugcina ngenkathalo nangemfihlo kangangoko sinako ulwazi lwakho.

ZEZIPHI INZUZO EZILINDELEKILEYO?
Akukho nzuzo zibhekise kuwe ngqo xa uthatha inxaxheba koluphando. Ulwazi olufumaneke koluphando lunganceda ekuphuhliseni amaziko okukhathalelwa kwezempilo kumakhosikazi akhulelweyo nabantwana babo eKapa, kwiphondo lase Ntshona Koloni nase Mzantsi Afrika jikelele.

ZEZIPHI INDLELA ZOKUTHATHA INXAXHEBA?
Indlela yokuthatha inxaxheba koluphando kukuqhubeleka njengesiqhelo nokhathalelo lwempilo yakho. Ukuba ugqibe ekubeni ungathathi nxaxheba koluphando, ukhathalelo lwakho lwempilo lwesiqhelo alusayi kutshintsha nangayiphi na indlela.

KUTHIWANI NGEMFIHLELO?
Ukuba uyavuma ukuthatha inxaxheba, lonke ulwazi oluqokelelwe ngexesha lophando luyakugcinwa luyimfihlo. Igama lakho alisayi kubhalwa kwimpepha zophando kwaye aliyikusetyenziswa ngokunxulumene nalo naluphi na ulwazi okanye incindi eziqokelewa elebhu njengenxalenye yophando.

Zonke ingcombolo zophando ziyakugcinwa kwikhabhathi etshixwayo. Ngabasebenzi kunye nabantu ababandakanyekayo kwinkqubo yophendlo abayakufikelela kwezi ngcombolo. Bonke abasebenzi abayinxalenye kwingqokelela yolwazi kunye nabaphathi bayakufumana uqeqesho olukhethekileyo kwimfihlelo.

Kuzo zona ezinkqubo ukuba umsebenzi wophando uthe wafumanisa ukuba usemngciphekweni wokuzonzakalisa okanye omnye umntu okanye uhlukumezo lomntwana/okanye ukulahlwa kwakhe, umsebenzi wophando uyakwazisa abasemagunyeni.

INGABA KUKHO INDLEKO EZIKHOYO?
Akukho ndleko ngokuba koluphando.

NDINGALUSHIYA NA UPHANDO?
Unelungelo lokugqiba ekubeni ungayithathi inxaxheba koluphando, wale ukuphendula imibuzo, okanye urhoxe kuphando nanini na ngaphandle kwesohlwayo. Ayiyikuchaphazela ukhathalelo olufumanayo e Gugulethu MOU okanye nakwawaphi na amanye amaziko ezempilo.

IKHONA INTO ENDIZAKUYINIKWA NGOKUTHATHA KWAM INXAXHEBA?
Akukho ntlawulo yokuthatha inxaxheba. Ekupheleni kotyelelo ngalunye, uyakunikwa igrosari vawutsha exabisa iR100, iR20 yesithuthi, kunye nokutya nesiselo ngelixesha ukutyelelo.

Ukuba wosuleleke yi Ntsholongwane ka Gawulayo, uyakucelwa ukuba unikezela ngesampuli yechaphaza legazi elomileyo (DBS) kutyelelo ngalunye. Oku kuquka ukutsalwa kwegazi kwitiphu yomnwe wakho ngenaliti, kwaye amaqabaza egazi asetyenziswa ukugcwalisa umlinganiselo wamachaphaza amahlanu akwiqweqwe lephepha.

Isampuli ye DBS iyakugcinwa kwaye isetyenziswe ukujonga amajoni akho omzimba (ilungu lomzimba wakho elilwa ukosuseleka njenge Ntsholongwane ka Gawulayo), ivayirasi kunye nezinga le ARV kwixesha elizayo. Iziphumo zoluvavanyo zenzelwe nje uphando kwaye aziyikufumaneka kuwe, iklinikhi, okanye abasebenzi bophando. Ukuba abanikezeli benkathalo yezempilo baseklinikhi bafuna ukujonga igazi lakho, bayakuthatha incindi ezahlukileyo zegazi. Xa zigciniwe, igazi lakho kunye neziphumo zovavanyo aziyikubanalo igama lakho okanye nayiphi na enye indlela ekhombisa ukuba unento yokwenza nalo.

Nceda utyikitye onobumba ngezantsi ukubonakalisa ukuba uyinikile na okanye hayi imvume yokuba sithathe isampuli yeDBS kuwe. Ungahlala kulo uphando, nokuba ukhethe ukunganikeli ngencindi yakho.

_____ (onobumba) Ndiyavuma ukuba nifumane isampuli yeDBS njengenxalenye yoluphando.

_____ (onobumba) Andivumi ukuba nifumane isampuli yeDBS njengenxalenye yoluphando.

UKUSETYENZISWA KWENCINDI KWIXESHA ELIZAYO:
Ukuba wosuleleke yi Ntsholongwane ka Gawulayo kwaye uyavuma, elinye igazi elitsalwe kuwe (isampuli ye DBS) njengenxalenye yophando lingasetyenziswa kuphando lwexesha elizayo olwayamene ne Ntsholongwane ka Gawulayo. Ngelixesha, asinakunikezela ngenkcukacha zokuba uvavanyo luyakuqhutywa nini, okanye loluphi kanye-kanye uvavanyo esizakulenza. Yaye, uvavanyo olwangezelelweyo aluyi kwenziwa kusetyenziswe ezi sampuli zigciniweyo ngaphandle kwemvume ye komiti ye ethics ebandakanyeka koluphando.

Ukuba uyavuma sigcine isampuli zakho ukwenzela uphando lwexesha elizayo, zingatshixelwa kwisikhenkcezisi kangangeminyaka emihlanu. Ukuba sithe sazisebenzisa ezisampuli kwixesha elizayo, amagama okanye ezinye izazisi aziyi kuqukwa kolu lwazi (njengolunye uluwazi esiluqokelelayo loluphando).

Nceda utyikitye onobumba ngezantsi ukubonakalisa ukuba uyinikile na okanye hayi imvume yokuba sithathe imvume yezincindi ukuze zisetyenziswe kuphando lwexesha elizayo.

_____(onobumba) Ndiyavuma ukuba nifumane igaxi lam niligcinele uphando lwexesha elizayo.

_____(onobumba) Andivumi ukuba nifumane igazi lam niligcinele uphando lwexesha elizayo.

UNAYO IMIBUZO ONAYO?
Ukuba kukho into engacacanga okanye ukuba ufuna ulwazi oluphangaleleyo, nceda ucele sikunike lona

Unayo imibuzo onayo?

ULWAZI OLONGEZELELEKILEYO:
Ukuba unayo nayiphi na imibuzo okanye unengxaki ngelixesha uthathe inxaxheba koluphando, ungaqhagamshelana:

Professor Landon Myer
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Ukuba unayo nayiphi na imibuzo malunga namalungelo akho njengomthathi nxaxheba wophando, ungaqhagamshelana neli lungu lekomiti ye ethics lilandelayo:

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

IKHASI LOKUTYIKITYA

Umthathi nxaxheba makagcwalise (nceda phawula):

☐ Ndilufundile ulwazi lwalomqulu (okanye ndilufundelwe). Ndiye ndayinikwa ikopi yesisivumelwano sokungenela uphando. Ndiye ndakhuthazwa kwaye ndanikwa ithuba lokuba ndibuze imibuzo malunga nophando kwaye nokuthatha inxaxheba kwam kuyo iye yaphendulwa. Ndivuma ngokukhululekileyo ukuba koluphando kaye ndiyavuma ukuthatha inxaxheba ndisazi ukuba ndingarhoxa nangeliphi na ixesha. Ndingene ngokuzithandela kuphando. Ndiyaqonda ukuba ndingenele okanye ndingangenelanga lonto ayizukuchaphazela inkonzo zokhathalelo lwempilo lwam lwanamhlanje, okanye nezexesha elizayo.

☐ Ndiyavuma ukuba iqela lophando lingafikelela kumarekhodi am ezempilo kwesi sibhedlela okanye kwesinye isibhedlela ukuba kuyimfuneko yoluphando. Ulwazi lwam luyakugcinwa luyimfihlo.

☐ Ndiyavuma ukunikezela ngenkcukacha zam eziyakugcinwa ziyimfihlo liqela lophando.

☐ Ndiyavuma ukuba nditsalelwe umnxeba ngelixesha lophando

Igama lomthathi nxaxheba (Nceda uprinte)	Isignitsha yomthathi nxaxheba	Umhla/Ixesha

Igama lomvavanyi (Nceda uprinte)	Isignitsha yomvavanyi	Umhla/Ixesha

Ukuba eliphepha-mvume lokuthatha inxaxheba liye lafundelwa umthathi nxaxheba ngenxa yokuba engakwazi ukulifunda okanye ukuba umthathi nxaxheba kufuneka anyathelise ubhontsi kwi gama lakhe, ingqina elingelolungu lophando okanye labaphandi malibekhona luzokusayina lengxelo ilandelayo:

Ndiyaqinisekisa ukuba ulwazi olukwisivumelwano sokungenela uphando kunye nalo naluphi na olunye ulwazi olubhaliweyo lucaciswe ngokucacileyo, kwaye lwaqondwa, ngumthathi nxaxheba. Umthathi nxaxheba uye wavuma ngokukhululekileyo ukuba koluphando.

