COMPARING HEALTH OUTCOMES IN INFANTS BORN TO MOTHERS INITIATED ON ART DURING PREGNANCY AND RANDOMISED TO RECEIVE POSTPARTUM ART SERVICES FROM PRIMARY HEALTH CARE FACILITIES OR ADHERENCE CLUBS

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DECLARATION

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ABSTRACT

Introduction: Adherence clubs (ACs) increase retention in care among postpartum women living with HIV. However, the effect of maternal antiretroviral therapy (ART) provision through ACs on infant health remains unknown.

Methods: This study utilised data from a parallel-arm randomised controlled trial that enrolled women who initiated ART during pregnancy, were within 70 days postpartum, and who met standard AC eligibility criteria (clinically stable and viral load <400 copies/mL). Consenting women were randomised to community-based ACs (n = 201) or routine primary healthcare (PHC) clinics (n = 194) for ART service delivery and followed for two years. Infant care was provided separately at "well baby" clinics. Outcome frequencies were calculated by summing the number of visits at which lower respiratory tract infection, diarrhoeal illness, care-seeking, and overnight hospitalisation were self-reported. Multivariate Poisson regression was then used to quantify the associations between each trial arm and study outcome, controlling for various maternal demographic and infant health covariates.

Results: Data were available for 395 mother-infant pairs, representing 1681 visits. There were 27 and 20 instances of lower respiratory tract infection and 60 and 55 occurrences of diarrhoeal illness in PHC and AC trial arms, respectively. Lower respiratory tract infection (aIRR 0.73; 95% CI 0.39–1.32) and diarrhoeal illness (aIRR 0.87; 95% CI 0.60–1.27) were self-reported at equivalent rates between trial arms. Mothers attending ACs were less likely to report seek care (205 *vs*. 247 times) for their infants compared to mothers receiving ART from PHC clinics (aIRR 0.80; 95% CI 0.66–0.97). Infants of mothers attending ACs were reported as being hospitalised less frequently (15 *vs*. 26 times) compared to those within the PHC study arm (aIRR 0.55; 95% CI 0.28–1.07; p value = *0.083*) but this was not statistically significant.

Conclusions: Occurrence of illness was similar in both groups. However, mothers receiving ART from ACs were less likely to access care for their infants than those receiving ART from PHC clinics. While this may reflect the increased care demands associated with community-based ART service delivery, further research is needed to clarify the mechanisms underlying these differences in care-seeking behaviour.

LIST OF ABBREVIATIONS

AC	Adherence club
AIDS	Acquired Immunodeficiency Syndrome
aIRR	Adjusted incidence rate ratio
ART	Antiretroviral therapy
ARV	Antiretroviral
CHC	Community Health Centre
CHW	Community health worker
CI	Confidence interval
DI	Diarrhoeal illness
DSD	Differentiated service delivery
HIV	Human Immunodeficiency Virus
IQR	Interquartile range
IRR	Incidence rate ratio
LRTI	Lower respiratory tract infection
MOU	Midwife Obstetric Unit
MTCT	Mother-to-child transmission
PACART	Postpartum adherence clubs for antiretroviral therapy
PHC	Primary healthcare
PLH	People living with HIV
PMTCT	Prevention of mother-to-child transmission
SOC	Standard of care
VL	Viral load
WLH	Women living with HIV

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

MANUSCRIPT

Comparing health outcomes in infants born to mothers initiated on ART during pregnancy and randomised to receive postpartum ART services from primary healthcare facilities or adherence clubs

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Keywords: HIV, differentiated service delivery, adherence clubs, retention in care.

INTRODUCTION

Without an effective vaccine or curative treatment, successful management of Human Immunodeficiency Virus (HIV) infection requires rapid diagnosis, long-term treatment, and viral suppression among people living with HIV (PLH) [1]. Despite not hitting all 90–90–90 targets by 2020 – that is, the percentages of individuals who know their status, are receiving antiretroviral therapy (ART), and who are virologically suppressed while on ART – the drive to end AIDS by 2030 has necessitated updating these targets to 95–95–95 by 2025 [2]. It is evident, however, that a "one-size-fits-all" approach to HIV services will not sustainably provide access to ART among all vulnerable communities [3].

Globally, pregnant and postpartum women living with HIV (WLH) represent a key vulnerable population for whom ART-services need to be tailored. Early motherhood is associated with social, economic, physiological, and psychological changes that promote high levels of healthcare disengagement, including loss to follow-up and reduced adherence to treatment [4-9]. Poor treatment adherence results in the development of viremia, which, in turn, increases the risk of mother-to-child transmission (MTCT) of HIV during breastfeeding as well as leading to adverse maternal health outcomes [10-13].

The current standard of care (SOC) provides ART services at primary healthcare (PHC) facilities [14]. This includes visits once a month for the first four months, followed by regular visits for ART collection every two months. Due to the scale of the HIV/AIDS epidemic in South Africa, the frequency and centralization of ART collection overwhelm PHC facilities and promote disengagement of patients from the health system [15]. This effect is pronounced among vulnerable populations [9].

One potential alternative to the current SOC, differentiated service delivery (DSD), is a patient-centred approach intended to simplify and adapt HIV services at all levels to better serve PLH [16]. Adherence clubs (AC) are the primary form of DSD in South Africa. They involve groups of 20–30 patients meeting every two months for 60 minutes at community venues, where community health workers lead guided health discussions and provide pre-packaged ART [14, 17]. ACs are designed to reduce the burden of chronic HIV-care on clinically stable PLH and PHC facilities [15, 18]. They typically provide ART services to low-risk clinically stable adults who have been on ART for at least six months, have a suppressed viral load (<400 copies/mL), and have no comorbidities necessitating more extensive clinical follow up [14, 17]. Until recently, however, limited data existed that demonstrated the effectiveness of ACs among pregnant and postpartum women.

The Postpartum Adherence Clubs for Antiretroviral Therapy (PACART) trial sought to investigate if the scope of ACs could be increased to include women initiating ART during pregnancy. This was done by comparing the incidence of healthcare disengagement and viremia between mothers randomised to ACs (intervention arm) or SOC (control arm) [14]. ACs were well accepted and improved ART-service engagement, thereby reducing the risk of viremia in women through 24 months postpartum compared to women in the SOC trial arm [19, 20]. Although these data strongly support the use of ACs among postpartum women, no specific provisions for infant care were made in this study [14]. In both trial arms, infant care was provided per the SOC at well-baby clinics rather than being integrated into ART services at PHC facilities or ACs [19]. Well-baby clinics may or may not have been located at the same health facilities where mothers in the SOC arm received HIV care. However, the venues where mothers in the AC arm received treatment were always different from the well-baby clinics, as these participants received treatment at community venues.

Provision of care to infants is an important consideration. Although the effect of in-utero ART exposure on infant outcomes remains a matter of debate [21], exposure to HIV and/or ARVs *in utero* has been associated with adverse health outcomes; including small-for-gestational age infants with a higher risk of severe respiratory tract infections and mortality during their first year [5, 22-27]. Factors that prevent or delay care-seeking and HIV-testing severely impact infant health [28, 29], whereas simplifying postpartum care through service integration (*e.g.*, ART provision) improves infant health outcomes [30, 31]. ART service delivery through community-based ACs modified the standard requirements for care-seeking, which may over-burden mothers and negatively impact infant health. Therefore, we investigated the effect of providing ART to clinically stable WLH through ACs on infant health by comparing the frequency of infant symptoms, maternal care-seeking, and infant hospitalisations between the PACART trial arms across the 24-month postpartum period.

METHODS

Ethical review

Women who provided written informed consent for the PACART trial were eligible for inclusion into this secondary analysis. Ethical approval for this secondary analysis was obtained from the Human Research Ethics Committee of the University of Cape Town (REF: 424/2024).

Study design

The study was secondary analysis of data already collected during the PACART trial [14, 19]. Briefly, the PACART trial – a pragmatic randomised controlled trial – was conducted between January 2016 and August 2019 and sought to compare two strategies for ART service delivery among women initiated onto ART during pregnancy.

All consenting postpartum women attending the Midwife Obstetric Unit at the Gugulethu Community Health Centre who had initiated ART during pregnancy and met the eligibility criteria were enrolled in the trial. Mother-infant pairs were randomly allocated (1:1) to either the current SOC for ART services (control group) or to community-based ART services at ACs (intervention group). In addition to standard AC admission criteria – including having a suppressed viral load (<400 copies/mL) and no comorbidities necessitating more extensive clinical follow up [14, 17] – eligibility included being ≥18 years old and within 70 days postpartum.

General adult ART services – control

Per routine care, postpartum women are referred from the Midwife Obstetric Unit to a PHC facility for general adult ART care. These women usually present to the PHC facility within one month of referral. This includes visits for clinical assessment once a month for the first four months, followed by regular visits for ART collection every two months. Three months of medication are dispensed over the December holiday period. Except for individuals with clinical or psychological concerns, clinical screening occurs six monthly. Once ART has been initiated, routine laboratory investigations occur at four and 12 months and annually thereafter.

Adherence clubs – intervention

ACs involve groups of 20–30 patients meeting every two months for 60 minutes at community venues, where community health workers lead guided health-related discussions [14, 17]. Four months of medication are dispensed over the December holiday period. Participants are weighed, screened for symptoms, and receive ART during regular visits and have an annual viral load and general clinical assessment by a visiting nurse from the Gugulethu Community Health Centre. If patients have lost weight, are symptomatic, have an elevated viral load, or have failed to collect their ART within five days of any visit, they are immediately referred to the general ART clinic associated with the AC [17]. Except for clinical visits, patients can periodically opt to send a "buddy" (*i.e.,* a partner, friend, or relative) to attend club visits and collect their medication, however, patients must attend every second session.

In both trial arms, infants were referred to the well-baby child health services that are provided at PHC facilities per the SOC.

Measurements

Study visits – at which questionnaires were administered, and biological samples were collected – were scheduled separately to visits at Department of Health facilities at which participants received medical care in both arms. Study visits were scheduled at approximately three, six, 12, 18 and 24 months postpartum (recorded as visits 2–6, with visit 1 representing baseline). Questionnaires were administered at every study visit by trained interviewers in the participant's preferred language (either English or isiXhosa) [14]. For this secondary analysis, previously validated questionnaires were utilised that collected information on maternal and infant demographics, maternal and infant medical history, maternal ART adherence, and infant feeding [32].

Infant HIV status was self-reported and analysed as part of the primary study. No vertical transmission of HIV was observed through 24 months postpartum.

Outcomes

Lower respiratory tract infections and diarrhoea are major causes of childhood morbidity and mortality [33, 34] and are commonly used outcomes to assess child health [35, 36]. In line with le Roux *et al.*, the occurrence of a lower respiratory tract infection (LRTI) was defined as the self-reported presence of both cough and fever as well as wheeze, while the occurrence of a diarrhoeal illness (DI) was defined as increased or loose stools [32]. Reports of LRTI and DI were only considered within two weeks of each study visit [32]. Limiting the recall period for these outcomes was done to minimise bias [37].

To assess the frequency with which mother-infant pairs engaged with the health system, study visits reporting any care-seeking were counted. This included any consultation at a healthcare facility for treatment or advice about an illness occurring between study visits. Facilities included clinics, community health centres, hospitals, traditional healers, and pharmacies. The facilities attended and the diagnoses received were recorded and reported on separately.

To assess the severity of infant health outcomes, any overnight hospital stay that occurred between visits was recorded. Reporting of care-seeking and hospitalisation were not limited to within two weeks of each study visit as longer periods of recall are preferable for aggregate measures, such as hospitalisation [37].

Data analysis

Data were analysed in RStudio using R version 4.3.3 [38, 39]. Baseline characteristics were summarised as numbers and percentages (categorical), medians with interquartile ranges (continuous, non-symmetrical), or means with standard deviations (continuous, symmetrical). These data were compared between trial arms using Fisher's Exact Tests for categorical variables or Wilcoxon Rank Sum Tests for asymmetrical continuous data. A t-test was used for comparing symmetrical continuous data between trial arms. An alpha level of 0.05 was used to define statistical significance.

The two-year frequency of all study outcomes (LRTI, DI, care-seeking, and overnight hospital stay) was calculated by summing the number of reported events across all visits. Poisson regression was used to compare the frequency at which each outcome occurred, while using the total time observed per participant as a model offset. Baseline demographic variables that had borderline differences between groups (i.e., p value ≤ 0.1) as well as breast-feeding duration [32, 40] and birthweight [22, 41] – which are important determinants of infant health – were included in subsequent analyses. This was done to control for possible confounding effects. Suffering from a DI is an independent risk factor of pneumonia in infants [42]. As such, the effect of DI on LRTI was also assessed. For each Poisson regression model, the mean and variance were compared to ensure model appropriateness.

RESULTS:

Screening and enrolment for the PACART study occurred between January 2016 and December 2017, with 409 mothers included in the modified intention-to-treat population [19]. In this secondary analysis, infant health data were available from at least one follow-up visit among 401 mother-infant pairs (1878 visits, median = 6 visits per mother-infant pair). When asked about infant health outcomes, mothers were more likely to respond "no" or "unsure" if the infant was living elsewhere (Table S1–S4). As such, visits where the mother-infant pairs were living separately were excluded (Table S5), leaving 395 mothers (1681 visits) in the study sample (Table 1).

Characteristics at enrolment

Overall, 41% of women were married or cohabiting with a partner, 30% had completed any secondary education, 31% were currently working or studying, 42% lived in formal housing, and 25% were primiparous. The median time postpartum was 11 days (IQR, 14), with 63% of births by

Table 1: Characteristics at enrolment. N, % unless otherwise specified.

Variable	Clinic	Club	Total	P value
Study arm	194(49.1)	201 (50.9)	395 (100)	
Married or cohabiting with a partner	70 (36.1)	91 (45.3)	161 (40.8)	*0.067*
Completed any secondary education	65 (33.5)	55 (27.3)	120 (30.4)	0.191
Currently working/studying	64 (33.0)	57 (28.4)	121 (30.6)	0.327
Formal housing	82 (42.3)	85 (42.3)	167 (42.3)	1.000
Flush toilet inside home	83(42.8)	77 (38.3)	160 (40.5)	0.412
Running water inside home	101 (52.1)	111 (55.2)	212 (53.7)	0.546
Electricity inside home	184 (94.8)	190 (94.5)	374 (94.7)	1.000
Refrigerator inside home	156 (80.4)	160 (79.6)	315 (80.0)	0.900
Household crowding (≥10)	6 (3.1)	13 (6.5)	19 (4.8)	0.158
Primiparous	51 (26.3)	46 (22.9)	97 (24.6)	0.483
Delivery in hospital	126 (64.9)	112 (55.7)	238 (60.3)	*0.065*
Previously on ART	20 (10.3)	27 (13.4)	47 (11.9)	0.569
Previously experienced child loss	12 (6.2)	18 (9.0)	30 (7.6)	0.345
Normal vaginal delivery	116 (59.8)	133 (66.2)	249 (63.0)	0.211
Infant female sex	95 (49.0)	95 (47.3)	190 (48.1)	0.763
Breast feeding (ever)	187 (96.4)	196 (97.5)	383 (97.0)	0.569
Breast feeding at enrolment	167 (86.1)	176 (87.6)	343 (86.8)	0.681
Infant experienced symptoms* since birth	19 (9.8)	14 (7.0)	33 (8.4)	0.364
Infant referred to any health facility since birth	5 (2.6)	3 (1.5)	8 (2.0)	0.495
Median duration of ART in pregnancy (IQR), days	152 (72)	145 (70)	149 (71)	0.490
Median time postpartum (IQR), days	12 (16)	11 (13)	11 (14)	0.250
Mean reported birth weight (SD), grams	3105 (600)	3031 (534)	3067 (568)	0.199

*symptoms include at least one of the following: fever, cough, rash, diarrhoea; IQR: interquartile range; SD: standard deviation

normal vaginal delivery, and 87% of infants being breastfed at enrolment. On average, mothers were on ART for 149 days during pregnancy and the mean reported birthweight was 3067 g. Altogether, 8.4% of infants had experienced symptoms since birth (either fever, cough, rash, or diarrhoea), while 2.0% had been referred to any health facility prior to study enrolment.