Igama le Ngqina (Nceda uprinte)	Isignitsha ye Ngqina	Umhla/Ixesha

Enkosi!

Appendix B: Immunization

B-POS: Infant Medical Events
Version 2.0, 7th April 2017

I-IMMZ

PCID: __ __ __ __ __ - __ __

INFANT IMMUNISATIONS

To be completed at EVERY Study Visit

Visit Date					
D	**D**	**M**	**M**	**M**	

Visit Code
ALL P-visits

PLEASE NOTE: These immunisations should be checked-off by a Study Team Member at every visit even if they have been recorded in the RTHC. **All RTHC to be photocopied at each visit.**

For Multiple Births → **Complete this CRF for EACH infant.**
i.e. for twins, complete for each child

Age of child	Vaccine needed	How and where it is given on body	Date given dd/mmm/yyyy	Signed by nurse	Study Visit code when vaccines checked e.g. P2
Birth	**BCG** Bacilles Calmette Guerin	Right arm			
	OPV-0 Oral Polio Vaccine	Drops by mouth			
6 weeks	**OPV-1** Oral Polio Vaccine	Drops by mouth			
	RV-1 Rotavirus Vaccine	Liquid by mouth			
	DTaP-IPV-Hib-HBV-1 Diphtheria, Tetanus. Acellular Pertussis, Inactivated Polio Vaccine and Haemophilus Influenza Type B & Hepatitis B Combined	Intramuscular/Left thigh			
	PCV-1 Pneumococcal Conjugated Vaccine	Intramuscular/Right thigh			
10 weeks	**DTaP-IPV-Hib-HBV-2** Diphtheria, Tetanus. Acellular Pertussis, Inactivated Polio Vaccine and Haemophilus Influenza Type B & Hepatitis B Combined	Intramuscular/Left thigh			
14 weeks	**RV-2*** Rotavirus Vaccine	Liquid by mouth			
	DTaP-IPV-Hib-HBV-3 Diphtheria, Tetanus. Acellular Pertussis, Inactivated Polio Vaccine and Haemophilus Influenza Type B & Hepatitis B Combined	Intramuscular/Left thigh			
	PCV-2 Pneumococcal Conjugated Vaccine	Intramuscular/Right thigh			
6 months	**Measles Vaccine -1****	Subcutaneous/ Left thigh			
9 months	**PCV-3** Pneumococcal Conjugated Vaccine	Intramuscular/Right thigh			
12 months	**Measles Vaccine -2****	Subcutaneous/ Right arm			

Signed Interviewer: _____ Date: _____ / _____ / _____
DD MMM YYYY

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

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

Appendix C: Questionnaires

B-POS: Infant Birth Info Form
English-Version 1.0, 4th April 2017

IME-P1

PWID: __ __ __ __ __ - __ __

INFANT BIRTH INFORMATION FORM

THIS CRF APPLIES TO ALL ENROLLED INFANTS
To be completed during the >7 days Postpartum Study visit

Visit Date								
D	**D**	**M**	**M**	**M**	**Y**	**Y**	**Y**	**Y**

Visit Code	
P	**1**

PLEASE NOTE: These measurements should still be carried out by a Study Team Member even if they have been recorded in the RTHC.

For Multiple Births ⟶ Complete this CRF for EACH infant
i.e. for twins, complete for each child

We are going to ask you a few questions about your baby/babies' birth	
INFANT #:_____ Initials**:** ____ ____	
1. What is your baby/babies' sex	☐ Male ☐ Female
2. Was your baby alive after birth?	☐ Ewe *Yes* ☐ Hayi *No* → **If NO, or if TWINS and both died. Please complete a *STUDY EXIT FORM***
3. What is your baby's birth weight?	Weight: ____ ____ ____ ____ g ***Confirm with RTHC**

Signed Interviewer: _____ Date: _____ / _____ / _____
DD MMM YYYY

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

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

PWID: __ __ __ __ __ - __ __

INFANT ANTHROPOMETRY

THIS CRF APPLIES TO ALL ENROLLED INFANTS
To be completed during the >7 days Postpartum Study visit

Visit Date								
D	D	M	M	M	Y	Y	Y	Y

Visit Code	
P	1

Please on note: These measurements should still be carried out by a Study Team Member even if they have been recorded in the RTHC.

For Multiple Births ⟶ Complete this CRF for EACH infant
i.e. for twins, complete for each child

INFANT #:_____ Initials____ ____

ANTHROPOMETRY		
Weight	____ ____ ____ kg	☐ Not measured
Length 1	____ ____ . ____ cm ☐	Not measured
Length 2	____ ____ . ____ cm ☐	Not measured
Head Circumference 1	____ ____ . ____ cm ☐	Not measured
Head Circumference 2	____ ____ . ____ cm ☐	Not measured
MUAC 1	____ ____ . ____ cm ☐	Not measured
MUAC 2	____ ____ . ____ cm ☐	Not measured

Please compare these measurements to the ones in the RTHC and consult the local clinic if the growth curve is flattening or crossing centiles.

PWID: _ _ _ _ _ _ - _ _

Additional Notes:

Please write down anything suspicious that you might take note off while taking these measurements.

Signed Assessor of Measurements: _____ Date: _____ / _____ / _____
DD MMM YYYY

Signed Assessor of Measurements: _____ Date: _____ / _____ / _____
DD MMM YYYY

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

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

PWID: __ __ __ __ __ - __ __

INFANT MEDICATION USE AND SIDE EFFECTS

To be completed during the This CRF applies to <u>ALL</u> enrolled infants
Complete during <u>>7 days Postpartum</u> Study visit

Visit Date								
D	D	M	M	M	Y	Y	Y	Y

Visit Code	
P	**1**

PLEASE READ OUT TO PARTICIPANT

The following questions will refer to any medicines and/or remedies you given to your baby. This includes <u>ANY</u> 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 given your baby **<u>in the past 7 days</u>**.

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

You will be asked to list all medications you are <u>you recently gave your baby</u>. Please include all prescription medicines (If any was given at any point) non-prescription medicines (i.e. over the counter medicines and remedies), complementary medicines (e.g. Vitamins), traditional and/or herbal medicines and remedies.

Table 1: PREVIOUS/CURRENT SYMPTOMS

These questions relate to any health problems your baby might have had since s/he was born.

Since your baby was born, did your baby experience ANY of the following symptoms? If s/he did we would like to know what medications and/or remedies gave him/her. These could be medications and/or remedies from a doctor, clinic, pharmacist, traditional healer, spiritual healer, supermarket/grocery store, friend or family member?

PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 7, pg. 13) FOR EACH MEDICATION MENTIONED!!!

Symptom	Did you give the baby something for this?	Name of medication or remedy	State date for each medication used
1. Hyperbilirubinaemia (Jaundice) ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
2. Fever (Xhosa "Ubushushu") ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
3. Vomiting (not spills/posset) ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
4. Diarrhoea ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
5. Cough ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY

PWID: _ _ _ _ _ - _ _

Symptom	Did you give the baby something for this?	Name of medication or remedy	State date for each medication used
6. Fast breathing ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
7. Wheezing (whistling noise) ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
8. Persistent crying ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
9. Tummy ache ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
10. Distended stomach ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
11. Inflamed cord ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY

Symptom	Did you give the baby something for this?	Name of medication or remedy	State date for each medication used
12. Colic reflux ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
13. Oozing eye ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
14. Seizures ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
15. Oral thrush ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
16. Nappy rash ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
17. Body rash ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY
18. Itchy rash in the skin folds ☐Ewe *Yes* ☐Hayi *No*	☐Ewe *Yes* ☐Hayi *No*	a. b.	____ / ____ / _____ DD MMM YYYY ____ / ____ / _____ DD MMM YYYY

PWID: _ _ _ _ _ - _ _

		c.	____/ ____ / _____ DD MMM YYYY
19. Other rash ☐Ewe *Yes* ☐Hayi *No* Cacisa:_____ *Specify*	☐Ewe *Yes* ☐Hayi *No*	a. b. c.	____/ ____ / _____ DD MMM YYYY ____/ ____ / _____ DD MMM YYYY ____/ ____ / _____ DD MMM YYYY

Table 2: HOSPITAL ATTENDANCE/ADMISSIONS

We are now going to ask you about any health problems that your baby may have had or currently have.

***Since your baby was born**, have you taken him/her to visit a hospital?*

☐Ewe *Yes* ☐Hayi *No* (If NO, continue to **Table 3**)

List reasons for attendance/admission and associated medications received.
PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 7, pg. 13) FOR EACH MEDICATION MENTIONED!!!

What made you take him/her to the hospital?	Did s/he sleep over (in a ward) at the Hospital? If YES, when was this and for how long?	Which hospital did you visit?	Medicine name: It can be any medication, including drips, syrups and injections.
1.	____/ ____ / _____ DD MMM YYYY Ixesha (iiyure/iintsuku): _____ *Period (*hrs/days)		
2.	____/ ____ / _____ DD MMM YYYY Ixesha (iiyure/iintsuku): _____ *Period (*hrs/days)		
3.	____/ ____ / _____ DD MMM YYYY Ixesha (iiyure/iintsuku): _____ *Period (*hrs/days)		
4.	____/ ____ / _____ DD MMM YYYY Ixesha (iiyure/iintsuku): _____ *Period (*hrs/days)		

Table 3: CLINIC ATTENDANCE

We are now going to ask you about any health problems that the baby may have had or currently have.

***Since your baby was born**, have you taken him/her to visit the clinic?*

☐Ewe *Yes* ☐Hayi *No* (If NO, skip to **Table 4**)

List reasons for attendance and associated medications received.

PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 7, pg. 13) FOR EACH MEDICATION MENTIONED!!!

What made you take him/her to the clinic?	When was this?	Which clinic did you visit?	Medicine name: It can be any medication, including drips, syrups and injections.
1.	____/ ____ /____ DD MMM YYYY		
2.	____/ ____ /____ DD MMM YYYY		
3.	____/ ____ /____ DD MMM YYYY		
4.	____/ ____ /____ DD MMM YYYY		
5.	____/ ____ /____ DD MMM YYYY		
6.	____/ ____ /____ DD MMM YYYY		
7.	____/ ____ /____ DD MMM YYYY		
8.	____/ ____ /____ DD MMM YYYY		
9.	____/ ____ /____ DD MMM YYYY		
10.	____/ ____ /____ DD MMM YYYY		

PWID: _ _ _ _ _ _ - _ _

Table 4: OVER-THE-COUNTER MEDICATION

Since your baby was born, did you use any medications and/or remedies from a chemist or pharmacy, or supermarket including pills, liquids, injections, ointments, creams or anything else?

☐ Ewe *Yes* ☐ Hayi *No* (*If NO, skip to* **Table 5**)

If **YES**, then PLEASE PROVIDE DETAILS BELOW.

PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 7, pg. 13) FOR EACH MEDICATION MENTIONED!!!

Medicine and/or Remedy name	**What was the reason for use?**	**When last and for how long did you take this medicine?** State period. If on-going (tick)
1. Gripe water		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
2. Lennons		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
3. Druppels		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
4. Herman's drops		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
5. Immune boosters		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
6. Clement drops		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
7. Disprin for cord		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY
8. Other		**Start:** ____ / ____ / _____ DD MMM YYYY **Stop:** ____ / ____ / _____ DD MMM YYYY

Table 5: SPECIFIC MEDICATIONS

We are now going to ask you whether you have given the baby any of these specific medicines and/or remedies.

Since your baby was born, *have you taken or used any of the following? If YES, please SPECIFY?*

PLEASE REMEMBER TO COMPLETE M EDICATION TABLE (TABLE 7, pg. 13) FOR EACH MEDICATION MENTIONED!!

Specific Medicine and/ or Remedy	***How often do you take this medicine, treatment or remedy?***	***When last did you take this medicine?*** *State period. If on-going (tick)*	***Medicine name***
1. Nevirapine ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
2. AZT ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
3. Multivitamins ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	

PWID: _ _ _ _ _ - _ _

Specific Medicine and/ or Remedy	***How often do you take this medicine, treatment or remedy?***	***When last did you take this medicine?*** *State period. If on-going (tick)*	***Medicine name***
4. Bactrim ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
5. Iron ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
6. Antibiotics ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	

7. Nose drops ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
8. Zinc ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
9. Bum cream (Fissan, Bennetts) ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	
10. Surgical spirit on cord ☐Ewe *Yes* ☐Hayi *No*		Ukuqala: *Start:* ____ / _____ / _____ DD MMM YYYY Uyokuma: *Stop:* ____ / _____ / _____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	

PWID: _ _ _ _ _ - _ _

Table 6: USE OF TRADITIONAL MEDICINE

We will now ask you questions about any traditional medicines which you may have received from a traditional, spiritual healer, prophet, friend or family member to give to the baby.

Since the baby was born have you given her any traditional medicines and /or remedies to drink, to rub, to inhale, to chew, to steam with, to wash with or to "snuff" etc.?

☐ Ewe *Yes* ☐ Hayi *No* (If NO, skip to **Table**)

If **YES**, then PLEASE PROVIDE DETAILS BELOW

PLEASE REMEMBER TO COMPLETE MEDICATION TABLE (TABLE 7, pg. 13) FOR EACH MEDICATION MENTIONED!

Medicine and/or Remedy name	**When was this taken?**	**Method of use** Please choose from list below. Tick **ALL** that apply
1.	____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY	☐ Elokuxuba nokutya *To mix with food* ☐ Elokusela *To drink* ☐ Elokuhlafuna *To chew* ☐ Elokuhlamba ngayo *To wash with it* ☐ Elokurhogola *To inhale* ☐ Elokuthambisa emzimbeni *To apply to the body* ☐ Elokufutha *To steam with* ☐ Elokugabha/elokuphalaza *To puke* ☐ Elokuhambisa *To clean the stomach with* ☐ Enye *Other* Cacisa: _____ *Specify*
2.	____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY	☐ Elokuxuba nokutya *To mix with food* ☐ Elokusela *To drink* ☐ Elokuhlafuna *To chew* ☐ Elokuhlamba ngayo *To wash with it* ☐ Elokurhogola *To inhale* ☐ Elokuthambisa emzimbeni *To apply to the body* ☐ Elokufutha *To steam with* ☐ Elokugabha/elokuphalaza *To puke* ☐ Elokuhambisa *To clean the stomach with* ☐ Enye *Other* Cacisa: _____ *Specify*

Medicine and/or Remedy name	**When was this taken?**	**Method of use** Please choose from list below. Tick **ALL** that apply
3.	____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY	☐ Elokuxuba nokutya *To mix with food* ☐ Elokusela *To drink* ☐ Elokuhlafuna *To chew* ☐ Elokuhlamba ngayo *To wash with it* ☐ Elokurhogola *To inhale* ☐ Elokuthambisa emzimbeni *To apply to the body* ☐ Elokufutha *To steam with* ☐ Elokugabha/elokuphalaza *To puke* ☐ Elokuhambisa *To clean the stomach with* ☐ Enye *Other* Cacisa: _____ *Specify*
4.	____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY	☐ Elokuxuba nokutya *To mix with food* ☐ Elokusela *To drink* ☐ Elokuhlafuna *To chew* ☐ Elokuhlamba ngayo *To wash with it* ☐ Elokurhogola *To inhale* ☐ Elokuthambisa emzimbeni *To apply to the body* ☐ Elokufutha *To steam with* ☐ Elokugabha/elokuphalaza *To puke* ☐ Elokuhambisa *To clean the stomach with* ☐ Enye *Other* Cacisa: _____ *Specify*
5.	____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY ____ / _____ / _____ DD MMM YYYY	☐ Elokuxuba nokutya *To mix with food* ☐ Elokusela *To drink* ☐ Elokuhlafuna *To chew* ☐ Elokuhlamba ngayo *To wash with it* ☐ Elokurhogola *To inhale* ☐ Elokuthambisa emzimbeni *To apply to the body* ☐ Elokufutha *To steam with* ☐ Elokugabha/elokuphalaza *To puke* ☐ Elokuhambisa *To clean the stomach with* ☐ Enye *Other* Cacisa: _____ *Specify*

PWID: _ _ _ _ _ - _ _

Table 7: DETAILED MEDICATION LIST

This is a list of the medicines and remedies you have given your baby since s/he was born. I would like to go through this list again with you just to make sure that everything is correct.

Please let me know if there is a mistake or if you remember something we have not mentioned.

PLEASE REMEMBER TO COMPLETE THIS MEDICATION TABLE FOR EACH MEDICATION MENTIONED EARLIER!