Of the mother-infant pairs remaining in this secondary analysis, 194 and 201 were randomised to PHC and AC arms, respectively. Although none of the measured variables were significantly different between the trial arms, there were two noteworthy trends: mothers randomised to ACs were more likely to be married or cohabiting (45.3% *vs*. 36.1%, p = 0.067) and less likely to deliver in hospital (55.7% *vs*. 63.9%, p = 0.065) compared to mothers randomised to PHC.

Two-year frequency of LRTI and DI

Self-reporting of LRTI was less common than DI during the PACART study. There was a total of 27 and 20 LRTI cases reported by 22 and 19 mothers randomised to PHC and AC, respectively

(Figure 1A). DI episodes were reported on 60 and 55 occasions by 47 and 49 mothers randomised to PHC and AC, respectively (Figure 1B). Except for LRTI among mother-infant pairs randomised to ACs – where most instances occurred within the first year – no notable time trends in symptom reporting were present (Figure S1A & B). No differences were observed in the frequency of LRTI cases (aIRR 0.73; 95% CI 0.39–1.32) or instances of DI (aIRR 0.87; 95% CI 0.60–1.27) by study arm (AC vs PHC, Tables 2 & 3), suggesting that the mode of ART service delivery does not impact the frequency of self-reported LRTI or DI 24 months postpartum.

Table 2: Results of univariable and multivariable Poisson regression models assessing the association between trial arm and self-reported lower respiratory tract infection (LRTI) frequency, adjusting for baseline characteristics in the intention to treat population.

	Crude IRR	Adjusted IRR	P value
Study arm (AC vs PHC)	0.72 (0.4-1.27)	0.73 (0.39-1.32)	0.298
Relationship (other vs cohabiting)	1.28 (0.71-2.41)	1.49 (0.80-2.96)	0.228
Birth weight (low vs normal)	2.14 (1.00-4.17)	2.23 (1.04-4.36)	**0.027**
Breast feeding (>5 months vs ≤5 months)	1.02 (0.56-1.82)	0.98 (0.52-1.79)	0.950
Place of delivery (hospital vs other)	0.79 (0.45-1.42)	0.78 (0.43-1.44)	0.418

IRR: incidence rate ratio; AC: adherence club; PHC: primary health care; low birth weight < 2500g; AC (n = 201); PHC (n = 194)

Infants with low-birth weight were twice as likely (aIRR 2.23; 95% CI 1.04–4.36) to suffer from LRTI compared to infants of normal birth weight (Table 2). When accounting for ever having reported an episode of DI (Table S6), the relationship between low birth weight and LRTI frequency remained unchanged (aIRR 2.33; 95% CI 1.04–4.39), while there was an additional positive association (aIRR 2.54; 95% CI 1.39–4.60) between reporting DI and LRTI.

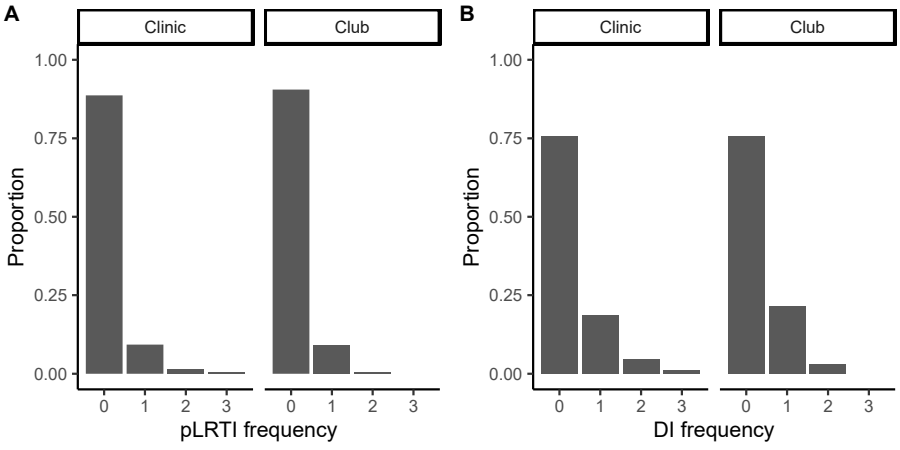

Figure 1: Two-year frequency of (A) presumed lower respiratory tract infections (pLRTI) and (B) diarrhoeal illness (DI).

Two-year frequency of care-seeking and overnight hospital stays

Mothers primarily sought care for their infants at a PHC clinics or CHCs (Table S7). Diarrhoea was the most reported diagnosis, followed by cough and lower respiratory tract infection (Table S8).

Care-seeking occurred most frequently between six and 18 months (Figure S2A), while overnight hospital stays were most common during the first 12 months (Figure S2B).

Table 3: Results of univariable and multivariable Poisson regression models assessing the association between trial arm and self-reported diarrhoeal illness (DI) frequency, adjusting for baseline characteristics in the intention to treat population.

	Crude IRR	Adjusted IRR	P value
Study arm (AC vs PHC)	0.89 (0.61-1.28)	0.87 (0.60-1.27)	0.477
Relationship (other vs cohabiting)	0.93 (0.64-1.35)	0.88 (0.61-1.29)	0.512
Birth weight (low vs normal)	1.02 (0.56-1.72)	1.06 (0.58-1.80)	0.837
Breast feeding (>5 months vs ≤5 months)	1.02 (0.70-1.48)	1.00 (0.68-1.46)	0.980
Place of delivery (hospital vs other)	0.83 (0.57-1.20)	0.80 (0.55-1.16)	0.232

IRR: incidence rate ratio; AC: adherence club; PHC: primary health care; low birth weight < 2500g; AC (n = 201); PHC (n = 194)

There were 247 and 205 visits at which care-seeking was reported over two years for mother-infant pairs randomised to PHC (n = 139 mothers) and AC (n = 128 mothers), respectively (Figure 2A). Mother-infant pairs randomised to receive ART through ACs were 20% less likely (aIRR 0.80; 95% CI 0.66–0.97) to report having sought any care between study visits, compared to those in the control arm (Table 4).

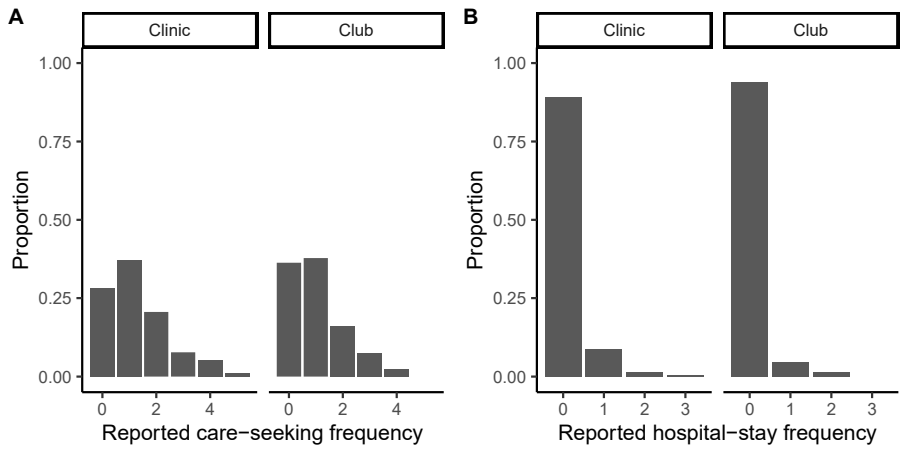

Figure 2: Two-year frequency of (A) care-seeking and (B) overnight hospital stays.

Only 41 overnight hospital stays were reported across 1681 visits (Figure 2B). Infants were hospitalised 26 and 15 times among 21 and 12 mothers randomised to PHC and AC study arms, respectively. Of those, lower respiratory tract infection (42%) was the most common diagnosis, followed by diarrhoea (21%) (Table S9). Infants of mothers randomised to ACs were 45% less likely (IRR 0.55; 95% CI 0.28–1.07; p value = 0.083) to require an overnight hospital stay between study visits compared to those in the PHC arm (Table 5) but this was not statistically significant.

Table 4: Results of univariable and multivariable Poisson regression models assessing the association between trial arm and care-seeking frequency, adjusting for baseline characteristics in the intention to treat population.

	Crude IRR	Adjusted IRR	P value
Study arm (AC vs PHC)	0.80 (0.67-0.96)	0.80 (0.66-0.97)	**0.022**
Relationship (other vs cohabiting)	1.05 (0.87-1.27)	1.07 (0.88-1.30)	0.522
Birth weight (low vs normal)	1.13 (0.85-1.48)	1.14 (0.86-1.49)	0.344
Breast feeding (>5 months vs ≤5 months)	0.89 (0.74-1.08)	0.87 (0.71-1.05)	0.154
Place of delivery (hospital vs other)	0.96 (0.80-1.17)	0.96 (0.79-1.17)	0.704

IRR: incidence rate ratio; AC: adherence club; PHC: primary health care; low birth weight < 2500g; AC (n = 201); PHC (n = 194)

Table 5: Results of univariable and multivariable Poisson regression models assessing the association between trial arm and overnight hospital stay frequency, adjusting for baseline characteristics in the intention to treat population.

	Crude IRR	Adjusted IRR	P value
Study arm (AC vs PHC)	0.56 (0.29-1.04)	0.55 (0.28-1.07)	*0.083*
Relationship (other vs cohabiting)	0.63 (0.34-1.17)	0.65 (0.34-1.25)	0.192
Birth weight (low vs normal)	1.14 (0.39-2.67)	1.21 (0.41-2.86)	0.695
Breast feeding (>5 months vs ≤5 months)	1.17 (0.62-2.16)	0.99 (0.50-1.90)	0.976
Place of delivery (hospital vs other)	0.74 (0.40-1.38)	0.75 (0.39-1.48)	0.404

IRR: incidence rate ratio; AC: adherence club; PHC: primary health care; low birth weight < 2500g; AC (n = 201); PHC (n = 194)

DISCUSSION

Ensuring the long-term engagement of postpartum women with ART services has proven exceptionally challenging [5]. Poor treatment adherence has profound consequences on long-term maternal health and vertical during breastfeeding [10-13]. The recent PACART trial demonstrated that ACs – a broadly implemented form of DSD in South Africa – effectively reduce healthcare disengagement of mothers initiating ART during pregnancy [19]. While the main study reported no differences in breastfeeding at six months, uptake of infant-HIV testing, vertical transmission of HIV (no infants were diagnosed with HIV upon the study's conclusion), or infant deaths between trial arms, this secondary analysis sought to compare the frequency at which infants experienced symptoms (LRTI and DI), mothers sought care for their infants, and infants were hospitalised between the trial arms over a 24-month postpartum period. We found no differences between the two-year frequency of self-reported LRTI (aIRR 0.73; 95% CI 0.39–1.32) or DI (aIRR 0.87; 95% CI 0.60–1.27) between mother-infant pairs in each trial arm. However, women attending ACs were 20% less likely (aIRR 0.80; 95% CI 0.66–0.97) to seek any care, while their infants were almost 50% as likely to require an overnight hospital stay (IRR 0.55; 95% CI

0.28–1.07) compared to mother-infant pairs in SOC. These data warrant further research into the effects of ACs on mother-infant wellbeing.

Using self-reported symptoms as study outcomes represents a limitation of this research and may explain the similarity in symptom reporting between trial arms. However, multiple attempts were made to mitigate bias. Firstly, visits were excluded when mother-infant pairs were no longer cohabiting. Mothers who were living separately from their infants were more likely to respond either "no" or "unsure" when asked about the presence of symptoms compared to mothers cohabiting with their infants. Secondly, the self-reporting of symptoms was limited to within two weeks of each study visit. Although this reduced the number of possible outcomes, this time period was selected to reduce bias [37] and based on previous research [32]. Furthermore, the associations identified in this study – independently linking low birthweight and diarrhoea with an increased risk of LRTI – have been reported previously [25, 42]. We are confident, therefore, in the conclusion that service provision through ACs did not increase the frequency at which infants experienced symptoms compared to current standard of care.

Given the increased risk of adverse health outcomes among HIV-exposed but uninfected infants, it is important to mitigate factors that prevent or delay care-seeking and HIV-testing, as these severely impact on infant health, well-being, and risk of mortality [28, 29]. As the implementation of ACs among the intervention arm altered the standard approach to service delivery for this population, it was important to investigate what, if any, knock on effects this might have on care-seeking. While those in the ACs were less likely to seek care, ART service provision via ACs did not change the nature of care-seeking in this trial: mothers who sought care for their infants primarily attended PHC clinics or CHCs. While not affecting the internal validity of these results, there are two important considerations when interpreting these data: 1) participants in this study were recruited from PHC facilities within a periurban setting, and 2) psychosocial and systemic barriers to care-seeking exist across South Africa [43]. It is important that these factors are considered and accounted for before implementing ACs for ART service delivery among postpartum mothers across the country.

Interestingly, despite the lack of differences in symptom reporting and the similarity in diagnoses at care, mothers randomised to ACs were less likely to seek care for their infants compared to mothers in the control arm. It is difficult to determine whether this was due to mothers being overburdened by attending ACs and thus less likely to seek care, because of an increased perception of support while attending ACs, or because of all-round better infant health outcomes in the experimental arm. A further limitation of this study was the discrepant time intervals considered for symptom reporting and care-seeking, which prevented any analysis linking

symptom reporting to care-seeking. As such, it is not possible to directly assess the reasons for care-seeking (or lack thereof) among mothers with symptomatic infants from these data. It is worth noting, however, that infants of these mothers were also less likely to require an overnight hospitalisation – indicative of more severe health outcomes.

The results of this study ought to be interpreted in the light of its several limitations – additionally to the limitations already discussed. As a secondary analysis, this study was not powered to exhaustively investigate the outcomes in question. As such, the absence of differences in symptom reporting between trial arms could simply be due to an insufficient sample size. This is evident especially when considering hospitalisation, which was a rare outcome (41/1681) with a large, yet statistically insignificant (aIRR 0.55; 95% CI 0.28–1.07; p value = 0.083) difference in the multivariate model. This study also suffered from a lack of empirical results relating to infant health and wellbeing, relying heavily on self-reported symptoms, care-seeking, and hospitalisation. As ACs are implemented throughout the Western Cape, future work could include patient monitoring via the Provincial Health Data Centre, which consolidates all person-level health data throughout the province and would allow an empirical investigation of infant health outcomes and hospitalisations [44].

Considering these limitations, we interpret our results as indicating that the occurrence of illness was similar in both groups. However, mothers receiving ART from ACs were less likely to access care for their infants compared to those receiving ART from PHC clinics. Further research is required to explore how ART service provision through ACs affects infant health and access to care. These data support the implementation of ACs among postpartum mothers initiating ART during pregnancy.

AUTHORS' CONTRIBUTIONS

RD and JO conceptualised the study and defined the study objectives; RD cleaned and analysed the data; RD wrote and formatted the manuscript; JO provided edits.

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SUPPLEMENTARY INFORMATION

FIGURES

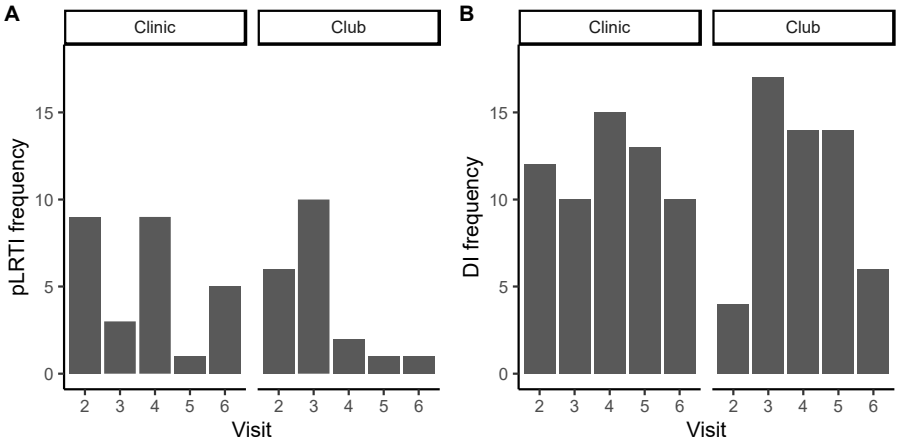

Figure S1: Per visit frequency of (A) presumed lower respiratory tract infections (pLRTI) and (B) diarrhoeal illness (DI). Visits were scheduled at approximately three, six, 12, 18, and 24 months postpartum.

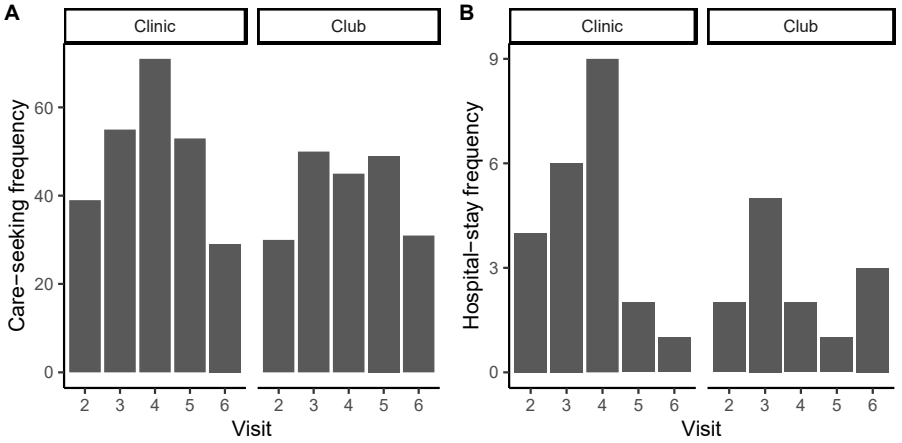

Figure S2: Per visit frequency of (A) care-seeking and (B) overnight hospital stays. Visits were scheduled at approximately three, six, 12, 18, and 24 months postpartum.

TABLES

Table S1: Frequency of self-reported lower respiratory tract infection (LRTI) per visit stratified by the infant's residence.

Visit		Reported LRTI		
		No outcome n (%)	Outcome n (%)	Unsure n (%)
2	Child apart from mother	7 (100)	0 (0)	0 (0)
	Child with mother	362 (96)	15 (4)	0 (0)
3	Child apart from mother	18 (78)	0 (0)	5 (22)
	Child with mother	347 (96)	13 (4)	1 (0)
4	Child apart from mother	27 (75)	0 (0)	9 (25)
	Child with mother	326 (97)	11 (3)	0 (0)
5	Child apart from mother	37 (64)	1 (2)	20 (34)
	Child with mother	310 (99)	2 (1)	1 (0)
6	Child apart from mother	55 (79)	1 (1)	14 (20)
	Child with mother	285 (97)	6 (2)	2 (1)
Total[†]	Child apart from mother	144 (74)	2 (1)	48 (25)
	Child with mother	1630 (97)	47 (2)	4 (1)

[†]Fisher's exact test p value on data pooled over visits <0.001

Table S2: Frequency of self-reported diarrhoeal illness (DI) per visit stratified by the infant's residence.

Visit		Reported DI		
		No outcome n (%)	Outcome n (%)	Unsure n (%)
2	Child apart from mother	7 (100)	0 (0)	0 (0)
	Child with mother	360 (95)	16 (4)	1 (0)
3	Child apart from mother	16 (70)	2 (9)	5 (22)
	Child with mother	334 (93)	27 (7)	0 (0)
4	Child apart from mother	26 (72)	2 (6)	8 (22)
	Child with mother	308 (91)	29 (9)	0 (0)
5	Child apart from mother	36 (62)	1 (2)	21 (36)
	Child with mother	286 (91)	27 (9)	0 (0)
6	Child apart from mother	55 (79)	2 (3)	13 (19)
	Child with mother	276 (94)	16 (5)	1 (1)
Total[†]	Child apart from mother	140 (72)	7 (4)	47 (24)
	Child with mother	1564 (93)	115 (7)	2 (0)

[†]Fisher's exact test p value on data pooled over visits <0.001

Table S3: Frequency of self-reported care seeking per visit stratified by the infant's residence.

Visit		Reported care seeking		
		No outcome n (%)	Outcome n (%)	Unsure n (%)
2	Child apart from mother	6 (86)	1 (14)	0 (0)
	Child with mother	308 (82)	69 (18)	0 (0)
3	Child apart from mother	15 (65)	4 (17)	4 (17)
	Child with mother	256 (71)	105 (29)	0 (0)
4	Child apart from mother	25 (69)	2 (6)	9 (25)
	Child with mother	221 (66)	116 (34)	0 (0)
5	Child apart from mother	35 (60)	5 (9)	18 (31)
	Child with mother	211 (67)	102 (33)	0 (0)
6	Child apart from mother	48 (69)	7 (10)	15 (21)
	Child with mother	232 (79)	60 (20)	1 (1)
Total[†]	Child apart from mother	129 (66)	19 (10)	46 (24)
	Child with mother	1228 (73)	452 (27)	1 (0)

[†]Fisher's exact test p value on data pooled over visits <0.001

Table S4: Frequency of self-reported overnight hospital stay per visit stratified by the infant's residence.

Visit		Reported hospital stay		
		No outcome n (%)	Outcome n (%)	Unsure n (%)
2	Child apart from mother	7 (100)	0 (0)	0 (0)
	Child with mother	369 (96)	8 (2)	0 (0)
3	Child apart from mother	23 (100)	0 (0)	0 (0)
	Child with mother	350 (97)	11 (3)	0 (0)
4	Child apart from mother	35 (97)	1 (3)	0 (0)
	Child with mother	325 (96)	12 (4)	0 (0)
5	Child apart from mother	57 (98)	1 (2)	0 (0)
	Child with mother	310 (99)	3 (1)	0 (0)
6	Child apart from mother	67 (96)	2 (3)	1 (1)
	Child with mother	289 (99)	4 (1)	0 (0)
Total[†]	Child apart from mother	189 (96)	4 (2)	1 (1)
	Child with mother	1643 (98)	38 (2)	0 (1)

[†]Fisher's exact test p value on data pooled over visits = 0.0791

Table S5: Characteristics at enrolment between included and excluded mother-infant pairs. N, % unless otherwise specified.

Variable	Included	Excluded	P value
Total	395 (94.7)	22 (5.3)	
Married or cohabiting with a partner	161 (40.8)	8 (36.4)	0.824
Completed any secondary education	120 (30.4)	11 (50.0)	*0.061*
Currently working/studying	121 (30.6)	14 (63.6)	**0.002**
Formal housing	167 (42.3)	6 (27.3)	0.188
Flush toilet inside home	160 (40.5)	5 (22.7)	0.118
Running water inside home	212 (53.7)	(40.9)	0.277
Electricity inside home	374 (94.7)	21 (95.5)	1.000
Refrigerator inside home	316 (80)	20 (90.9)	0.275
Household crowding (≥10)	19 (4.8)	0 (0.0)	---
Primiparous	97 (24.6)	6 (27.3)	0.800
Delivery in hospital	238 (60.3)	10 (45.5)	0.185
Previously on ART	47 (11.9)	3 (13.6)	0.742
Previously experienced child loss	30 (7.6)	0 (0.0)	---
Normal vaginal delivery	249 (63.0)	15 (68.2)	0.827
Infant female sex	190 (48.1)	10 (45.5)	0.830
Breast feeding (ever)	383 (97.0)	22 (100)	---
Breast feeding at enrolment	343 (86.8)	22 (100)	---
Infant experienced symptoms* since birth	33 (8.4)	3 (13.6)	0.423
Infant referred to any health facility since birth	8 (2.0)	0 (0.0)	---
Median duration of ART in pregnancy (IQR), days	149 (71)	145 (66)	0.926
Median time postpartum (IQR), days	11 (14)	9 (15)	0.373
Mean reported birth weight (SD), grams	3067 (568)	3037 (711)	0.849

Table S6: Results of univariable and multivariable Poisson regression models assessing the association between trial arm and self-reported lower respiratory tract infection (LRTI) frequency, adjusting for frequency of diarrhoeal illness (DI) as well as baseline characteristics in the intention to treat population.

	Crude IRR	Adjusted IRR	P value
Study arm (AC vs PHC)	0.72 (0.4-1.27)	0.71 (0.39-1.3)	0.274
Relationship (other vs cohabiting)	1.28 (0.71-2.41)	1.55 (0.83-3.09)	0.187
Birth weight (low vs normal)	2.14 (1.00-4.17)	2.23 (1.04-4.39)	**0.028**
Breast feeding (>5 months vs ≤5 months)	1.02 (0.56-1.82)	0.93 (0.49-1.71)	0.825
Place of delivery (hospital vs other)	0.79 (0.45-1.42)	0.81 (0.44-1.50)	0.488
Reported DI (Ever vs never)	2.26 (1.25-4.01)	2.54 (1.39-4.60)	**0.002**

IRR: incidence rate ratio; AC: adherence club; PHC: primary health care; low birth weight < 2500g; AC (n = 201); PHC (n = 194)

Table S7: All reported instances of care-seeking[§] over two years among mother-infant pairs by trial arm.

	Clinic n (%)	Club n (%)	P value[†]
Clinic/CHC	246 (84.8)	202 (84.2)	0.795
GP	15 (5.2)	17 (7.1)	
Hospital	19 (6.6)	14 (5.8)	
Pharmacy	10 (3.4)	7 (2.9)	

CHC: community health centre; GP: general practitioner; AC (n = 201); PHC (n = 194)
[†]Chi squared test p value on data pooled over visits
[§]Occasionally, multiple healthcare facilities were visited between study visits, resulting in more facilities attended than reports of care-seeking

Table S8: Infant diagnoses at health facilities by trial arm.

	Clinic n (%)	Club n (%)	P value[†]
Diarrhoea	59 (23.1)	47 (21.6)	0.167
Cough	48 (18.8)	41 (18.8)	
LRTI	47 (18.4)	31 (14.2)	
Other*	47 (18.4)	51 (23.4)	
Skin rash	33 (12.9)	39 (17.9)	
Fever	21 (8.2)	9 (4.1)	

LRTI**:** Lower respiratory tract infection; AC (n = 201); PHC (n = 194)
*Including injuries, vomiting, pain, poor weight gain, swollen glands, poor appetite, blocked nose, *etc.*.
[†]Chi squared test p value on data pooled over visits

Table S9: Diagnoses among infants requiring an overnight hospital stay.

	n (%)
LRTI	16 (42.1)
Diarrhoea	8 (21.1)
Other	7 (18.4)
Fever	4 (10.5)
Cough	3 (7.9)

LRTI – Lower respiratory tract infection

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PROTOCOL AND RESEARCH APPENDICES

Comparing health outcomes among infants of women living with HIV obtaining postpartum ART care at routine primary health care services versus adherence clubs in Cape Town, South Africa

Master of Public Health in Epidemiology and Biostatistics:

Protocol

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Table of Contents

Synopsis

The Human Immunodeficiency Virus (HIV) is a significant cause of morbidity in South Africa, with an estimated 7.5 million people living with HIV (PLH) in 2019. Without an effective vaccine or cure, successful management of HIV infection requires rapid diagnosis, long-term treatment, and viral suppression of PLH. However, given the differing needs of all PLH, there is a growing appreciation that a “one-size-fits-all” approach will not sustainably provide access to antiretroviral therapy (ART) among all vulnerable communities.

Preventing the mother-to-child transmission (PMTCT) of HIV is an essential component in controlling the HIV/Acquired Immunodeficiency Syndrome (AIDS) epidemic. Despite recent successes in the PMTCT, mothers initiating ART during pregnancy are at an increased risk of disengaging from ART services, and therefore poor treatment adherence, postpartum. Ultimately, disengaging from ART services increases the risk of viremia and HIV transmission during breastfeeding. Moreover, HIV infection during pregnancy increases the risk of adverse health outcomes among infants. As such, when tailoring approaches for ART service delivery among mothers initiating ART during pregnancy, it is essential to account for the needs of both postpartum mothers and their infants.

The recent Postpartum Adherence Clubs for Antiretroviral Therapy (PACART) trial sought to investigate if adherence clubs (AC) – an already successful form of differentiated service delivery (DSD) – could reduce the risk of viremia postpartum among women initiating ART during pregnancy, when compared to the current standard of care (SOC). Although successful in achieving its primary aim (viral load [VL] suppression to less than 1000 copies/mL through 24 months), no provisions for infant care were made in the PACART trial. Rather, mothers in both arms were referred to local “well-baby” clinics. A reasonable hypothesis, therefore, is that changing the care-seeking requirements for mothers will impact the health outcomes of their infants. This is an important consideration, as any delays or barriers to care-seeking can severely impact infant health and well-being. As such, the aim of this study – a secondary analysis of data collected during the PACART trial – is to investigate if ACs influence infant health during the first 24 months postpartum when born to mothers initiated onto ART during pregnancy, compared to the SOC.

The PACART trial was conducted in Gugulethu, a township in Cape Town, South Africa, with high rates of poverty and unemployment, and an HIV prevalence of around 23%. Recruitment occurred at the Gugulethu Community Health Centre (CHC) as well as the affiliated Midwife Obstetric Unit (MOU). Potentially eligible women were informed about the study in their preferred language (isiXhosa or English), and those interested and willing provided informed consent. Eligibility included being ≥18 years old and within 70 days postpartum, as well as

having a suppressed VL (<400 copies/mL) and no comorbidities necessitating more extensive clinical follow up. Women who were enrolled into this study were randomised to receive ART services either through the current SOC (control) or ACs (intervention). Importantly, however, infants in both arms received the current SOC at local “well-baby” clinics.

General infant health and wellbeing was assessed during the PACART study through the administration of questionnaires to postpartum mothers. Data were collected on infant delivery, demographics, medical history, and feeding. This exploratory study will investigate the impact that the provision of ART services through ACs has on infant health, compared to the SOC, through 24 months postpartum. As data on infant health were collected through questionnaires, we will be using the timing of symptom onset and frequency of reported symptoms (including cough, fast breathing, wheezing, diarrhoea, fever, poor feeding, or rash), as well as the frequency of reported care seeking (both referral to any specialist facility and overnight hospital stays) as estimates for disease frequency and severity, respectively. Together, these variables should give an insight into how frequently infants randomised to both arms were unwell, and how severe the illness was.

This secondary analysis of the PACART trial poses limited risk to study participants: no further visits are required, no additional data will be collected, and the data to be used in this study are appropriately de-identified. Although this study poses no direct benefits to the participants of the PACART trial, its objective to promote infant health and wellbeing has indirect benefits for infants born of women living with HIV. The findings of this study will inform future iterations of ACs, ensuring that they are designed to best serve both postpartum WLH and their infants.