Name of medication	From where was the medication received? Select appropriate code	When did you start and stop using the medication? State period. If on-going (tick)	Reason for stopping use? Select appropriate code	Did you experience any side effects? If YES, please specify what you took for it
1.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify:* _____	Ukuqala: *Start:* ____ / ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____ / ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*
2.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify:* _____	Ukuqala: *Start:* ____ / ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____ / ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*

Name of medication	**From where was the medication received?** Select appropriate code	**When did you start and stop using the medication?** State period. If on-going (tick)	**Reason for stopping use?** Select appropriate code	**Did you experience any side effects?** If YES, please specify what you took for it
3.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify*: _____	Ukuqala: *Start:* ____/ ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____/ ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*
4.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify*: _____	Ukuqala: *Start:* ____/ ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____/ ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*
5.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify*:	Ukuqala: *Start:* ____/ ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____/ ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*

	_____		☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	
6.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify:* _____	Ukuqala: *Start:* ____/ ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____/ ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*
7.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify:* _____	Ukuqala: *Start:* ____/ ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____/ ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*

Name of medication	**From where was the medication received?** Select appropriate code	**When did you start and stop using the medication?** State period. If on-going (tick)	**Reason for stopping use?** Select appropriate code	**Did you experience any side effects?** If YES, please specify what you took for it
8.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional Healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify:* _____	Ukuqala: *Start:* ____ / ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____ / ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe *Yes* Cacisa:_____ *Specify:* ☐Hayi *No*
9.	☐1 Ugqirha *Doctor* ☐2 Unesi *Nurse* ☐3 Khemesti *Chemist* ☐4 Igqirha *Traditional healer* ☐5 Ivenkile yokutya *Grocery store* ☐6 Enye *Other* Ukuba kukho enye into nceda ucacise: *If other, please specify:* _____	Ukuqala: *Start:* ____ / ____ / ____ DD MMM YYYY Uyokuma: *Stop:* ____ / ____ / ____ DD MMM YYYY ☐Iyaqhubeleka *Ongoing*	☐1 Ndabangcono *Felt better* ☐2 landiphelela *Ran out* ☐3 Ndaligqiba *Completed course* ☐4 Ndaxelelwa ukuba ndiliyeke *Told to stop* Waxelelwa ngubani ukuba liyeke? *If "told to stop" please say by whom* _____ ☐5 Lalingasebenzi *Was not working* ☐6 Imiphumela *Side effects*	☐Ewe*Yes* Cacisa:_____ *Specify:* ☐Hayi *No*

PWID: _ _ _ _ _ _ - _ _

Reminder:

PLEASE COULD YOU BRING ALONG YOUR CLINIC CARD OR YOUR MEDICINES AND REMEDIES WITH YOU NEXT TIME WE SEE YOU. KINDLY ALSO BRING ALONG EMPTY MEDICINE CONATINERS IF YOUR MEDICINES ARE FINISHED.

PWID: _ _ _ _ _ _ - _ _

NOTES:

Please write notes and/or any other comments here.

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

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

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

PWID: _ _ _ _ _ _ - _ _

INFANT MEDICAL EVENTS

This CRF applies to ALL enrolled infants
Complete during >7 days Postpartum Study visit

Visit Date								
D	D	M	M	M	Y	Y	Y	Y

Visit Code	
P	1

INFANT #:_____ Initials: _____

A: INFANT HEALTH ON DAY OF VISIT

We are going to ask you a few questions about how your baby is doing today. If you have any concerns about your baby today, we will provide you with a referral letter to your clinic.

1. Is your baby here today?	☐ Yes → **Skip to Q3** ☐ No
2. Where is your baby?	☐ At home ☐ Outpatient/clinic visit ☐ Inpatient at RXH ☐ Inpatient at GSH ☐ Inpatient at NSH ☐ Inpatient at MMH ☐ Other, Specify: _____

3. Does your bay have any of the following **TODAY**?
Please read all, tick **ALL** that apply and indicate for how long this has been.

Coughing ☐ Yes #_____ days ☐ No	Fast breathing ☐ Yes #_____ days ☐ No
Wheezing (whistling chest) ☐ Yes #_____ days ☐ No	Diarrhoea ☐ Yes #_____ days ☐ No
Fever (baby is warm or hot to the touch) ☐ Yes #_____ days ☐ No	Poor Feeding ☐ Yes #_____ days ☐ No
Itchy rash in the skin folds ☐ Yes #_____ days ☐ No	Other, Specify: _____ ☐ Yes #_____ days ☐ No

B: INFANT HEALTH SINCE BORN			
We are going to ask you some questions about your baby's health since <u>birth.</u>			
4. **Since birth**, has your baby been referred to any other health facility for <u>infant-related care</u>	☐Yes ☐No → **If NO, Skip to Q5**	a. Where were you referred for your baby?	Location: _____
		b. What was the date of the referral?	____ /____ /____ DD MMM YYYY
		c. What was the reason for the referral?	Reason: _____
		d. Did your baby receive any new treatment or medications as a result of this referral?	☐ Yes, Specify:_____ ☐ No
5. Since **birth**, has your baby had any vaccinations?		☐Yes ☐ No → **Skip to Q6**	→**Complete Immunization sheet** **Confirm in RTHC (tick)** ☐
NOTE: If the baby is unwell, please let the Study Nurse fill out a **<u>REFERRAL LETTER</u>** and send the baby to their usual health care provider for assistance.			

PWID: _ _ _ _ _ _ - _ _

We will now ask you some questions about your baby's breathing

Note to Interviewer:
"How many times" refers to Number of Episodes of Illness, NOT the number of days the baby was ill. One episode could last for more than one day.

The "last two weeks" refers to the preceding 14 days; e.g. if today is Wednesday 28th, it refers back to the period since "last before last Wednesday" i.e.: Wednesday 14th

6. **Since birth**, has your baby been ill with a fever "ubushushu"? (including today)	☐Yes ☐No → **Skip to Q10** ☐Unsure → **Skip to Q10**
7. **Since birth**, how many times has your baby been ill with a fever "ubushushu"?? (including today)	# times: _____
8. When your baby was ill with a fever "ubushushu", did he/she breathe with difficulty, or faster than usual with short, fast breaths?	☐Yes ☐No ☐Unsure
9. Did you at any time seek treatment or advice for this fever "ubushushu"?	☐Yes ☐No ☐Unsure
10. **Since birth**, has your baby been ill with a cough? (Including today)?	☐Yes ☐No → **Skip to Q14** ☐Unsure → **Skip to Q14**
11. **Since birth**, how many times has your baby been ill with a cough? (including today)	# times: _____
12. When your baby was ill with a cough, did he/she breathe with difficulty, or faster than usual with short, fast breaths?	☐Yes ☐No ☐Unsure
13. Did you at any time seek treatment or advice for this cough?	☐Yes ☐No ☐Unsure
14. Has your baby had any wheezing (whistling in the chest) at any time since birth? (including today)	☐Often (≥1 day a week) ☐Sometimes (<1 day a week) ☐No → **Skip to Q17** ☐Unsure → **Skip to Q17**

15. How many attacks of wheezing has your baby had **since birth**?	☐None ☐1-3 Attacks ☐3-12 Attacks ☐More than 12 Attacks ☐Unsure
16. Has the wheeze ever made it difficult for your baby to sleep?	☐Often (≥1 day a week) ☐Sometimes (<1 day a week) ☐No ☐Unsure
17. Sometimes babies get an itchy rash in their skin folds (especially behind the ears, in the neck, in the elbow fold, and/or behind the knee). Has the baby had a rash like this at any time since birth?	☐Yes ☐No ☐Unsure
We are now going to ask you some questions about your baby's stools	
18. **Since birth**, has your baby had any illness with diarrhoea? (including today)	☐Yes ☐No → **Skip to Q22** ☐Unsure → **Skip to Q22**
19. **Since birth**, how many times has your baby had a diarrhoeal illness? (including today) **PLEASE NOTE**: This is referring to periods of illness, NOT to the number of days with diarrhoea.	# diarrhoeal illnesses: _____ ☐Unsure
20. On the worst day of the diarrhoea, how many bowel movements did the baby have?	# bowel movements: _____ ☐Unsure
21. Please describe the <u>nature</u> of the stool on the worst day.	i. Watery ☐Yes ☐No ☐Unsure ii. Soft ☐Yes ☐No ☐Unsure iii. Bloody ☐Yes ☐No ☐Unsure iv. Mucous ☐Yes ☐No ☐Unsure

PWID: _ _ _ _ _ - _ _

C: HEALTHCARE VISITS

We are now going to ask you questions about who you get help from when the baby is sick.

Please answer for all illnesses that the baby has had **since birth**, including coughing or diarrhoea.

Notes to Interviewer: This is NOT for routine well baby or vaccination visits, but only for **ILLNESS** related visits There may be more than one diagnosis and treatment per visit.