Introduction

Background

South Africa is the global epicentre of the HIV epidemic, with an estimated 7.5 million PLH in 2019 (UNAIDS, 2020). In the absence of an effective vaccine or curative treatment, control of HIV/AIDS is heavily predicated on the successful diagnosis, treatment, and viral suppression of PLH (Frescura et al., 2022). Focussing on all tiers of the HIV testing and treatment cascade, the ambitious 90–90–90 targets (set to be achieved by 2020) aimed to ensure that 90% of all PLH were aware of their HIV status, 90% of PLH who were aware of their status were accessing treatment, and 90% of those individuals accessing treatment were virologically supressed (UNAIDS, 2014). Although modelling data suggests that South Africa achieved the first 90 (*i.e*., the diagnosis of 90% of all HIV infected individuals) (Woldesenbet et al., 2021), the initiation of, and adherence to successful treatment (the second and third 90s, respectively) proved more challenging (Marinda et al., 2020).

Despite not hitting all 90–90–90 targets by 2020, the drive to end AIDS by 2030 has necessitated updating these targets to 95–95–95 by 2025 (UNAIDS, 2023). There are growing concerns, however, that a "one-size-fits-all" approach to HIV services will not sustainably provide access to ART among vulnerable communities (Grimsrud et al., 2016). Pregnant women and their infants in South Africa represent a key vulnerable population for whom ART-services need to be tailored.

Antenatal HIV in South Africa

The antenatal HIV prevalence in South Africa is 30% and has remained relatively unchanged since 2004 (Woldesenbet et al., 2021). The importance of successfully managing HIV during pregnancy is threefold; 1) the presence of infection during pregnancy risks the vertical transmission of HIV and the perpetuation of the epidemic (Abrams and Myer, 2013), 2) women initiating ART during pregnancy are at an increased risk of loss to follow up and therefore poor treatment adherence postpartum (Larsen et al., 2019), and 3) infants born to mothers with antenatal HIV are at an increased risk of poor health outcomes (Pfeifer and Bunders, 2016). These are important barriers that need to be overcome if we hope to reduce the impact of the HIV/AIDS epidemic and achieve the aspirational goal of ending AIDS by 2030 (UNAIDS, 2023).

Antenatal diagnosis of HIV infection & initiation of ART

The integration of provider-initiated HIV testing and counselling into standard antenatal services has improved the detection of HIV during pregnancy (UNAIDS, 2007, de Beer et al., 2020). In 2013, the barriers to treatment access were lowered further when the WHO issued

a recommendation (termed “Option B+”) to initiate all HIV-infected pregnant women onto lifelong ART regardless of clinical symptoms (WHO, 2016). Option B+ has since been superseded by universal ART, whereby all PLH are initiated onto ART regardless of clinical symptoms, viral load, or CD4 count (WHO, 2016). The integration HIV testing into antenatal services and the introduction of option B+ (subsequently updated to universal ART) significantly impacted the HIV/AIDS epidemic, increasing the percentage of pregnant and postpartum women accessing ART (UNAIDS, 2018), thereby reducing the mother-to-child transmission of HIV (Kalua et al., 2017).

Maintaining virological suppression postpartum

The recent successes in the first two targets during pregnancy and postpartum have not been matched by sustained virological suppression, especially among women initiated onto ART during pregnancy (Larsen et al., 2019). During early motherhood, women undergo social, economic, and psychological changes that are not catered for through the current ART services (Nachega et al., 2012). These changes promote disengagement from the health system and limit access and adherence to treatment (Kaplan et al., 2008, Nachega et al., 2012, Phillips et al., 2014, Tenthani et al., 2014, Haas et al., 2016, Larsen et al., 2019). Poor treatment adherence contributes to the development of viremia, which has significant implications for the risk of vertical transmission during breastfeeding and negatively impacts long-term maternal health (Myer et al., 2017, Abrams and Myer, 2013, Garcia et al., 1999, Katzenstein et al., 1999).

Infant health and well-being

Successful pregnancy outcomes are critically dependent on the homeostasis of several maternal and foetal systems (Arck and Hecher, 2013). Antenatal HIV infection significantly disrupts this homeostasis, promoting elevated cytokine levels within the placental plasma and increased inflammation (Deeks et al., 2013, Kumar et al., 2012). Even in cases of HIV exposure without infection, this disrupted homeostasis can lead to small-for-gestational age infants and delayed cognitive development (Pfeifer and Bunders, 2016, le Roux et al., 2019, le Roux et al., 2018, Newell and Bunders, 2013). These infants remain at a higher risk of severe respiratory tract infections and mortality during their first year, among other health complications (Ndirangu et al., 2012, Newell and Bunders, 2013, Nachega et al., 2012, le Roux et al., 2019, McNally et al., 2007, Herce et al., 2021). ART administration during pregnancy greatly reduces the risk of vertical transmission (Chasela et al., 2010) and has generally improved infant well-being (Schulte et al., 2007), however, systematic inflammatory responses remain elevated in adults receiving ART (Deeks et al., 2013). Moreover, the drugs themselves increase the risk of adverse health outcomes among ART-exposed infants (Newell

and Bunders, 2013); an important consideration since the implementation of option B+ (Kieffer et al., 2014).

The implementation of Option B+ and universal ART have successfully reduced the risk of the vertical transmission of HIV (Kalua et al., 2017). However, the unmatched success in retaining mothers initiating ART during pregnancy (Larsen et al., 2019) and the risk of adverse health outcomes faced by their infants (Pfeifer and Bunders, 2016) necessitate a tailored approach to ART services that accounts for the needs of mothers and their infants.

Differentiated Service Delivery

The current SOC provides ART services at PHC facilities (Odayar et al., 2019). This includes an intensive follow up phase with visits once a month for the first four months, followed by a continuation phase with regular visits for ART collection every two months. Due to the scale of the HIV/AIDS epidemic in South Africa, the frequency and centralization of ART collection overwhelm primary healthcare (PHC) facilities and promote disengagement of patients from the health system (El-Sadr et al., 2017). This effect is pronounced among vulnerable populations (Larsen et al., 2019).

One potential alternative to the SOC, DSD, is a patient-centred approach intended to simplify and adapt HIV services at all levels to better serve people living with HIV (Grimsrud et al., 2017). This approach seeks to provide client-centred services that encourage engagement, adherence, and retention in care. A parallel benefit of DSD is a reduced burden on the health system by maximizing the efficiency of ART service delivery (El-Sadr et al., 2017, Grimsrud et al., 2017). Whereas earlier care approaches broadly categorized adults living with HIV as either pregnant or nonpregnant, DSD seeks to recognize more categories of people living with HIV and tailor the type of care to each of them (Ehrenkranz et al., 2019).

Many approaches to DSD have been attempted on clinically stable adults (Ehrenkranz et al., 2019, Bemelmans et al., 2014), including mobile phone communication, psychological counselling, and ACs (Clouse et al., 2020, Wilkinson et al., 2016). Although limited, evidence is beginning to emerge that suggests DSD may be effective in vulnerable populations, including pregnant women (Macdonald et al., 2017, Myer and Phillips, 2017, Ehrenkranz et al., 2019, Myer et al., 2018). However, further research is required to unequivocally demonstrate the impact of DSD on vulnerable communities when implemented at scale (Ehrenkranz et al., 2019).

Adherence clubs in South Africa

ACs, the primary form of DSD in South Africa, are designed to reduce the burden of chronic HIV-care on clinically-stable PLH and PHC facilities (Wilkinson et al., 2016). Although similar

in frequency to the ART services at PHC facilities, ACs involve groups of 20–30 patients meeting every two months at community venues, where CHWs lead guided discussions (Odayar et al., 2019, Wilkinson, 2013). They typically provide ART services to low-risk clinically stable adults who have been on ART for at least six months, have suppressed VL (<400 copies/mL), and have no comorbidities necessitating more extensive clinical follow up (Odayar et al., 2019, Wilkinson, 2013). Until recently, limited data existed that demonstrated the efficacy of ACs among pregnant and postpartum women.

The PACART trial sought to investigate if the scope of ACs could be increased from clinically stable adults with low risk of loss to follow up to include pregnant mothers initiating ART during pregnancy (Odayar et al., 2019). This trial provided strong evidence that ACs improve ART-service engagement and reduce risk of viremia through 24 months among mothers attending ACs compared to SOC. (Myer et al., 2022). Moreover, a pilot study had already demonstrated that ACs were well accepted among pregnant women initiating ART during pregnancy (Trafford et al., 2018), further supporting the use of ACs among vulnerable populations.

Despite the success of the PACART trial in achieving its primary aim – reducing the risk of viremia 24 months postpartum – no provisions for infant care were made in this study, with mothers in both arms referred to local “well-baby” clinics (Odayar et al., 2019), a point to which some mothers have raised concern (Trafford et al., 2018). This is an important consideration, as integrating maternal and infant care postpartum provides health benefits to both mothers and infants (Myer et al., 2018), whereas factors that prevent or delay care-seeking and HIV-testing severely impact on infant health, well-being, and risk of mortality (Lassi et al., 2019, Violari et al., 2008). As such, the aim of this study is to analyse data collected during the PACART trial to investigate if ACs influence infant health during the first 24 months postpartum among infants born to mothers initiated onto ART during pregnancy when compared to the SOC.

Study rationale

South Africa remains the global epicentre of the HIV/AIDS epidemic despite significant effort to increase the access and adherence to successful treatment (UNAIDS, 2023). To date, efforts to eradicate HIV/AIDS have been thwarted as a “one-size-fits-all” approach to ART services is insufficient to provide access to all vulnerable communities (Grimsrud et al., 2016). Pregnant women in South Africa represent a key vulnerable population for whom ART services need to be tailored.

The PMTCT of HIV is critical to the realisation of an “AIDS free generation” (Abrams and Myer, 2013), however, the antenatal HIV prevalence in South Africa is 30% and has remained relatively unchanged since 2004, highlighting the magnitude of this challenge (Woldesenbet

et al., 2021). Despite the successes of Option B+ and universal ART in the PMTCT (Kalua et al., 2017), the unmatched success in retaining mothers initiating ART during pregnancy in the health system (Larsen et al., 2019) and the risk of adverse health outcomes faced by their infants (Pfeifer and Bunders, 2016) necessitate a tailored approach to ART services that accounts for the needs of both mothers and their infants.

The PACART trial sought to investigate if ACs – an already successful form of DSD – could reduce the risk of viremia postpartum among women initiating ART during pregnancy, compared to SOC (Odayar et al., 2019). Although successful in achieving its primary aim, no provisions for infant care were made in this study, with mothers in both arms referred to local "well-baby" clinics (Odayar et al., 2019). A reasonable hypothesis, therefore, is that changing the care-seeking requirements for mothers will impact the health outcomes of their infants. This is an important consideration, as any delays or barriers to care-seeking can severely impact infant health and well-being (Lassi et al., 2019, Violari et al., 2008). As such, the aim of this study is to investigate if maternal care via ACs influence infant health during the first 24 months postpartum when born to mothers initiated onto ART during pregnancy, compared to the SOC.

Aims and objectives

This study aims to investigate if ACs influence infant health during the first 24 months postpartum when compared to the SOC, among infants born to mothers initiated onto ART during pregnancy. This study will be conducted as a secondary analysis of data collected during the PACART study, according to the following aim and objectives:

1) To compare the general health of infants between mothers randomised to receive ART services via ACs or SOC, by assessing the presence of symptoms and the frequency of referral to specialist medical facilities. Symptoms include cough, fast breathing, wheezing, diarrhoea, fever, poor feeding, or rash.
    i. Compare the time to first symptom onset between mothers randomised to ACs or SOC.
    ii. Compare the proportion of infants with symptoms at each visit between mothers randomised to ACs or SOC.
    iii. Compare the frequency at which infants have experienced symptoms since birth between mothers randomised to ACs or SOC.
    iv. Compare the frequency at which infants were referred to specialist medical facilities for treatment since birth between mothers randomised to ACs or SOC.
    v. Compare the proportion of infants requiring an overnight hospital stay since birth between mothers randomised to ACs or SOC.

Hypothesis

The AC model of HIV service delivery, which is designed to increase the adherence of women living with HIV initiating ART during pregnancy, will not negatively impact the health of their infants 24 months postpartum when compared to the SOC.

Methodology

Study design

The proposed study will be conducted as a secondary analysis of data already collected during the PACART trial, for which the methods and main results have already been published (Odayar et al., 2019, Myer et al., 2022). Briefly, the PACART trial – a pragmatic randomised controlled trial – sought to compare two strategies for ART service delivery among women initiated onto ART during pregnancy. Women enrolled into the trial were randomly allocated (1:1) to either referral to the current SOC for ART services (control group) or to community-based ART services at ACs (intervention group). Additional study visits were scheduled approximately three-monthly for participants in both arms through 24 months postpartum. The trial's primary objective was to compare maternal HIV viral suppression between the control and intervention groups through 24 months postpartum, specifically defining viral suppression as a viral load (VL) of less than 1,000 copies/mL. Data were collected for the assessment of several secondary outcomes, including infant general health and wellbeing (detailed below).

Study setting and population

Community

This study was conducted in Gugulethu, a township in Cape Town, South Africa, with a population of approximately 350,000 individuals. In addition to the high rates of poverty and unemployment prevalent in this community, around 23% of the general population are living with HIV (Myer et al., 2015). The Gugulethu CHC, responsible for PHC within the community, has an ART clinic that provides the general adult population with HIV care. Affiliated with the CHC, the MOU provides both antenatal and postnatal care, as well as PMTCT and ART services, to more than 4,000 women annually (Myer et al., 2016). This service is critical, as approximately 33% of the women presenting at the MOU are HIV-positive (Myer et al., 2015).

Eligibility criteria

All consenting pregnant women attending the CHC or MOU, who had initiated ART during pregnancy, and who met the eligibility criteria (outlined below) were enrolled and randomised

to either the control or intervention arm. The primary criteria for eligibility included being ≥18 years old and within 70 days postpartum. In addition, eligibility was based on standard AC admission criteria. These included having a suppressed VL (<400 copies/mL) and no comorbidities necessitating more extensive clinical follow up (Odayar et al., 2019, Wilkinson, 2013). Although admission into an AC typically requires six-months of uninterrupted ART, an exception was made for this study allowing participants to be on ART for at least three months pre-enrolment. Women intending to relocate out of Cape Town or who had lost their infant were excluded from the study.

Postnatal and MOU ART services

The Gugulethu MOU houses an integrated ART clinic that provides PMTCT services, including the first-line ART regimen (tenofovir [300 mg], emtricitabine [200 mg], and efavirenz [600 mg] taken once daily). During pregnancy, clinical follow up as part of routine care services occurs every one to two months, with VL measured after three months on ART.

Basic neonatal support and infant feeding monitoring are provided to mother-infant pairs within seven days of delivery. Mothers on ART and their infants are then scheduled to attend the MOU ART clinic within one month of delivery. This visit allows for counselling, review of maternal and infant health, and collection of ART. At this point, mothers are referred to the Gugulethu CHC for general adult ART services and the infants are referred to “well baby” services at separate clinics for vaccinations and HIV testing.

General adult ART services

Women present for general adult ART care at the CHC within one month of referral from the MOU. This includes an intensive follow up phase with visits for clinical assessment once a month for the first four months, followed by a continuation phase with regular visits for ART collection every two months. Three months of medication are dispensed over the December holiday period. Except for individuals with clinical or psychological concerns, clinical screening occurs six monthly. Once ART has been initiated, routine laboratory investigations occur at four and 12 months and annually thereafter.