22. **Since birth**, have you taken your baby to any health care providers for treatment or advice about any illness	☐ Yes ☐ No → **Skip to Q23** ☐ Unsure → **Skip to Q23**			
a. Where was baby seen? Select **ALL** that apply	b. What was the diagnosis? Select **ALL** that apply	c. What treatment did baby receive? Select **ALL** that apply	d. Did the baby have to sleep in the hospital?	e. When was this? Please give approximate date
☐ Clinic ☐ CHC ☐ Hospital ☐ Traditional Healer ☐ GP ☐ Other Name: _____ ☐ Unsure	☐ Cough ☐ Wheeze ☐ Chest Infection ☐ Diarrhoea ☐ Poor weight gain ☐ Poor feeding ☐ Rash ☐ Other Name: _____ ☐ Unsure	☐ Antibiotics ☐ Cough syrup ☐ Inhaler ☐ Oxygen ☐ Oral fluids ☐ Fluid by drip/IV ☐ Cream/Ointment ☐ Other Name: _____ ☐ Unsure	☐ Yes ☐ No ☐ Unsure	DD : _____ MMM: _____ YYYY : _____
☐ Clinic ☐ CHC ☐ Hospital ☐ Traditional Healer ☐ GP ☐ Other Name: _____ ☐ Unsure	☐ Cough ☐ Wheeze ☐ Chest Infection ☐ Diarrhoea ☐ Poor weight gain ☐ Poor feeding ☐ Rash ☐ Other Name: _____ ☐ Unsure	☐ Antibiotics ☐ Cough syrup ☐ Inhaler ☐ Oxygen ☐ Oral fluids ☐ Fluid by drip/IV ☐ Cream/Ointment ☐ Other Name: _____ ☐ Unsure	☐ Yes ☐ No ☐ Unsure	DD : _____ MMM: _____ YYYY : _____

a. Where was baby seen? Select **ALL** that apply	b. What was the diagnosis? Select **ALL** that apply	c. What treatment did baby receive? Select **ALL** that apply	d. Did the baby have to sleep in the hospital?	e. When was this? Please give approximate date
☐ Clinic ☐ CHC ☐ Hospital ☐ Traditional Healer ☐ GP ☐ Other Name: ___________ ☐ Unsure	☐ Cough ☐ Wheeze ☐ Chest Infection ☐ Diarrhoea ☐ Poor weight gain ☐ Poor feeding ☐ Rash ☐ Other Name: ___________ ☐ Unsure	☐ Antibiotics ☐ Cough syrup ☐ Inhaler ☐ Oxygen ☐ Oral fluids ☐ Fluid by drip/IV ☐ Cream/Ointment ☐ Other Name: ___________ ☐ Unsure	☐ Yes ☐ No ☐ Unsure	DD : ___________ MMM: ___________ YYYY : ___________
☐ Clinic ☐ CHC ☐ Hospital ☐ Traditional Healer ☐ GP ☐ Other Name: ___________ ☐ Unsure	☐ Cough ☐ Wheeze ☐ Chest Infection ☐ Diarrhoea ☐ Poor weight gain ☐ Poor feeding ☐ Rash ☐ Other Name: ___________ ☐ Unsure	☐ Antibiotics ☐ Cough syrup ☐ Inhaler ☐ Oxygen ☐ Oral fluids ☐ Fluid by drip/IV ☐ Cream/Ointment ☐ Other Name: ___________ ☐ Unsure	☐ Yes ☐ No ☐ Unsure	DD : ___________ MMM: ___________ YYYY : ___________
☐ Clinic ☐ CHC ☐ Hospital ☐ Traditional Healer ☐ GP ☐ Other Name: ___________ ☐ Unsure	☐ Cough ☐ Wheeze ☐ Chest Infection ☐ Diarrhoea ☐ Poor weight gain ☐ Poor feeding ☐ Rash ☐ Other Name: ___________ ☐ Unsure	☐ Antibiotics ☐ Cough syrup ☐ Inhaler ☐ Oxygen ☐ Oral fluids ☐ Fluid by drip/IV ☐ Cream/Ointment ☐ Other Name: ___________ ☐ Unsure	☐ Yes ☐ No ☐ Unsure	DD : ___________ MMM: ___________ YYYY : ___________

HIV	
23. Has your baby had a HIV test **since born**?	☐ Yes ☐ No → **Skip to Q28** ☐ Unsure → **Skip to Q28**
24. What was the date of the test?	_____ /_____ /_____ DD MMM YYYY ☐ Unsure
25. What was the result of the test?	☐ HIV-positive ☐ Awaiting results → **Skip to Q28** ***Note: Check results at Room 21 at the MOU*** ☐ HIV-negative → **Skip to Q28** ☐ Unknown → **Skip to Q28**
26. Has your baby been started on Antiretrovirals (ART)? **PLEASE Note: This is not referring to the NVP prophylaxis, but to full treatment from the paediatric ART team at the CHC.**	☐ Yes, please specify date: _____ /_____ /_____ → **Skip to Q28** DD MMM YYYY ☐ No- Baby is HIV-positive but not yet on ART ☐ Unsure → **Skip to Q28**
27. Why not? Select **ALL** that apply ***If baby is HIV-positive but has not yet started ART, please follow-up why not and refer urgently.**	☐ Not yet referred to ART clinic ☐ Mother does not want baby to have ART ☐ Mother has not yet been able to go to ART clinic ☐ Doctors/nurses are waiting for blood results ☐ Other, Specify: _____ ☐ Unsure
TUBERCULOSIS (TB)	
28. **Since birth**, has anyone tested your baby for TB?	☐ Yes ☐ No → **Skip to END** ☐ Unsure → **Skip to END**
29. When was the baby tested for TB?	_____ /_____ /_____ DD MMM YYYY

30. At which clinic/hospital was the baby tested?	☐ Red Cross Children's Hospital ☐ Groote Schuur Hospital ☐ New Somerset Hospital ☐ Clinic Name of clinic: _____ ☐ Other, specify: _____ ☐ Unsure
31. What was the result of the test?	☐ Baby does not have TB and does not need medicine ☐ Baby does not have TB but needs medicine to prevent TB ☐ Baby does have TB and needs medicine to treat TB ☐ Other, Specify: _____ ☐ Unsure
32. Did a doctor or nurse tell you that your baby has TB?	☐ Yes → **Skip to Q34** ☐ No
33. **Since born**, has the baby been given any TB prevention medication? **Note: Even if the baby does not have TB, if an adult close by has TB, the baby may be receiving medicine to protect the baby from getting TB; this medicine is called Isoniazid (INH).**	☐ Yes, the baby has been given INH TB prevention ☐ Yes, the baby has been given full TB treatment ☐ Other, Specify: _____ ☐ No, the baby has not had ANY TB medicine →**Skip to END** ☐ Unsure → **Skip to END**
34. When did the baby start the TB medicine (Full treatment **or** INH)?	_____ /_____ /_____ DD MMM YYYY
35. From where does your baby receive the TB medicine? (Full treatment **or** INH)?	Name of Hospital/Clinic: _____

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

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

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

Appendix D: Ethics Approval Forms

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

19 October 2023

HREC REF: 764/2023

A/Prof U Mehta
Division of Public Health Medicine
Falmouth Building-FHS
Email: ushma.mehta@uct.ac.za
Student: MLNHIL002@myuct.ac.za

Dear A/Prof Mehta

PROJECT TITLE: A COMPARATIVE ANALYSIS OF THE MEDICINE USE AND EXPOSURES IN INFANTS WHO ARE HIV EXPOSED UNINFECTED AND HIV UNEXPOSED UNINFECTED IN THE FIRST YEAR IN CAPE TOWN, SOUTH AFRICA-SUB-STUDY LINKED TO 541/2015; 749/2015; 197/2020-
(MASTERS CANDIDATE-MS HILKKA M'LUNGA)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 October 2024.

You are required to submit a progress report form, using the standardised Annual Report Form (FHS016) or (FHS017) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Ms Hilkka M'Lunga will also be involved in this study.

Please quote HREC REF 764/2023 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007

HREC/ref 764.2023

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC/ref 764.2023

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

HUMAN RESEARCH ETHICS COMMITTEE 26 AUG 2020 HEALTH SCIENCES FACULTY UNIVERSITY OF CAPE TOWN

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	30.8.21
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	28/8/2020

Note: Please note that incomplete submissions will not be reviewed.
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

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)			
HREC REF Number	749/2015	Current Ethics Approval was granted until	30/08/2020
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?		x Yes ☐ No	
If yes, could you please provide the HREC Ref's for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study.		HREC REF: 541/2015 (separate FHS016 enclosed)	
Principal Investigator	Professor Andrew Boulle		

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

Department / Office Internal Mail Address	Centre for Infectious Disease Epidemiology & Research, School of Public Health & Family Medicine, 5th floor Falmouth Building, UCT FFHS, Anzio Road

1.1 Does this protocol receive US Federal funding?	x Yes	☐ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval? **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-enquiries@uct.ac.za)	☐ Yes	x No
If yes in 1.2 please complete section 1.3 below for invoicing purposes		
1.3 Annual Approval for **full committee** review	- R 3450 (inclusive of vat)	

For invoicing purposes, please provide:	
Sponsor's name	
Contact person	
Address	
Telephone number	
Email Address	

2. List of documentation for approval

N/A

3. Protocol status (tick ✓)

x	Open to enrolment PER
x	Closed to enrolment (tick ✓) Cohort
x	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

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

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
224 participants did not complete all 4 postnatal visits (last visit at 12 months postnatal), mainly because they relocated out of the area. However, 699 completed at least 1 ante- and postnatal visit. The last study visit was scheduled for end of February 2020 and further retention attempts were disrupted by the SARS-CoV-2 pandemic and subsequent lockdown.	
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	0

7. Progress of study

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

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)

x	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
x	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.
6 maternal deaths • 1 car crash • 1 kidney failure • 3 "sick" – no further details provided • 1 unknown Unrelated to study procedures.

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	x Not applicable

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

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	x Not applicable

11.2 Did a Data and Safety Monitoring Board publish a report?		
☐ Yes	☐ No	x 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	x 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
x	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.

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

13. 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	x No
If yes, please explain and if necessary, attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form FHS013):	

14. Signature

My signature certifies that the above is complete and correct.			
Signature of PI	Boulle	Date	29 July 2020

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

13. 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	x No
If yes, please explain and if necessary, attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form FHS013):	

14. Signature

My signature certifies that the above is complete and correct.			
Signature of PI		Date	29 July 2020

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

Appendix E: Supplementary Material

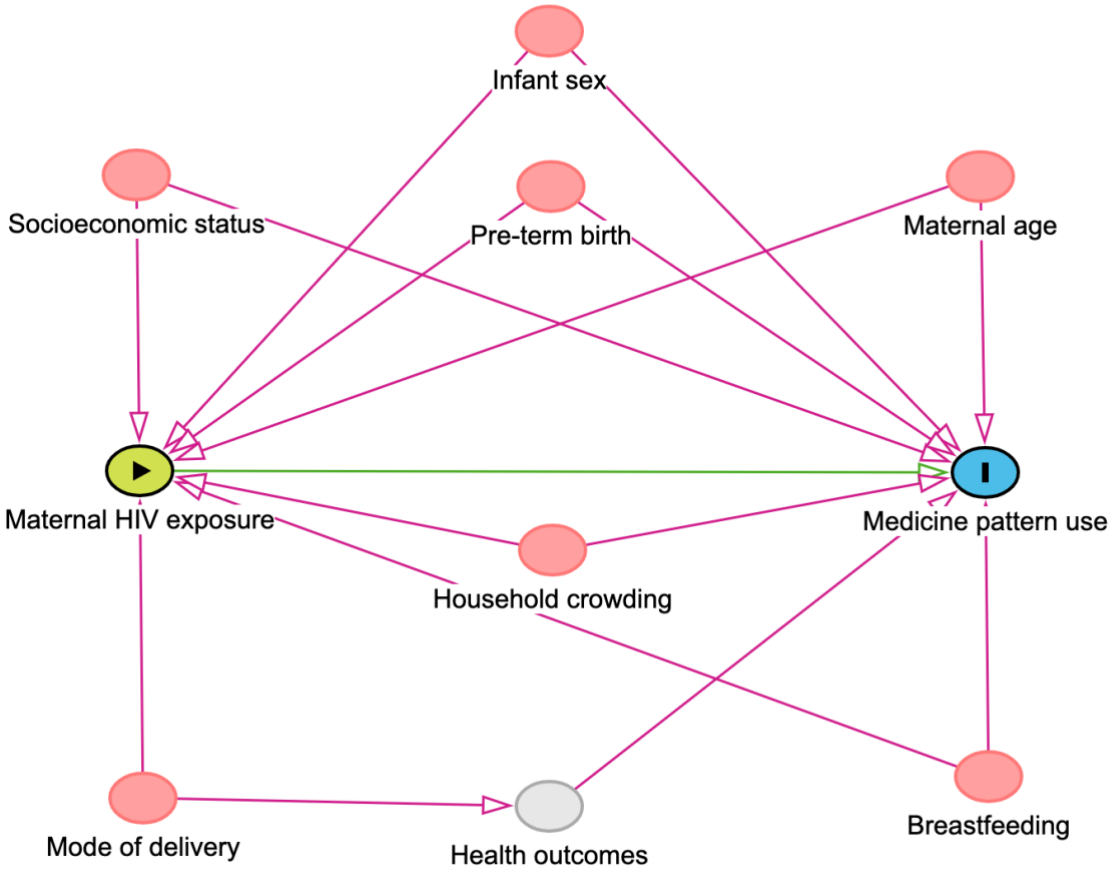

Figure 5: *Directed Acyclic Graph (DAG) illustrating the causal relationships between the impact of maternal HIV status exposure (infants who are HEU and HUU - green), mediator (ever breastfed - blue), confounders (like maternal age, pre-term birth, infant sex, mode of delivery and socioeconomic status-pink), and the outcome (medication pattern usage- blue) observed in the infants within the study's scope.*

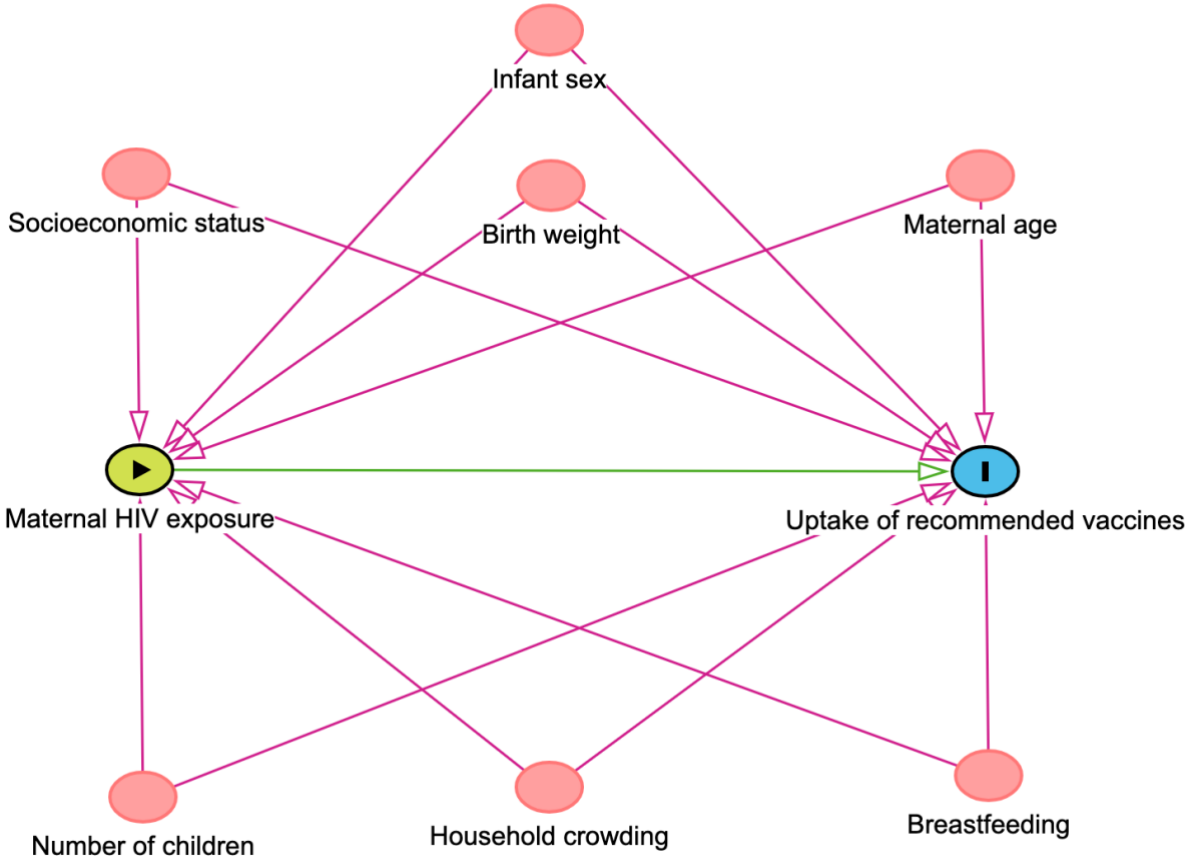

Figure 6: *Directed Acyclic Graph (DAG) illustrating the causal relationship between the impact of maternal HIV Status exposure (Infants who are HEU and HUU - green), confounders (like maternal age, birthweight, breastfeeding, household size, number of children, infant sex, and socioeconomic status - pink), and outcome (uptake of recommended vaccines- blue) observed in the infants within the cohort.*