Adherence clubs

ACs involve groups of 20–30 patients meeting every two months for 60 minutes at community venues, where CHWs lead guided discussions (Odayar et al., 2019, Wilkinson, 2013). Four months of medication are dispensed over the December holiday period. Participants are weighed, screened for symptoms, and receive ART during regular visits and have an annual VL and general clinical assessment by a visiting nurse from the CHC. If patients have lost weight, are symptomatic, have an elevated VL, or have failed to collect their ART within five

days of any visit, they are immediately referred to the general ART clinic associated with the AC (Wilkinson, 2013). Except for clinical visits, patients can periodically opt to send a "buddy" (*i.e.,* a partner, friend, or relative) to attend club visits and collect their medication, however, patients must attend every second session.

Description of the control and intervention

Control

ART care was provided to mothers and infants in the control arm by government health services and based on the local standard of care according to the public sector policies. This involved referral of mothers from the MOU ART service to PHC ART facilities, including the ART clinic at the CHC, for general adult care. Whereas infants were referred to the "well-baby" child health services.

Intervention

ART services were provided through ACs to women randomised to the intervention arm. As in the control arm, infants were referred to "well-baby" health services.

Study procedures

Recruitment, enrolment, and randomisation

Recruitment occurred at both the MOU ART clinic and postnatal clinical visits and consecutive, potentially eligible women were considered. These women were informed about the study and, if interested, were screened. Women who were eligible for enrolment were referred to study counsellors, and consenting women were then randomised to either the control or intervention arm of the study.

Once enrolled, all study participants were seen at the MOU ART clinic, at which point they were referred to either the current SOC or AC clubs for follow up. Infant care was provided via "well baby" clinics in both study arms.

Measurements

Study visits were scheduled separately from ART services in both arms, at approximately three, six, 12, 18 and 24 months postpartum. Blood was collected at each study visit to determine participant VL in accordance with the primary aim of the study. In addition to phlebotomy, various questionnaires were administered by trained interviewers in the preferred language of the participant (either English or isiXhosa). These interviews were conducted at every visit to collect data on both maternal and infant demographics, medical history, ART adherence and infant feeding (Odayar et al., 2019). To assess factors that may be related to poor treatment adherence among women initiating ART during pregnancy, various

questionnaires were administered at every visit to collect data on behavioural, psychosocial, and mental health status (Odayar et al., 2019).

Outcomes and analysis plan

Variables used in this study

This exploratory study will be investigating what impact, if any, the provision of ART services through ACs has on infant health compared to the SOC 24 months postpartum. As data on infant health were collected through questionnaires, we will be using the timing of symptom onset, proportion of infants with symptoms, and the frequency of reported symptoms (including cough, fast breathing, wheezing, diarrhoea, fever, poor feeding, or rash), as well as the frequency of reported care seeking (both referral to any specialist facility and overnight hospital stays) as estimates for disease frequency and severity, respectively. Given the exploratory nature of this secondary study and the fact that the PACART study was powered for its primary objective (n = 412), an additional sample size calculation will not be performed.

All analyses in this study will be by intention-to-treat and all relevant demographic and clinical variables for mother-infant pairs will be compared between the groups.

Analysis plan

For the outlined objectives, the main exposure of interest is the random assignment of mothers to either receive ART services at ACs or PHC facilities. Each objective will evaluate the relationship of this exposure with various outcomes, requiring different analytical methods as detailed below. While the primary exposure was randomly assigned, potential confounding variables will be addressed through multivariable models, where appropriate.

The first objective will be assessed using Kaplan-Meier curves to compare the time to first symptom onset (either cough, fast breathing, wheezing, diarrhoea, fever, poor feeding, or rash) between infants of mothers randomised to receive ART services at ACs or PHC facilities. The curves will be compared using a log-rank test.

For the second objective, the outcome is the proportion of infants experiencing symptoms, which is a binary outcome. Consequently, logistic regression will be employed to compare the odds of experiencing symptoms between infants of mothers randomised to receive ART services at ACs or PHC facilities. Separate regression analyses will be conducted to assess the associations at each visit.

Objectives three and four both evaluate the frequency of the outcome occurring during the study period and are thus suited to Poisson regression. The outcomes for objectives three and four are the frequency at which infants experience symptoms since birth and the frequency at which infants are refereed to specialist medical facilities, respectively. In both cases, the

outcomes will be compared between infants of mothers randomised to receive ART services at ACs or PHC facilities, and both analyses will control for duration of observation. If the data are overdispersed, a negative-binomial regression will be conducted instead.

The final objective will compare the proportion of infants requiring an overnight hospital stay during their first 24 months postpartum. Since this is a binary outcome, logistic regression will be performed comparing the odds of requiring a hospital stay between infants of mothers randomised to receive ART services at ACs or PHC facilities.

Data management

All data that will be utilized in this study were collected on paper during the PACART trial. Original documents are securely stored in locked filling cabinets, while the electronic records are managed according to already-established standard operating procedures and stored in a password-protected Microsoft Access database. Electronic records will be shared with the investigator for the extraction of data relevant to the proposed study onto a password-protected MacBook Pro. Data analyses will be conducted in R version 4.3.3 (RCoreTeam, 2020).

Ethical considerations

Ethical review

The PACART study received ethical approval from the Human Subjects Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town (REF 194/2015). In addition, local government and the facility manager approved the study.

Informed consent

Trained counsellors took participants through the informed consent process in their preferred language (IsiXhosa or English) in a private room. This included time for potential participants to ask questions regarding the study, while the counsellors informed them that their decision would not impact the care they would receive and that they could withdraw from the study at any time. Consenting participants were given a copy of the signed document. No additional data was collected for the purpose of this study, and as such, no further informed consent will be collected.

Risks and benefits

Pregnant mothers living with HIV and their infants represent a vulnerable population for whom special care must be taken to ensure no harm is brought to them through the study. The PACART trial sought to minimize risks in several ways. Firstly, by monitoring if participants indicated thoughts or behaviour of self-harm. Secondly, by ensuring that phlebotomies were

performed under sterile conditions, and lastly, to ensure that data obtained were kept confidential and safe. This study will pose no additional physical harm to the participants, and data utilised will remain de-identified. This will ensure that participant information will remain confidential.

This study poses no direct benefit to the participants. However, the findings of this research will contribute to a broader understanding of the potential risks or benefits that the provision of ART through ACs pose on infants of mothers initiating ART during pregnancy. Moreover, this study will be submitted as a partial fulfilment of the requirement for the Master of Public Health in Epidemiology and Biostatistics degree at the University of Cape Town. Once completed, the results of this study will be readily accessible in the public domain.

Time schedule

Table 1: Proposed time schedule for this project during 2024.

	April	May	June	July	August
Ethical approval					
Data management					
Analyses					
Writing results					
Writing discussion					
Final write-up					
Final submission					

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Appendices

PACART informed consent documents

Informed Consent Form Version 3

Isihloko Soluphando: Amaqumrhu asekuhlaleni zokutyiwa kwamachiza okuthomalalisa intsholongwane ngendlela eyiyo emva kokubeleka

Title of Research: Postpartum Adherence Clubs for Antiretroviral Therapy (PACART)

YINTONI INJONGO YOLUVAVANYO?
WHAT IS THE PURPOSE OF THE STUDY?

Sisuka kwiDyunivesithi yaseKapa. Senza uvavanyo ukuthelekisa iindlela ezimbini ezahlukileyo zokunikezela unyango lweNtsholongwane kaGawulayo kubafazi abaphila nale Ntsholongwane kaGawulayo emva kokuba bebelekile. Uyacelwa ukuba uthathe inxaxheba kolu vavanyo, olwenziwa kwiCandelo lokuBelekisa lase Gugulethu. (MOU)

We are from the University of Cape Town. We are doing a research study to compare two different ways of providing HIV treatment to HIV-positive women after they deliver a baby. You are being asked to take part in this study, which is being done at the Gugulethu Midwife Obstetric Unit (MOU).

Siyazi ukuba kubalulekile ukuba abafazi abaphila neNtshlongwane kaGawulayo nabantwana babo bafumane ukhathalelo lwe Ntsholongwane kaGawulayo emva kokubeleka. Kolu vavanyo sithelekisa indlela ezimbini zokunikezela ngolunyango. Ulwazi esilufumana koluvavanyo luyakunceda ukuphucula amaziko onyango luka Gawulayo kubafazi abasanda kubeleka, ukwenzela ukuba bahlale bekukhathalelo nonyanzeleko lonyango.

We know that it is essential for HIV-positive women and their babies to receive HIV care and treatment after delivery. In this study we are comparing two different ways of providing this treatment. Information learned in this study will help us to improve HIV services for women who have recently delivered a baby, so that they can remain in care and adherent to treatment.

Uyacelwa uthathe inxaxheba koluvavanyo ngoba ungumama onesimo esaziwayo solosuleleko lweNtsholongwane kaGawulayo, oqale ukuthatha amachiza okuthomalalisa kolukhulelo lakho lokugqibela, nonyamezeleyo kuzo. Injongo yale fomu yesivumelwano kukunika iinkcukacha ezizakunceda ukuba uthathe isigqibo sokuba uyafuna na ukuthatha inxaxheba koluphando okanye hayi.

You are being asked to take part in this study because you are a woman with known HIV-infection who started taking HIV drugs during your last pregnancy, and who is adherent to them. The purpose of this consent form is to give you information to help you decide if you want to take part in this study or not.

KWENZEKA NTONI UKUBA NDIYAVUMA UKUTHATHA INXAXHEBA?
WHAT HAPPENS IF I AGREE TO TAKE PART?

Ungenelelo no kungacetywa
Enrolment and randomization

Ukuba uyavuma ukuthabatha inxaxheba uyakwenza oku kulandelayo:

- Phendula imibuzo edibene nezihloko eziquka oku kulandelayo: indlu yakho, inombolo zakho zomnxeba, ukukhulelwa kwakho kwaye neenkcukacha zakho zempilo, ukusebenzisa kwakho amachiza eNtsholongwane kaGawulayo, nokondliwa kosana.
- Kuzakutsalwa igazi elingange 5ml (itispuni enye) engalweni yakho
- Uzakukhethwa ngokungacetywanga (oku kokuguqulwa kwengqekembe) kwenye yalamaqela mabini, ayakunikwa unyango ngendlela ezahlukeneyo.
    1. **Amaqumrhu asekuhlaleni okutya amachiza ngendlela eyiyo:** Abafazi abakhethelwe kweli qela bayakufumana ukhathalelo lweNtsholongwana kaGawulayo namachiza kumaqela asekuhlaleni, (iklabhu) ahlanganela kwiziko lasekuhlaleni, kumgama ongange 600m ukusuka kwiziko lempilo laseGuguletu. Abantwana babo bayakuthunyelwa kumaziko amancinci empilo akufutshane ukwenzela unyango lwesiqhelo luqhubekeke.
    2. **Ikliniki kawonke-wonke yonyango lweNtsholongwane kaGawulayo:** Abafazi abakhethelwe kweli iqela bayakuthunyelwa kwiziko labatya amachiza eNtsholongawe kaGawulayo e Guguletu Day Hospital bafumane ukhathalelo nonyango lweNtsholongwane kaGawulayo. Abantwana babo bayakuthunyelwa kwiziko elincinci lokhathalelo lwesiqhelo lwabantwana. Oku luqhubekeko lwesiqhelo lwabafazi abaphila neNtsholongwane kaGawulayo nabantwana babo abahamba kwiziko lokubelekisa.

If you agree to take part you will do the following today:

- *Answer questions about a number of topics including: your household, your contact details, your pregnancy and medical history, your HIV testing history, your use of HIV medications and infant feeding.*
- *Have 5mls (1 teaspoon) of blood taken from your arm.*
- *You will then be randomized (like a flip of a coin) to one of two groups, who will each receive their HIV treatment in different ways:*
    1. ***Community-based adherence club**: Women assigned to this group will receive HIV care and medicines at the adherence clubs, which meet at the community centre about 600m from the Gugulethu Community Health Centre (CHC). Their babies will be referred to their nearest primary health care clinic for routine baby care.*
    2. ***General antiretroviral therapy (ART) clinic**: Women assigned to this group will be referred to the ART clinic at the Gugulethu CHC for HIV care and treatment. Their babies will be referred to their nearest primary health care clinic for routine baby care. This is currently the standard of care for all HIV-positive women and their babies attending the MOU.*

"Ukhetho olungacetywanga" kuthetha ukuba uyakuba ne 50 yepesenti yokuba seqeleni oluyakufumana ukhathalelo kwiklabhu yasekuhlaleni/ Uyakuba ne50 yepesenti yokuba kwiqela elizakuthunyelwa kwikliniki yokuxilonga iNtsholongwane kaGawulayo. Lilonke amathuba okuyo kweliphi na iziko lempilo ayalingana. Abaphangeli bophando nabathathi nxaxheba abayi kukhetha ukuba uzakuya kweliphi iziko lempilo. . Izigqibo zenziwa yi kompyutha zifakwe emvulophini. Abasebenzi bophando abazi ukuba leliphi iqela elisemvulophini.

***"Randomized"** means that you will have a 50% chance of being in the group that will receive care at the adherence club. You will also have a 50% chance of being in the group that gets referred to an ART clinic. Neither the study staff nor you can choose which group you will be assigned to. The decisions are made by a computer and put into an envelope. The staff does not know which group is in each envelope.*

Amatyelelo ophando lomlinganiselo

Study measurements visits

Emva kokuba wena nomntwana wakho nikhethwe ngokungacetywanga,uyakucelwa ukuba utyelele amaxesha amayi 5 omlinganiselo emva inyanga eziyi 3, inyanga eziyi 6, nenyanga eziyi 12, nenyanga eziyi 18, nenyanga eziyi 24 emva kokubeleka. Lamatyelelo ovavanyo ohlukile kumatyelelo esiqhelo akho emva kokubeleka nokhathalelo lwakho lweNtsholongwane kaGawulayo. Utyelelo ngalunye luyakuthatha kangange mizuzu engamashumi amathathu ukuya kwiyure.

After you and your baby are randomized, you be asked to attend a further 5 study measurement visits at approximately 3 months, 6 months, 12 months, 18 months and 24 months after delivery. These study visits are separate from the usual clinic visits that you will have for your postpartum and HIV care. Each visit will take about 30-60 minutes.

Kula matyelelo uyakwenza oku kulandelayo:

- Ukuphendula uluhlu olwahlukeneyo lwemibuzo kutyelelo ngalunye. Imibuzo ingaquka ezi zihloko zilandelayo:
    - Ulwazi ngempilo yakho yakamva nje, amachiza akho eHIV, ukwaziwa kwesimo sakho seHIV, ubandlululo, isimo sengqondo (kuquka nokusetyenziswa iziyobisi notywala) ukusetyenziswa kocwangciso-ntsapho, impilo yomntwana, nokhathalelo lwempilo nokuba wena uziva njani ngokhathalelo lwe Ntsholongwane kaGawulayo olufumeneyo.
- Utsalo gazi olungange 5mls (itispuni enye) kwingalo yakho kuwo onke amatyelelo akho

At these visits, you will do the following:

- *Answer different sets of questions at each visit. Questions may include the following topics: your recent medical history, your HIV medications, HIV disclosure, stigma, mental health (including drug and alcohol use), family planning use, infant feeding, infant health and health care and how you feel about the HIV care that you have received.*
- *Have 5mLs (1 teaspoon) of blood will be drawn from your arm at every visit.*

Utyelelo lwakho lokugqibela lomlinganiselo luyakuba kwinyanga eziyi 24 emva kokubeleka. Emva koku akuyi kulindeleka ukuba utyelele uvavanyo, kodwa uyakuqhubeka ngokhathalelo lwesiqhelo lweNtsholongwane kaGawulayokwiqela lasekuhlaleni eklabhini okanye kwi kliniki yamachiza eHIV ngokufanelekileyo.

Your last study measurement visit will be at 24 months after delivery. After this you will no longer be required to attend study visits, but will continue with routine HIV care either at the adherence club or at the ART clinic as appropriate.

QAPHELA: Igazi elitsalwe kutyelelo ngalunye luya kugcinwa kuphononongwe ubungakanani beNtsholongwane ka Gawulayo egazini lakho kwixa elizayo. Iziphumo zeli gazi aziyi kwaziswa kuwe, kwi kliniki okanye kubasebenzi bovavanyo. Igazi lakho eligciniweyonazo naziphina iziphumo zovavanyo azisayi kuba nagama lakho nalo naluphina uhlobo lokuba unakanwe. Xa abasebenzi bezempilo abajongene notyelelo lwakho lolandelelwano ekliniki okanye eklabhini yokuthatha amachiza ngokufanelekileyo befuna ukujonga ubungakanani beNtsholongwane kaGawulayo bayakuthatha l spesimeni segazi esahlukileyo.

***NOTE**: The blood that is drawn at each visit will be stored and used to check your viral load (this is the amount of HIV in your blood) at a later time. Results from these tests will not be available to you, the clinic, or the study staff. Your stored blood and any study test results will not have your name or any other means of identifying you on it. When the health care workers who do your routine follow-ups at the clinic or the adherence club need to check your viral load, they will take a separate blood specimen.*

UKUPHONONONGWA KWE REKHODI ZONYANGO
REVIEW OF MEDICAL RECORDS

Ngokuyinxenye yolu vavanyo siyakujonga sithathe ulwazi lohlukuhlo, zecala lobelekiso, zekliniki ekhupha amachiza okuthomalalisa iNtsholongwane neze klabhu yokutya amachiza ngokufanelekileyo, ezase lebhu nerekhodi zase khemesti, nencwadana yendlela eya empilweni yomntwana. Kwezi rekhodi sinomdla kuhlukuhlo nokhathalelo kwiziko lobelekiso notyelelo lolwandelelwano lwakho nomntwana emva kokubeleka.

Lonke ulwazi esithe saluphononongo salutsala luyimfihlelo kwaye akukho gama lamthathi-nxaxheba eliyakubhalwa kwimiqulu yovavanyo.

As part of this study we will also be looking at and taking information from your antenatal, obstetric, ART clinic or adherence club, laboratory and pharmacy records as well as your baby's road to health booklet. From these records we are interested in your antenatal and obstetric care and the follow-up care that you and your baby receive postnatally.

All the data that we review and abstract is confidential and no participant names are recorded on study documents.

UTYELELO LOLANDELELWANO OLUPHOSAKELEYO
FOLLOW-UP OF MISSED VISITS

Uyakucelwa ukhuphe iinkcukatcha zakho zoqhagamshelwano ukuze sikwazi ukukuthinta ngeli xesha lovavanyo. Abasebenzi bovavanyo bayakuthetha nawe ngeyona ndlela iyiyo yoqhagamshelwano nawe. Ukuba uphose elinye lamaxesha amisiweyo ovavanyo, ilungu labasebenzi bovavanyo liyakukuthinta ukuze kufumaneke olunye usuku nexesha lotyelelo. Ukuba usoloko uphosa amaxesha otyelelo okanye umsebenzi wovavanyo akakufumani, esebenzisa iinkukacha ebezikhutshwe nguwe, kuya kubayimfuneko ukuba sikundwendwele ekhaya ukuze siphinde simise olunye utyelelo lovavanyo.

You will be asked to provide contact information so that we can get in touch with you during the study. Study staff will talk to you about the best way to contact you. If 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.

UQHAGAMSHELWANO KWIXA ELIZAYO LOVAVANYO
CONTACT FOR FUTURE STUDY

Emva kotyelelo lwakho lokugqibela emva kwenyanga eziyi 24 emva kokubeleka, singaphinde siqhagamshelane nawe kwixa elizayo ukuze uthathe inxaxheba kolunye uphando lovavanyo. Ngelo xeshauyakucelwa uphinde ujonge utyikitye olunye uxwebhu lwesivumelwano. Ungakhetha ukungathathi nxaxheba nakoluphi uvavanyo kwixesha elizayo ukuba uyacelwa. Uyakucelwa ukuba unikeze ngenkcukacha zakho zoqhagamshelwano ukuze sikwazi ukukuthinta ngophando lovavanyo olongezelelweyo. Abasebenzi bovavanyo baya kuthetha nawe ngeyona ndlela ingcono yokuqhagamshelana nawe.

After the completion of your last visit at 24 months postpartum, we might contact you again in the future to take part in other research studies. At that time, you would be asked to review and sign another consent form. You can choose not to take part in any future studies if you are asked. You will be asked to provide contact information so that we can get in touch with you regarding additional research studies. Study staff will talk with you about the best way to contact you.

YINTONI IMINGCIPHEKO ELINDELEKILEYO EKUTHATHENI INXAXHEBA KOLUPHANDO?
WHAT ARE THE POTENTIAL RISKS OF TAKING PART IN THE STUDY?

Ungaziva ungonwabanga ngeminye imibuzo emayela nawe oyakuthi uyibuzwe. Ungavumi ukuphendula nawuphina umbuzo ongafuni kuwuphendula.

Ukhona umngcipheko ekwabelaneni ngenkcukacha zakho nezonyango. Siya kulumka ekugcineni iinkcukacha zakho ziyimfihlo kangangoko esinokwenza ngako. Utsalo-gazi lwenziwa ngokwesiqhelo kukhathalelo lonyanga lwaye lunemingciphekwana engephi yokuziva ungonwabanga. Abasebenzi abanamava bayakutsala eligazi phantsi kwemeko zococeko ukuze ukhuseleke kulemingcipheko.

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.

Drawing blood is normally done as part of routine medical care and presents a slight risk of discomfort. Experienced staff will draw blood under sterile conditions in order to protect you against these risks.

YINTONI INZUZO ELINDELEKILEYO EKUTHATHENI INXAXHEBA KOLU VAVANYO
WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?

Akukho nzuzo engqamene nawe ekuthatheni inxaxheba kolu vavanyo, kodwa ukuba sibona ingxaki yokhathalelo lwempilo kuwe nakumntwana wakho ngeli xesha ukolu phando, siyakuqinisekisa ukuba uthunyelwa kwiziko lempilo elililo. Ulwazi olufunyenwe kolu vavanyo lunganceda ukuphucula iinkonzo ezinikeza amachiza okuthomalalisa iNtsholongwane ka Gawulayo kubafazi abaphila naleNtsholongwane eKapa, kwiPhondo leNtshona-Koloni, nakuMzantsi Afrika jikelele.

There is no direct benefit to you if you take part in this study, but if we identify any health care problem for you or your baby during the course of the study, we will make sure that you are referred to the appropriate health care services. In addition, the information gained in this study may help to improve ART services for HIV-infected pregnant women in Cape Town, the Western Cape Province, and across South Africa.

ZIINTONI EZINYE IINDLELA ZOKUTHABATHA INXAXHEBA?
WHAT ARE THE ALTERNATIVES TO TAKING PART?

Ezinye iindlela ekuthabatheni inxaxheba koluvavanyo kukuqhubeka ngokhathalelo lwakho lomlinganiselo lwabo bonke abafazi abaphila neHIV abakunyango lwamachiza entsholongwane emva kokubeleka, lo nto ithetha ukuba uyakuthunyelwa ukusuka kwicandelo lobelekiso ukuya kwikliniki yakho yonikezo machiza okuthomalalisa intshongwane eGuguletu CHC. Umntwana wakho uyakuthunyelwa ngokukhawuleza kwikliniki encinci ekufutshane kuwe azuze nolawulo olungaphezulu.

The alternative to taking part in this study is to continue with the standard of care for all HIV-positive women on ART postpartum, which means that you will be referred from the MOU to your nearest general ART clinic, which is the ART clinic at the Gugulethu CHC. Your baby will be referred as soon as possible to your nearest primary health care facility for further management.

KUTHIWANI NGEMFIHLELO
WHAT ABOUT CONFIDENTIALITY?

Ukuba uyavuma ukuthabatha inxaxheba, lonke ulwazi oluqokelelwe ngexesha lophando luyakugcinwa luyimfihlelo. Igama lakho aliyi kubhalwa kuma xwebhu ovavanyo lingasayi kusetyenziswa naluphina ulwazi okanye ispesimeni zaselebhu eziqokelelwe ngokuyinxenye yovavanyo.

Zonke izixhobo zophando ziya kugcinwa kwi khabhati etshixwayo. Ngabasebenzi bophando kuphela nabaphononongi boqhubeko abaya kuba nendlela yokufikelela kwezizixhobo. Bonke abasebenzi abaqokelela iinkcukacha nabolawulo bayakufumana uqeqesho lwemfihlelo.

Ngeli xesha kusenzwa le nkxamleko yokugcina iimfihlelo,ukuba abasebenzi bophando bafumanisa ukuba ungasemngciphekweni wokuzenzakalisa, okanye omnye umntu, okanye umntwana okwimpatho-mbi yabantwana okanye/nokungahoywa, abasebenzi bophando bayakwazisa abasemthethweni.

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 it will not be used in connection with any information or lab specimens 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.

While these efforts will be made to maintain confidentiality, if the study staff learns that you are a risk to yourself or someone else or of possible child abuse and/or neglect, study staff will tell the proper authorities.

KUTHIWANI NGE INSHORENSI?
WHAT ABOUT INSURANCE?

Akukho mayeza okuhlola asetyenzisiweyo koluvavanyo. Ngoko, akukho inshorensi iyakufumaneka. Nangona, uyakukhuseleka ngokwemiqathango yeinshorensi yabasebenzi ekhusela abasebenzi beDyunivesiti okanye inshorensi ekhusela ngexesha lengozi okanye ukugula okubangelwe kukuba uthatha inxaxheba kolu vavanyo (iinkcukacha zokhuselo zolu vavanyo zincanyathiselwe kumqukumbelo ekupheleni kweli xwebhu)

There are no experimental medicines being used in this study. Therefore, no insurance has been obtained. However, you will be protected in terms of the study staffs' personal malpractice insurance or the university's insurance cover in the event of injury or illness that is caused by you taking part in this study (details of this insurance cover are attached in the appendix at the end of this document).

IKHONA INTO ENDIYAKUYINIKWA NGOKUTHATHA INXAXHEBA
WILL I BE GIVEN ANYTHING FOR TAKING PART?

Ekupheleni kotyelelo ngalunye, uyakunikwa iR20 ukubuyekeza imali yokukhwela ukuza kolulandelayo uvavanyo, neR120 eyi voucher yegrosara kwaye nesipho esincinci. Kuyakubakho into etyiwayo kutyelelo ngalunye.

At the end of each visit, you will be given R20 in cash to cover the transport cost to your next scheduled study visit, an R120 grocery voucher and a small gift. Refreshments will be provided at all visits.

KUKHO INTLAWULO EKUTHABATHENI INXAXHEBA?
ARE THERE ANY COSTS TO TAKING PART IN THE STUDY?

Akukho ntlawulo ngokuthatha inxaxhaeba koluphando.

There is no cost for being in this study.

NDINGALUSHIYA UPHANDO?
CAN I LEAVE THE STUDY?

Unelungelo lokugqiba ekubeni ungathathi nxaxheba kuvavanyo, ukwala ukuphendula nayiphi imibuzo, okanye ukurhoxa nangaliphi ixesha ngaphandle kwesohlwayo. Ayikuchaphazela ukhathalelo olufumanayo eGuguletu CHC okanye naliphi elinye iziko lempilo.

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 penalty. It will have no effect on the care that you receive at the Gugulethu CHC or any other health facility.

UNAYO IMIBUZO?
DO YOU HAVE ANY QUESTIONS?

Ukuba kukho into engacacanga okanye udinga ulwazi olungaphezu koku, nceda usibuze siyakukunika iimpendulo. Unayo imibuzo ngoku?

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 currently?

ULWAZI OLUTHE VETSHE:
FOR ADDITIONAL INFORMATION:

Ukuba unayo imibuzo okanye ubenengxaki ngeli xesha ubuthatha inxaxheba kolu vavanyo lophando, ungaqhagamshelana no:

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

Prof 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

Ukuba unayo nayiphina imibuzo malunga namalungelo akho nje ngomthathi-nxaxheba wophando, ungaqhagamshelana neli lungu lilandelayo lekomiti yophengululo:

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

INGXELO YESIVUMELWANO:
CONSENT STATEMENT:

Ndilifundile olu xwebhu, okanye ukhona umntu ondifundeleyo. Ndinikiwe ikopi yolu xwebhu. Ndomeleziwe ndanikwa ixesha lokubuza imibuzo. Ndiyavuma ukuthatha inxaxheba koluvavanyo. Ndiyayazi ukuba ukuba nangona ndikhethe ukuba koluvavanyo ndingarhoxa nangaliphi ixesha. Ukuthatha inxaxheba koluvavanyo kukuzikhethela ngokuzithandela kwam. Ndiyaqonda ukuba nokuba ndithatha inxaxheba okanye andiyithathi akuyi kuchaphazela iinkonzo zempilo endizifumane apha namhlanje, okanye nanini na kwixesha elizayo.

I have read this form, or someone has read it to me. I have been offered a copy of this consent form. I was encouraged and given time to ask questions. I agree to be in this study. I know that after choosing to be in this study, 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.

NCEDA BONISA UKUVUMA NGEZANTSI NGOKUTYIKITYA:

PLEASE INDICATE YOUR CONSENT BELOW WITH YOUR SIGNATURE.

Ivolontiya / ***Volunteer:***

Igama kunye Nefani / *Name and Surname* _____

Tyikitya / *Signature* _____ Umhla / *Date* _____

Umsebenzi wophando / ***Staff member:***

Igama kunye Nefani / *Name and Surname* _____

Tyikitya / *Signature* _____ Umhla / *Date* _____

UKUBA IVOLONTIYA ALIKWAZI KUFUNDA OKANYE UKUBHALA, IVOLONTIYA LIYAKUBONAKALISA IMVUME NGOMNWE NAYO YONKE INKQUBO YODLIWANO-NDLEBE IYAKUQWALASELWA LINGQINA ELIZIMELEYO ELIYA KUNGQINA INKQUBO EMVA KOKUBA IMVUMELWANO YENZIWE

IF THE VOLUNTEER IS UNABLE TO READ OR WRITE, THE VOLUNTEER MUST INDICATE CONSENT WITH A FINGERPRINT AND THE ENTIRE COUNSELLING PROCESS MUST BE OBSERVED BY AN INDEPENDENT WITNESS WHO CAN CONFIRM THE PROCEDURE ONCE CONSENT HAS BEEN GIVEN.

Umnwe wevolontiya / ***Fingerprint of volunteer:***

Ingqina / *Witness*:

Ndiyavuma ukuba ndizimele andikho kuphando kwaye ndiyayingqina yonke inkqubo yekhawunseling yoxwebhu lwesivumelwano ngolwimi lwasekhaya lwevolontiya.