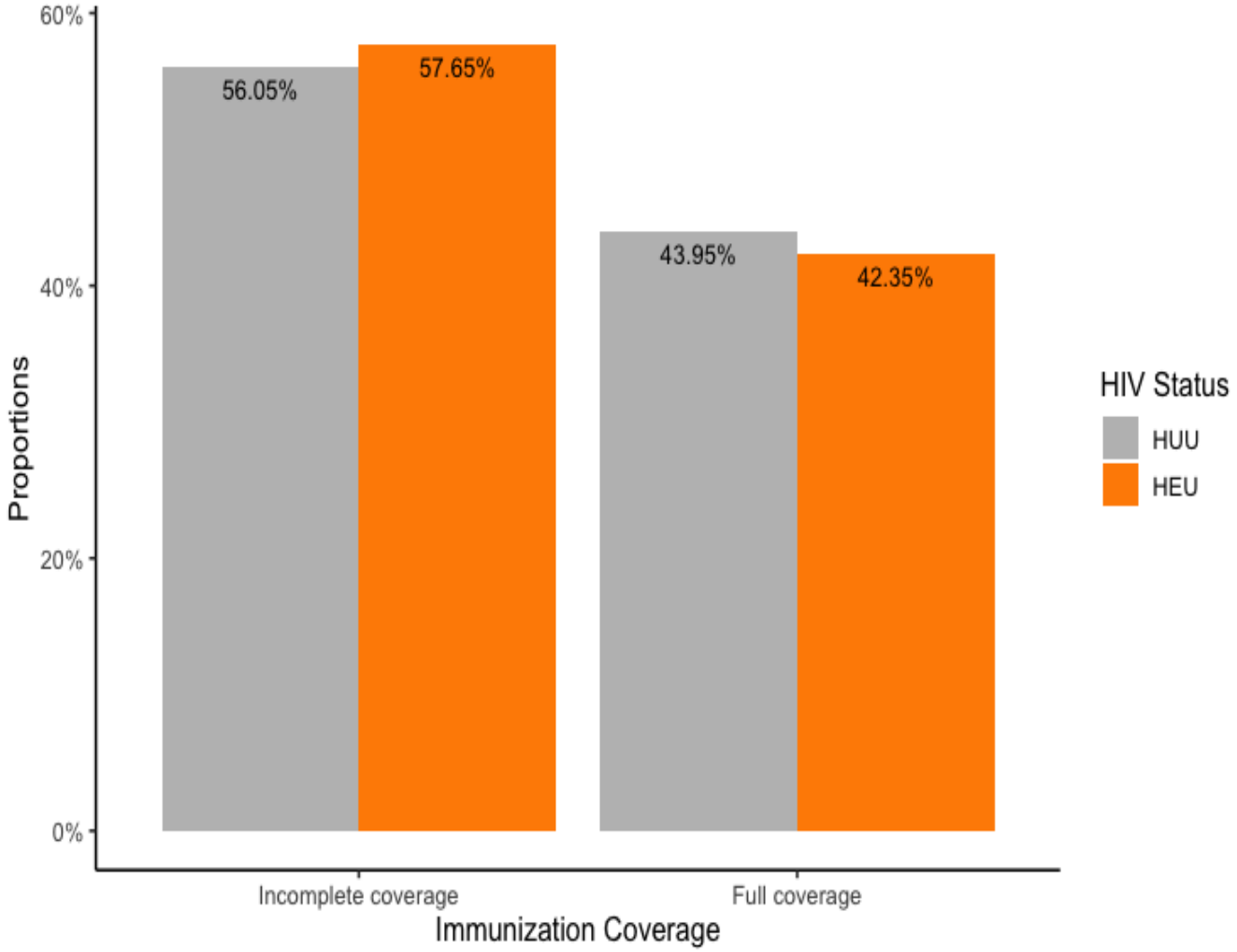

Figure 7: *Compares the vaccine coverage among infants who are HUU and HEU in their first year of life. This plot highlights the distribution of the vaccination status among infants who are HEU and HUU, allowing for a clearer comparison between full and incomplete vaccine coverage.*

Appendix F: Maternal and Child Health Journal Guidelines

Maternal Child Health Journal

Instructions for Authors

Editorial Procedure

Double-Blind Peer Review

All manuscripts are anonymously reviewed. Each copy of a manuscript should include a separate title page with authors' names and affiliations, and these should not appear elsewhere in the manuscript. Footnotes that identify the authors should be typed on a separate page. Authors should make every effort to ensure that the manuscript contains no clues to their identities.

When you are ready to submit a manuscript to MCHJ, please be sure to upload these 2 separate files to the Editorial Manager site to ensure timely processing and review of your paper:

- A title page with the running head, manuscript title, and complete author information. Followed by (page break) the Abstract page with keywords, significance, and the corresponding author e-mail information.
- The blinded abstract and manuscript containing no author information (no name, no affiliation, and so forth) which adheres to all standards described below.

Two-tiered Review Process

The MCHJ implements a two-tiered review process. Manuscripts are first reviewed by an Editorial Board member for suitability for the Journal, general quality, and potential contribution. Editorial Board members then recommend further peer review, or rejection. Those papers recommended for full peer review are then sent for review to appropriate reviewers.

Authors should note that only papers of the very highest quality and importance to the field of maternal and child health will be considered for the Journal.

Time to Review from Submission

As a matter of equity and fairness to all authors, the policy of the Journal Editorial Board is to work through the queue in sequence. The Journal cannot prioritize authors based on their queries. Reviewers are selected deliberately to match each paper, which is a process that takes some time to ensure that each paper is handled equitably.

Reviewers are given several weeks from the initial invitation to review until the due date for the review. If a reviewer does not respond to the initial invitation, another reviewer is chosen. In the case where multiple reviewers are invited to review a paper, authors can expect a long delay before receiving news of the decision regarding their article. The Journal requires three detailed reviews to be received before a decision can be made.

Authors will be asked to classify their article in the Editorial Manager site. These classifications are crucial to the choice of reviewers for the article. The Journal encourages authors to choose classification categories with care to expedite the review process.

If the paper has significant grammar or stylistic concerns, authors will be encouraged to utilize a service such as Edanz as no copy-editing support from the publisher is available to the editors. Authors should carefully proof-read their submissions or ask colleagues to assist.

To expedite the review of your submission, please ensure that your manuscript conforms to the format details outlined below. Submissions in another format will be returned to the author for correction before proceeding to the peer review process.

Resubmission Review Process

As a matter of equity and fairness to all authors, the policy of the Journal Editorial Board is to work through the resubmitted paper queue in sequence. The Journal cannot prioritize authors based on their queries. Reviewers are selected deliberately to match each paper, which is a process that takes some time to ensure that each paper is handled equitably.

The editors of the Journal recommend that authors respond thoughtfully to the recommendations of the reviewers, carefully check their grammar and spelling, and ensure that their paper conforms to the guidelines below. The original reviewers will often be invited to review the resubmitted paper. Authors should document their changes thoroughly and explain whether they made suggested changes or declined to make those changes and why. Additional reviewers may also be invited to review the resubmitted article.

If the paper has significant grammar or stylistic concerns, authors will be encouraged to utilize a service such as Edanz as no copy-editing support from the publisher is available to the editors. Authors should carefully proof-read their submissions or ask colleagues to assist.

Page Charges

The journal makes no page charges. Reprints are available to authors, and order forms with the current price schedule are sent with proofs.

- Springer Open Choice

  In addition to the normal publication process (whereby an article is submitted to the journal and access to that article is granted to customers who have purchased a subscription), Springer now provides an alternative publishing option: Springer Open Choice. A Springer Open Choice article receives all the benefits of a regular subscription based article, but in addition is made available publicly through Springer's online platform SpringerLink. To publish via Springer Open Choice, upon acceptance please visit the link below to complete the relevant order form and provide the required payment information. Payment must be received in full before publication or articles will publish as regular subscription model articles. We regret that Springer Open Choice cannot be ordered for published articles.
  www.springeronline.com/openchoice

  Publishing Open Choice involves an open access publication fee of US$ 3000/EUR 2200 (excl. VAT). You can choose to pay by credit card or to receive an invoice.

  Customers providing payment from the Americas will be charged in US$ sales tax will be charged if applicable. Customers providing payment from Europe, Africa, and Asia will be charged in EUR. VAT is not included in the price and will be added, at a standard rate, if applicable.

- NIH Open Access Policy

  If you receive research funding from the US National Institutes of Health (NIH), you will be required to deposit the final manuscript of your journal articles in PubMed Central and ensure their free availability (open access) within 12 months of publication. Springer complies with the NIH Open Access Policy using Method B. Please indicate your NIH funding when submitting your article for consideration to ensure that your article will be made available.

  If you would rather have your article made available immediately or if your funding is from another source and you want to ensure access, please choose Springer Open Choice.

  For more on the NIH Open Access Policy, please visit
  http://publicaccess.nih.gov/index.htm

Changes to Accepted Papers

Once a paper is accepted and the final proofs are approved, no changes can be made to the final version. Any changes must be submitted as erratum. Please carefully check your paper to ensure accuracy.

Types of Papers

The Journal is interested in original research in the area of maternal and child health, both within the US and from other countries. As this is primarily a journal devoted to population health, we are not interested in clinical case studies, in papers that are exclusively clinically focused, or in research that does not have an obvious public health focus. Research or practice-based articles from communities within the United States and from countries outside the US are welcome as long as they address issues of maternal and child health that will be of interest to more than a local audience.

Manuscripts of the following types are welcome:

Original Research reports (3500 word limit) results from an empirical research study, whether quantitative or qualitative, on a focused topic, presented consistent with international guidelines for research reporting (see http://www.equator-network.org/reporting-guidelines). *Original Research* may also take the format of a systematic review.