I confirm that I am independent of the study and that I witnessed the entire informed consent counselling process in the home language of the volunteer

Igama kunye Nefani / *Name and Surname* _____

Tyikitya / *Signature* _____ Umhla / *Date* _____

ENKOSI / *THANK YOU*

UMQUKUMBELEO: INGCACISO YEDYUNIVESITI YASE KAPA YEINSHORENSI ENGENASIPHENE
APPENDIX: EXPLANATION OF THE UNIVERSITY OF CAPE TOWN'S NO FAULT INSURANCE POLICY

KWENZEKA NTONI XA KUKHO INTO ENGAHAMBANGA KAKUHLE?
WHAT IF SOMETHING GOES WRONG?

Idyunivesiti yase Kapa ine inshorensi ekhusela kwixa lokwenzakala ngexesha uthatha inxaxheba kuvavanyo. Umntu welnshorensi uyakuhlawula zonke iindleko ezinxulumene nonyango ngokwe migaqo ye Good Clinical Practice Guidelines zaseMzantsi Afrika, ezisekwe phantsi kwe British Pharmaceutical Industry Guidelines (ABP) xa kukho umenzakalo okanye imiphumela eyenzeke ngokuthabatha inxaxheba ngqo kuvavanyo. Awuyikunyanzeleka ukuba ungqinisise ubutyala kwicala le Dyunivesiti.

Idyunivesiti ayiyi kuchaphazeleka kwilahleko, umenzakalo okanye/nengozi onokuthi uyifumane apho ilahleko iyakubangelwa koku kungezantsi:

- Kukusetyenziswa kwamachiza angagunyaziswanga
- Nawuphina umenzakalo ozizphumo zokungalandeli iimfuno zeprotokol okanye imiqathango obuyinikwe ngabasebenzi bophando
- Nawuphina umenzakalo obangelwe kukungakhathali kwakho.

The University of Cape Town (UCT) has insurance cover for the event that research-related injury or harm results from your participation in the study. The insurer will pay all reasonable medical expenses in accordance with the South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI) in the event of an injury or side effect resulting directly from taking part in the study. You will not be required to prove fault on the part of the University.

The University will not be liable for any loss, injuries and/or harm that you may sustain where the loss is caused by:

- *The use of unauthorised medicine or substances during the study;*
- *Any injury that results from you not following the protocol requirements or the instructions that the study staff may give you;*
- *An injury that results from negligence on your part*

[Researchers must bear in mind that it is unacceptable to impose a burden on participants who may not recognize symptoms or have the ready means to take action.]

By agreeing to take part in this study, you do not give up your right to claim compensation for injury where you can prove negligence, in separate litigation. In particular, your right to pursue such a claim in a South African court in terms of South African law must be ensured. Note, however, that you will usually be requested to accept that payment made by the University under the SA GCP guideline 4.11 is in full settlement of the claim relating to the medical expenses.

An injury is considered trial-related if, and to the extent that, it is caused by study activities. You must notify the study staff immediately of any side effects and/or injuries during the trial, whether they are research-related or other related complications.

UCT reserves the right not to provide compensation if, and to the extent that, your injury came about because you chose not to follow the instructions that you were given while you were taking part in the study. Your right in law to claim compensation for injury where you prove negligence is not affected. Copies of these guidelines are available on request.

Infant medical history at enrolment

PACART

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

18. INFANT MEDICAL HISTORY Visit 1, Version 3

IF MOTHER HAS HAD TWINS, THIS FORM IS FOR THE FIRSTBORN TWIN (THE OLDER TWIN)

Siza kubuza imibizo embalwa malunga nempilo yomntwana wakho namhlanje. Ukuba ikhona ingxaki anayo namhlanje ngokwasempilweni, siza kukunika ileta ukuze umthumele kwikliniki yakho.
We will now ask about how your baby is today. If there are any problems, we will refer you to your clinic.

1. Uphi umntwana wakho namhlanje? *Where is your baby today?*

☐ At Green Clinic with mother
☐ Usekhaya *At home*
☐ Ekliniki/kutyelelo ekliniki *Outpatient/clinic visit*
☐ Ulalisiwe eRedCross *Inpatient at Red Cross*
☐ Ulalisiwe eGSH *Inpatient at Groote Schuur Hosp*
☐ Ulalisiwe eNSH *Inpatient at New Somerset Hosp*
☐ Ulalisiwe eMMH *Inpatient at Mowbray Maternity Hospital*
☐ Okunye cacisa *Other* ***specify***:_____

2. Ingaba umntwana unazo na ezingxaki zilandelayo NAMHLANJE? *Does your baby have any of the following problems TODAY?*

a. Ukhohlokhohlo *Coughing* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

b. Ukuphefumla ngamandla *Fast breathing* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

c. Isifuba esitswinayo *Wheezing (whistling chest)*..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

d. Utyatyazo *Diarrhoea*..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

e. Ifiva (umntwana unobushushu okanye ushushu xa umbamba) *Fever (baby is warm or hot to the touch)*..
..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

f. Akatyi ngendlela eyiyo *Poor feeding* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

g. Urhawuzelelo apho kuphindene isikhumba *Itchy rash in the skin folds* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

h. Olunye *Other*..... ☐ Ewe/*Yes* ☐ Hayi/*No*
Uti ewe Cacisa, ***If yes specify***: _____ ***Number of days*** _____

CRF COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

NOTE TO INTERVIEWER: IF BABY IS UNWELL, REFER TO STUDY NURSE FOR A REFERRAL LETTER TO THEIR USUAL HEALTH CARE PROVIDER

Siza kubuza imibuzo nempilo yosana lwakho.oko lizelwe
We are going to ask you some questions about your baby's health care visits since he/she was born

3. Ingaba umntwana ukhe waxilongwa kumacandelo ezempilo emveni kokuba ezelwe uzothi ga ngoku? (Umz: utyelelo enkabeni eMOU okanye eMowbray Maternity Hospital)? *Has your baby been seen at any health care facility for a **postnatal visit** yet? (e.g. "cord care" visit at the MOU or at Mowbray Maternity Hospital)*

☐ Ewe *Yes* **Ukuba uthi ewe, phi** ***If Yes, where:*** _____

☐ Hayi okwangoku *Not yet*

☐ Hayi okwangoku, kodwa ndityelela namhlanje *Not Yet, but going today*

4. Oku ulubelekile usana lwakho, selukhe lwathunyelwa kwamanye amacandeo empilo kuba lugula zizifo zabantwana? *Since delivery, has your new baby been **referred** to any other health facility for infant-related care?*

..... ☐ Ewe/*Yes* ☐ Hayi/*No*

IF YES, PLEASE COMPLETE ONE ROW FOR EACH REFERRAL

	Isizathu sokumthumela *Reason for referral*	Iziko lezempilo omthumele kuyo *Referral facility*	Usutu omthumelele ngayo okanye oze ngayo *Date attended or to be attended*	Amayeza amatsha anikwe wona untwana wakho *New meds or treatments?*
1			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____ _____
2			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____ _____
3			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____ _____
4			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____ _____

CRF COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

5. Ingaba umntwana wakho wavavanyelwa iNtsholongwane kaGawulayo oko wazalwa? *Has your baby had an HIV test since birth?*

☐ Ewe *Yes* **Ukuba uthi ewe, caza indawo** *If yes, specify facility:* _____

Umhla *Date:* ☐☐/☐☐☐/☐☐☐☐

☐ Hayi *No*

☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 6b

6.

a. Zathini iziphumo zovavanyo? *What was the result of the test?*

☐ Zithi unalo ichaphaza *HIV positive*

☐ Azinachaphaza *HIV negative*

☐ Azikazeki *Unknown* ***OR*** Ndisandilindile iziphumo zovavanyo *Still waiting for test result*

IF ANSWER IS HIV POSITIVE, SKIP TO QUESTION 7

b. Bekukho kwakho iziphumo zovavanyo lwe HIV ezibuye zichaphazelekile? *Has any HIV test that the baby has had come back positive?*..... ☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Andiqinisekanga/*Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 9

7. Ingaba umntwana wakho waqaliswa amachiza okuthomalalisa iNtsholongwane kaGawulayo? (Nceda qaphela ukuba oku akubhekiselanga kwi-Nevirapine kodwa kubhekisele kwizithomalalisi zeNtsholongwane kaGawulayo kwiimveku apha ekliniki) *Has your baby been started on antiretrovirals? (NOTE this is not referring to NVP prophylaxis, but to full treatment from the paediatric ART team at the CHC)*

☐ Ewe *Yes* **Ukuba uthi ewe, caza indawo** *If yes, specify facility:* _____

Umhla *Date started:* ☐☐/☐☐☐/☐☐☐☐

☐ Hayi *No*

☐ Andiqinisekanga *Unsure*

IF YES OR UNSURE, SKIP TO QUESTION 9

CRF COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

8. Kutheni umntwana engekaqali ukutya amachiza eNtsholongwane kaGawulayo? *Why has baby not started ARVs?*

☐ Akakathunyelwa okwangoku kwi kliniki yamachiza okuthomalalisa *Not yet referred to ART clinic*

☐ Umama akafuni umntwana aqalise amachiza okuthomalalisa intsholongwane kagawulayo *Mother does not want baby to have ART*

☐ Umama akakwazi ukuya kwi kliniki yamachiza okuthomalalisa intsholongwane kagawulayo okwangoku *Mother has not yet been able to go to ART clinic*

☐ Oogqirha/abongikazi basalindele ingxelo zegazi *Doctors/nurses are waiting for blood results*

☐ Andiqinisekanga *Unsure*

☐ Okunye cacisa *Other specify:*_____

NOTE TO INTERVIEWER: IF BABY IS HIV-POSITIVE BUT HAS NOT YET STARTED ART, PLEASE FOLLOW-UP WHY NOT AND REFER URGENTLY

Siza kubuza imibuzo edibene nempilo yomntwana wakho oko wazalwa
We are going to ask you some questions about your baby's health since he/she was born

NOTE TO INTERVIEWER: "How many times" refers to number of episodes of illness, not the number of days the baby was ill; 1 episode could last for more than 1 day

9. Kwiveki ezimbini ezidlulileyo, ingaba umntwana wakho ebengaphilanga okanye ebene fiva edibene nokukhohlela? (Kuquka nemimi yanamhlanje) *Since birth, has your baby been ill or feverish with a cough? (including today)*..... ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

If Yes, how many times: _____

IF NO OR UNSURE, SKIP TO QUESTION 11

10. Ngelixesha umntwana ebengaphilanga okanye ene fiva edibene nokukhohlela, ingaba ebephefumla nzima okanye ephefumla ngamandla kunesiqhelo, umphefumlo unkqamka, ephefumla ngamandla? *When your baby was ill or feverish with a cough, did he/she breathe with difficulty, or faster than usual with short, fast breaths?*..... ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

CRF COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

11. Ingaba umntwana wakho ebekhe wanencwina (isifuba esitswinayo) oko wazalwa? (Kuquka nemini yanamhlanje) *Has your baby had any wheezing (whistling in the chest) at any time since birth? (including today)*

☐ Hayi *No*
☐ Ngamanye amaxesha *Sometimes (<1 day a week)*
☐ Qho *Often (≥ 1 day a week)*
☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 15

12. Ingaba umntwana ebene fiva ngexesha etswinelwa sisifuba? *Did the baby have a cold at the time of the wheeze?* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

13. Uhlaselwe kangaphi umntwana wakho sisifuba esitswinayo oko wazalwa? *How many attacks of wheezing has your baby had since birth? **Please note an "attack" of wheezing can last for more than 1 day continuously.***

☐ Akazange ahlaselwe *None*
☐ Ityeli elinye ukuya kumatyeli ayi-3 *One to three attacks*
☐ Amatyeli ayi-3 ukuya kumatyeli ayi-12 *Three to twelve attacks*
☐ Amatyeli agqithileyo ku-12 *More than 12 attacks*
☐ Andiqinisekanga *Unsure*

14. Ingaba ukutswina kwesifuba bekusenza kubenzima ukuba umntwana wakho alale? *Has the wheeze ever made it difficult for the baby to sleep?*

☐ Hayi *No*
☐ Ngamanye amaxesha *Sometimes (< 1 day a week)*
☐ Rhoqo *Often (≥ 1 day a week)*
☐ Andiqinisekanga *Unsure*

15. Umntwana wakho wakhe wabanerhashalala erhawuzelayo emiphindweni yesikhumba sakhe oko wazalwa? (ngakumbi emva kwendlebe, entanyeni, emiphindweni yengqiniba okanye nasemva kwamadolo). *Has the baby had an itchy rash in his/her skin folds e.g. behind the ears, in the neck, in the elbow fold, and/or behind the knee since birth?* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

CRF COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

16. Kwiveki ezimbini ezidlulileyo ingaba umntwana wakho ukhe wanesigulo sotyatyazo? (Kuquka nonamhlanje) *Since birth, has your baby had diarrhoea? (including today)*.....

..... ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

If Yes, how many times _____

IF NO SKIP TO QUESTION 18

17. Ngosuku olubi kakhulu lotyatyazo umntwana uzithume kangaphi? *On the worst day of the diarrhoea, how many bowel movements did the baby have?*

☐ Amatyeli ayezithuma ngayo *Number of bowel movements:*_____

☐ Andiqinisekanga *Unsure*

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Ngoku sizakubuza imibuzo ngokuba ulifumana kubani uncedo xa engaphilanga umntwana wakho. Sicela uchaze zonke izigulo umntwana wakho awakhe wanazo oko wazalwa, kwaye uquke nokhohlo-khohlo okanye utyatyazo

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

18. Oko umntwana wakho wazalwa, wakhe wamsa ekliniki ukuze afumane unyango okanye iingcebiso malunga nasiphi na isigulo? *Since birth, have you taken your baby to any health care providers for treatment or advice about any illness.* ..... ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 19

NOTES TO INTERVIEWER: Please complete the following information for each visit that has been made to a health care provider for the baby's illness

Ebebonwe phi umntwana? *Where was baby seen?* ***Select ALL that apply***	Wayegula yintoni? *What was the diagnosis?* ***Select ALL that apply***	Wafumana unyango olunjani? *What treatment did baby receive?* ***Select ALL that apply***	Ingaba umntwana kwafuneka alaliswe esibhedlele? *Did the baby sleep in the hospital?*	Kwenzeke nini oku? Nika umhla. *When was this?*
☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Whooze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe*Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: _____ MMM: _____ YYYY: _____

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☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* ***Specify***:_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Wheeze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* ***Specify***:_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* ***Specify***:_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe*Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: _____ MMM: _____ YYYY: _____

☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* ***Specify***:_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Wheeze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* ***Specify***:_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* ***Specify***:_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe*Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: _____ MMM: _____ YYYY: _____

CRF COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

19. Oko wazalwa umntwana ukhona umntu owakhe wamvavanyela iTB(isifo sephepha) umntwana wakho?

Since birth, has anyone tested your baby for TB?..... ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 23

20. Uvavanyo lwesifo sephephe lwenziwa kumntwana wakho? *When was the baby tested for TB?*.....

..... ☐☐/☐☐☐/☐☐☐☐

21. Umntwana wavavanywa kweyiphi na ikliniki/isibhedlele? *At which clinic/hospital was the baby tested?*

☐ Ekliniki, cacisa *Clinic, specify*:_____

☐ Red Cross Hospital

☐ Groote Schuur Hospital

☐ New Somerset Hospital

☐ Okunye cacisa *Other specify*:_____

☐ Andiqinisekanga *Unsure*

22. Zazisithini na iziphumo zovavanyo? *What was the result of the tests?*

☐ Umntwana akana- TB kwaye akukho mfuneko yokuba atye amayeza *Baby does not have TB and does not need medicine*

☐ Umntwana akana- TB kodwa ikhona imfuneko yokuba afumane amayeza okukhusela i-TB *Baby does not have TB but needs medicine to prevent TB*

☐ Umntwana unayo iTB kwaye uyawadinga amayeza okunyanga i-TB *Baby does have TB and needs medicine to treat TB*