Reviews on specific, defined topics (3500 word limit) are welcome if they are systematic and reported in a standardized format. When justified, Reviews may exceed 35 references. Reporting guidelines have been developed for different study designs. The Journal encourages authors to follow these guidelines because they help authors describe the study in enough detail for it to be evaluated by editors, reviewers, readers, and other researchers evaluating the medical literature. Authors of review manuscripts are encouraged to describe the methods used for locating, selecting, extracting, and synthesizing data; this is mandatory for systematic reviews. The Journal encourages authors to utilize the following standards:

For Observational Studies: STROBE http://strobe-statement.org/

For Qualitative Studies: COREQ http://www.equator-network.org/reporting-guidelines/coreq/

For Systematic Reviews and Meta-Analyses: PRISMA http://prisma-statement.org/

For Randomized Trials: CONSORT http://www.consort-statement.org/

For Quality Improvement in Healthcare: SQUIRE http://squire-statement.org/

Other guidelines are available here:
http://www.nlm.nih.gov/services/research_report_guide.html

For additional information, see http://www.equator-network.org/reporting-guidelines/

An example of an *Original Research* article is "New Evidence on Breastfeeding and Postpartum Depression: The Importance of Understanding Women's Intentions" by Cristina Borra, Maria Iacovou, Almudena Sevilla which is available here:
http://link.springer.com/article/10.1007%2Fs10995-014-1591-z

Another example is "Complex Calculations: How Drug Use During Pregnancy Becomes a Barrier to Prenatal Care" by Sarah C. M. Roberts and Cheri Pies available here:
http://link.springer.com/article/10.1007/s10995-010-0594-7

From the Field articles (2500 word limit) report novel programs, policies, or interventions of interest to a general maternal and child health audience, and may reflect evaluations, assessments, or other systematic description. *From the Field* articles may share a local experience that has potential

applicability to other communities. Authors are encouraged to describe the context clearly to ensure readers in other areas understand what is important and what has changed. Specific types of *From the Field* articles might include:

Field or practice-based articles (2500 word limit) that describe new models, demonstrate the effectiveness of new or modified interventions, discuss the development or impact of new policies, or evaluate large or small-scale programs.

Methodological Notes (2500 word limit) report upon focused, specific methodological issues of interest to maternal and child health researchers and practitioners, and can address qualitative, quantitative, policy, or other research modalities. Methodological notes may describe innovations in data gathering, measurement, study design, assessment and evaluation.

Professional Development manuscripts (2500 word limit) present systematic descriptions and analyses of aspects of maternal and child health career paths, skills, leadership, and training.

Policy Briefs (2500 word limit) describe the development and/or implementation of particular policies at any level of administration that may relate to maternal and child health.

Brief Reports (2500 word limit) are short analyses of specific topics, usually reflecting the results of empirical research of general interest.

Graduate Education pieces (2500 word limit) describe novel educational curricula development, educational interventions, or evaluations, broadly useful to maternal and child health and related fields.

Historical Notes (2500 word limit) present historical accounting and analysis of key developments in maternal and child health and may reflect aspects of clinical care, maternal and child health programming, education, or administration, or more general public health developments in the field.

An example of a *From the Field* article is "Routine Prenatal HIV Testing: Women's Concerns and Their Strategies for Addressing Concerns" by Pamela Rothpletz-Puglia, Deborah Storm, Carolyn Burr, and Deanne Samuels and is available here: http://link.springer.com/article/10.1007/s10995-011-0754-4.

Commentary or *Letters to the Editor* (2500 word limit) reflect a systematically presented opinion around a particular issue of maternal and child health interest, often promoting new ideas or directions. For specific guidance on how to prepare these, please see http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2647072/.

An example of a *Commentary* is "Racial and Ethnic Disparities in Birth Outcomes: A Life-Course Perspective" by Michael C. Lu and Neal Halfon and is available here: http://link.springer.com/article/10.1023/A%3A1022537516969

Article Length

As a general rule, the more concise the presentation, the better. Large-scale program evaluations, complex practice-based interventions, and some quantitative research may be allowed a few additional pages, if there is strong justification provided in a separate note to the editor. There is no need to repeat in text what is presented in tables and figures, and there is no need to repeat information from one section of the narrative to another.

- *Original Research* articles, which include *Review* articles, should be limited to 3500 words with no more than 35 references.

- *From the Field* and *Commentary* or *Letters to the Editor* should be limited to 2500 words with no more than 25 references.

Manuscript Submission

Submission is a representation that the manuscript has not been published previously and is not currently under consideration for publication elsewhere. A statement transferring copyright from the authors (or their employers, if they hold the copyright) to Springer will be required before the manuscript can be accepted for publication. The Editor will supply the necessary forms for this transfer. Such a written transfer of copyright, which previously was assumed to be implicit in the act of submitting a manuscript, is necessary under the U.S. Copyright Law in order for the publisher to carry through the dissemination of research results and reviews as widely and effectively as possible.

Permissions

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

Online Submission

Authors should submit their manuscripts online. Electronic submission substantially reduces the editorial processing and reviewing times and shortens overall publication times. Please follow the hyperlink "Submit online" on the right and upload all of your manuscript files following the instructions given on the screen.

Manuscripts should be submitted through the Editorial Manager Website for Maternal and Child Health Journal at: http://www.editorialmanager.com/maci/

APA Style

APA Publication Manual standards must be followed. Please visit http://www.apastyle.org/ for the guidelines.

Suggested Reviewers

Authors are asked to submit the names, current email addresses, and other contact information for three (3) suggested reviewers for their article. These potential reviewers should not be members of the authors' departments or institutions, must not have participated in writing, editing, or reviewing the submission, and should be qualified to address the topic of the article. The editors of the Journal reserve the right to invite the suggested reviewers or other reviewers.

Integrity of Research and Reporting

Ethical standards

Manuscripts submitted for publication must contain a statement to the effect that all human and animal studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

It should also be stated clearly in the text that all persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study should be omitted.

These statements should be described in the *Methods* or *Description* sections of submission. If these statements are not applicable, authors should state that the manuscript is not based upon clinical study or patient data.

The editors reserve the right to reject manuscripts that do not comply with the above-mentioned requirements. The author will be held responsible for false statements or failure to fulfill the above-mentioned requirements. Evidence of institutional review and approval may be requested if necessary.

Conflict of Interest

Authors must indicate whether or not they have a financial relationship with the organization that sponsored the research. This note should be added in a separate section before the reference list.

If no conflict exists, authors should state: The authors declare that they have no conflict of interest.

Formatting Requirements

Order of Manuscript Pages

- Title Page with all Author Contact Information and the corresponding author e-mail information.
- Blinded Abstract with Key Words and Significance Statement
- Blinded Manuscript
- Author Acknowledgements (including funding sources)
- References
- Tables, figures, footnotes, and legends should appear as separate sheets appended to the end of the manuscript.
- Figure caption sheet

Title Page

The title page should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) and address(es) of the author(s)
- The e-mail address, telephone and fax numbers of the corresponding author

Abstract

A structured abstract of up to 250 words is to be provided. The abstract should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study participants, settings, measurements, analytical methods), main findings (giving specific effect sizes and their statistical and clinical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations, note important limitations, and not overinterpret findings.

Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to ensure that they accurately reflect the content of the article.

- For *Original Research* articles using the headings: Objectives, Methods, Results, and Conclusions for Practice.
- For *From the Field* articles use the headings: Purpose, Description, Assessment, and Conclusion.
- Another acceptable format for all article types is: Introduction, Methods, Results, and Discussion.

Significance

Directly after the Abstract, the author should include a short paragraph (100 words or less) titled "Significance" which addresses what is already known about the topic of their article and what their article adds to the literature.

For example, the following paragraphs were included in "The educational gradient in coronary heart disease: the association with cognition in a cohort of 57,279 male conscripts" by Inger Ariansen, Laust Mortensen, Jannicke Igland, Grethe S Tell, Kristian Tambs, Sidsel Graff-Iversen, Bjørn Heine Strand, and Øyvind Næss in *J Epidemiol Community Health* available here: http://jech.bmj.com/content/early/2014/11/13/jech-2014-204597.full.pdf+html

> "What is already known on this subject?
> The socioeconomic gradient in coronary heart disease may not be fully explained by social differences in cardiovascular risk factors. Cognitive ability has been proposed to impact this gradient independently of cardiovascular risk factors.
>
> "What this study adds?
> Adjustment for established cardiovascular disease risk factors substantially attenuated the educational gradient in coronary heart disease. Although the remaining unexplained gradient was not further attenuated by cognitive ability, cognitive ability alone moderately attenuated the educational gradient. This suggests that cognitive ability may be linked to coronary heart disease through risk factors."

Key Words

A list of 4–5 keywords is to be provided directly below the abstract. Key words should express the precise content of the manuscript as they are used for indexing purposes.

Ethical Statement Required

Reports of original empirical research and *From the Field* articles must include a statement in the *Methods* or *Discussion* section certifying that the research was conducted in accord with prevailing ethical principles and reviewed by an Institutional Review Board or explaining the rationale for departures from those principles. The editors reserve the right to reject any submission which does not include this statement.

See the APA Publication Manual (1994) pp. 292 298.

Sections of the Text

Introduction, Objectives, Purpose

Provide a context or background for the study (that is, the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation. Cite only directly pertinent references, and do not include data or conclusions from the work being reported.

Methods, Description

The guiding principle of the Methods section should be clarity about how and why a study was done in a particular way. The section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section.

A note on Statistics: Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals).

Results, Assessment

Present your results in logical sequence in the text, tables, and figures, giving the main or most important findings first. Do not repeat all the data in the tables or figures in the text; emphasize or summarize only the most important observations.

Discussion, Conclusions, Conclusions for Practice

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- This effect has been widely studied (Abbott 1991; Barakat et al. 1995; Kelso and Smith 1998; Medvec et al. 1999).

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- Online document

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