☐ Andiqinisekanga *Unsure*

☐ Okunye cacisa *Other specify*:_____

23. Oko wazalwa umntwana wakhe wawanikwa amayeza e-TB? *Since birth, has the baby been given any TB medication?* ***Note: even if the baby does not have TB, if a close adult has TB, the baby may be getting medicine to protect him/her from getting TB; this is called Isoniazid (INH) or Isoniazid Preventive Therapy (IPT)***

☐ Ewe, umntwana ebeyinikwa i-INH ethintela isifo seTB *Yes, the baby has been given INH TB prevention*

☐ Ewe, umntwana uwafumene amayeza okunya iTB *Yes, the baby has been given full TB treatment*

☐ Hayi, umntwana akazange afumane nawaphi na amayeza e-TB *No, the baby hasn't had ANY TB pills*

☐ Andiqinisekanga *Unsure*

☐ Okunye cacisa *Other specify*:_____

IF NO OR UNSURE, SKIP TO QUESTION 26

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24. Umntwana wakho uwaqale nini amachiza e-TB, unyango olugcweleyo okanye amayeza athintela i-TB (INH)? *When was the TB medicine started? (Full treatment OR INH)* ☐☐/☐☐☐/☐☐☐☐

25. Uwafumana phi umntwana wakho amachiza eTB, unyango olugcweleyo okanye amayeza athintela i-TB (INH)? *From where does your baby receive the TB medicine? (Full treatment OR INH)*

Lesibhedlele/ikliniki ***Name of hospital/clinic:*** _____

26. Ngawaphi amayeza aselwa ngumntwana wakho? *Which of these medicines is your baby currently receiving:*

a. Iyeza labantwana /ezakhamzimba – multivitamins *Multivitamins (e.g. Kiddievite)* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

b. Iyeza lesakhamziba eliyi-Iron *Iron drops* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

c. Iyeza lesakhamziba eliyi-Zinc *Zinc syrup* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

d. Iyeza leNtsholongwane kaGawulayo eliyi-Nevirapine *Nevirapine* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

e. Iyeza leNtsholongwane kaGawulayo eliyi-Zidovudine *Zidovudine (AZT)* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

f. Cotrimoxazole / Bactrim Trimethoprim-Sulfamethoxazole / Resmed / Iantibiotic ukukhusela ulwasuleleko lwesifuba *Antibiotic to prevent chest infection* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

g. Iipilisi ze-TB *TB drugs* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

h. Iipilisi ezibulala iiNtsholongwane *Antibiotics* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

i. Okunye *Other* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*

Cacisa ***Specify:*** _____

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CRF COMPLETED BY: ☐☐☐

Infant medical history at follow-up visits

PACART

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

17. INFANT MEDICAL HISTORY 3 Month Visit, Version 3

IF MOTHER HAS HAD TWINS, THIS FORM IS FOR TWIN 1 (THE OLDER TWIN)

Siza kubuza imibizo embalwa malunga nempilo yomntwana wakho namhlanje. Ukuba ikhona ingxaki anayo namhlanje ngokwasempilweni, siza kukunika ileta ukuze umthumele kwikliniki yakho.
We will now ask about how your baby is today. If there are any problems, we will refer you to your clinic.

1. Ingaba uphi umntwana wakho namhlanje? *Where is your baby today?*

☐ At Green Clinic with mother
☐ Usekhaya *At home*
☐ Ekliniki/kutyelelo ekliniki *Outpatient/clinic visit*
☐ Ulalisiwe eRed Cross *Inpatient at Red Cross*
☐ Ulalisiwe e-GSH *Inpatient at Groote Schuur Hosp*
☐ Ulalisiwe e-NSH *Inpatient at New Somerset Hosp*
☐ Ulalisiwe e-MMH *Inpatient at Mowbray Maternity Hospital*
☐ Okunye cacisa *Other* ***specify***:_____

2. Ingaba umntwana unazo na ezingxaki zilandelayo NAMHLANJE? *Does your baby have any of the following problems TODAY?`*

a. Ukhohlokhohlo *Coughing* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

b. Ukuphefumla ngamandla *Fast breathing* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

c. Isifuba esitswinayo *Wheezing (whistling chest)*..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

d. Utyatyazo *Diarrhoea*..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

e. Ifiva (umntwana unobushushu okanye ushushu xa umbamba) *Fever (baby is warm or hot to the touch)*..
..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

f. Akatyi ngendlela eyiyo *Poor feeding* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

g. Urhawuzelelo apho kuphindene isikhumba *Itchy rash in the skin folds* ..... ☐ Ewe/*Yes* ☐ Hayi/*No*
If Yes, number of days _____

h. Olunye *Other*..... ☐ Ewe/*Yes* ☐ Hayi/*No*
Uti ewe Cacisa, ***If yes specify***: _____ ***Number of days*** _____

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INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

NOTE TO INTERVIEWER: IF BABY IS UNWELL, REFER TO STUDY NURSE FOR A REFERRAL LETTER TO THEIR USUAL HEALTH CARE PROVIDER

Siza kubuza imibuzo nempilo yosana lwakho.oko lizelwe
We are going to ask you some questions about your baby's health care visits since he/she was born

3. *Has your baby had his/her 10 week vaccination yet?*

☐ Ewe *Yes* Ukuba uthi ewe, phi ***If Yes, when?*** ☐☐/☐☐☐/☐☐☐☐

☐ Hayi okwangoku *Not yet*

☐ Hayi okwangoku, kodwa ndityelela namhlanje *Not Yet, but going today*

4. Ukugibela kwakho ukuzosibona, umntwana wakho ukhe wathunyelwa kwamanye amacandelo empilo kuba ukuze afumena uxilongo lweemveku? *Since we last saw you, has your baby been **referred** to any other health facility for infant-related care?*..... ☐ Ewe/*Yes* ☐ Hayi/*No*

IF YES, PLEASE COMPLETE ONE ROW FOR EACH REFERRAL

	Isizathu sokumthumela *Reason for referral*	Iziko lezempilo omthumele kuyo *Facility referred to*	Usutu omthumelele ngayo okanye oze ngayo *Date attended or to be attended*	Akhona amayeza amatsha anikwe wona untwana wakho *New meds or treatments?*
1			Imini *Day:*_____ Inyanga *Month:*_____ Unyaka *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet Attended *If yes, specify:* _____
2			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____
3			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____
4			*Day:*_____ *Month:*_____ *Year:*_____	☐ Ewe/*Yes* ☐ Hayi/*No* ☐ Not yet attended *If yes, specify:* _____

INFANT PID: ☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

5. Ingaba umntwana ukhe wenziwa uvavanyo lweNtsholongwane kaGawulayo ukugqibela kwethu ukukubona? *Has the baby had an HIV test since we last saw you?*

☐ Ewe *Yes* Ukuba uthi Ewe, chaza indawo ***If yes, specify facility:*** _____

Umhla ***Date:*** ☐☐/☐☐☐/☐☐☐☐

☐ Hayi *No*

☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 6b

6.

a. Ingaba ziye zathini iziphumo zovavanyo? *What was the result of this test?*

☐ Zithi unalo ichaphaza *HIV positive*

☐ Azinachaphaza *HIV negative*

☐ Azikazeki *Unknown OR* Ndisesemlindweni weziphumo zovavanyo *Still waiting for test result*

IF ANSWER IS HIV POSITIVE, SKIP TO QUESTION 7

b. Bekukho kwakho iziphumo zovavanyo lwe HIV ezibuye zichaphazelekile? *Has any HIV test that the baby has had come back positive?*..... ☐ Ewe/*Yes* ☐ Hayi/*No*

IF NO, SKIP TO QUESTION 9

7. Ingaba umntwana wakho waqaliswa amachiza okuthomalalisa iNtsholongwane kaGawulayo? (Nceda qaphela ukuba oku akubhekiselanga kwi-Nevirapine ekhusela umntwana kwiNtsholongwane kodwa kubhekisele kwizithomalalisi zeNtsholongwane kaGawulayo kwiimveku ezinaso isifo ezifumana amayeza apha ekliniki) *Has your baby been started on antiretrovirals? (NOTE this is not referring to NVP prophylaxis, but to full treatment from the paediatric ART team at the CHC)*

☐ Ewe *Yes* Ukuba uthi ewe, caza indawo ***If yes, specify facility:*** _____

Umhla ***Date started:*** ☐☐/☐☐☐/☐☐☐☐

☐ Hayi *No*

☐ Andiqinisekanga *Unsure*

IF YES OR UNSURE, SKIP TO QUESTION 9

INFANT PID: ☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

8. Kutheni umntwana engekaqali ukutya amachiza eNtsholongwane kaGawulayo? *Why has baby not started ARVs?*

☐ Akakathunyelwa okwangoku kwi kliniki yamachiza okuthomalalisa *Not yet referred to ART clinic*

☐ Umama akafuni umntwana aqalise amachiza okuthomalalisa intsholongwane kagawulayo *Mother does not want baby to have ART*

☐ Umama akakwazi ukuya kwi kliniki yamachiza okuthomalalisa intsholongwane kagawulayo okwangoku *Mother has not yet been able to go to ART clinic*

☐ Oogqirha/abongikazi basalindele ingxelo zegazi *Doctors/nurses are waiting for blood results*

☐ Andiqinisekanga *Unsure*

☐ Okunye cacisa *Other specify*:_____

NOTE TO INTERVIEWER: IF BABY IS HIV-POSITIVE BUT HAS NOT YET STARTED ART, PLEASE FOLLOW-UP WHY NOT AND REFER URGENTLY

Siza kubuza imibuzo edibene nempilo yomntwana wakho oko wazalwa
We are going to ask you some questions about your baby's health since he/she was born

NOTE TO INTERVIEWER: "How many times" refers to number of episodes of illness, not the number of days the baby was ill; 1 episode could last for more than 1 day

9. Kwiiveki ezimbini ezidlulileyo, ingaba umntwana wakho ebengaphilanga okanye enobu fiva obudibene nokhohlokhohlo (kuquka nemini yanamhlanje)? *In the last 2 weeks, has your baby been ill or feverish with a cough (including today)?* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

IF NO, SKIP TO QUESTION 12

10. Kwiiveki ezimbini ezidlulileyo, kukangaphi umntwana wakho engaphilanga okanye ene fiva edibene nokukhohlela (Kuquka nemini yanamhlanje)? *In the last two weeks, how many times has the baby been ill or feverish with a cough (including today)?* ☐☐

11. Ngelixesha umntwana ebengaphilanga okanye ene fiva edibene nokukhohlela, ingaba ebephefumla nzima okanye ebephefumla ngesantya esiphezulu nesifutshane? *When your baby was ill or feverish with a cough, did he/she breathe with difficulty, or faster than usual with short, fast breaths?* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

12. Ukugqibela kwethu ukubona, mangaphi amaxesha engaphilanga umntwana okanye enefiva nokhohlokhohlo? *Since we last saw you, how many times has the baby been ill or feverish with a cough? This will include the number of illnesses in Q10 as well as any earlier illnesses* ☐☐

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13. Ingaba umntwana ebekhe wanencwina (isifuba esitswinayo) ukugqibela kwethu ukubona (kuquka nemini yanamhlanje)? *Has your baby had any wheezing (whistling in the chest) at any time since we last saw you (including today)?*

☐ Hayi *No*
☐ Ngamanye amaxesha *Sometimes (<1 day a week)*
☐ Qho *Often (≥ 1 day a week)*
☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 17

14. Ingaba umntwana ebene fiva ngexesha etswinelwa sisifuba? *Did the baby have a cold at the time of the wheeze?* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

15. Uhlaselwe kangaphi umntwana wakho sisifuba esitswinayo ukugqibela kwethu ukukubona? *How many attacks of wheezing has your baby had since we last saw you?* ***Please note an "attack" of wheezing can last for more than 1 day continuously.***

☐ Akazange ahlaselwe *None*
☐ Ityeli elinye ukuya kumatyeli ayi-3 *One to three attacks*
☐ Amatyeli ayi-3 ukuya kumatyeli ayi-12 *Three to twelve attacks*
☐ Amatyeli agqithileyo ku-12 *More than 12 attacks*
☐ Andiqinisekanga *Unsure*

16. Ingaba ukutswina kwesifuba bekusenza kubenzima ukuba umntwana wakho alale? *Has the wheeze ever made it difficult for the baby to sleep?*

☐ Hayi *No*
☐ Ngamanye amaxesha *Sometimes (< 1 day a week)*
☐ Rhoqo *Often (≥ 1 day a week)*
☐ Andiqinisekanga *Unsure*

17. *Ukugqibela kwekhuukukubona, Ingaba umntwana ukhe wanerhashalala elirhawuzelelayo esikhumbeni sakhe esisongelweyo, umzekelo, emva kweendlebe, entanyeni, engqinibeni, okanye ngasemva kwedolo? Has the baby had an itchy rash in his/her skin folds e.g. behind the ears, in the neck, in the elbow fold, and/or behind the knee since we last saw you?* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

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INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

18. Kwiiveki ezimbini ezidlulileyo ingaba umntwana wakho ukhe wanesigulo sotyatyazo (kuquka usuku lwanamhlanje)? *In the last 2 weeks, has your baby had any illness with diarrhoea (including today)?*

☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE SKIP TO QUESTION 20

19. Kwiiveki ezimbini ezidlulileyo kukangaphi umntwana wakho esiba nesigulo sotyatyazo? *In the last 2 weeks, how many times has your baby had any illness with diarrhoea (including today)?* ☐☐

NOTE TO INTERVIEWER: Please note this is referring to periods of illness, not to the number of days with diarrhoea

20. Ukugqibela kwakho ukuzosibona, mangaphi amaxesha umntwana wakho okhe wanesigulo sotyatyazo? *Since we last saw you, how many times has your baby had a diarrhoeal illness?* ☐☐

IF BABY HAS HAD NO DIARRHOEA SINCE LAST SEEN, SKIP TO QUESTION 22

21. Ngosuku olubi kakhulu lotyatyazo umntwana uzithume kangaphi? *On the worst day of the diarrhoea, how many bowel movements did the baby have?*

☐ Amatyeli ayezithuma ngayo *Number of bowel movements:*_____

☐ Andiqinisekanga *Unsure*

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INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

Ngoku sizakubuza imibuzo ngokuba ulifumana kubani uncedo xa engaphilanga umntwana wakho. Sicela uchaze zonke izigulo umntwana wakho awakhe wanazo oko wazalwa, kwaye uquke nokhohlo-khohlo okanye utyatyazo

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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. Ukugqibela kwethu ukukubona, wakhe wamsa umntwana ekliniki kuba ufuna unyango okanye iingcebiso malunga nasiphi na isigulo? *Since we last saw you, have you taken your baby to any health care providers for treatment or advice about any illness.* ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 23

NOTES TO INTERVIEWER: Please complete the following information for each visit that has been made to a health care provider for the baby's illness

Ebebonwe phi umntwana? *Where was baby seen?* ***Select ALL that apply***	Wayegula yintoni? *What was the diagnosis?* ***Select ALL that apply***	Wafumana unyango olunjani? *What treatment did baby receive?* ***Select ALL that apply***	Ingaba umntwana kwafuneka alaliswe esibhedlele? *Did the baby sleep in the hospital?*	Kwenzeke nini oku? Nika umhla. *When was this?*
☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* *Specify:*_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Wheeze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* *Specify:*_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* *Specify:*_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe*Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: (Imini)_____ MMM: (Inyanga)_____ YYYY (Unyaka)_____

COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Wheeze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe*Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: _____ MMM: _____ YYYY: _____
☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Wheeze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe*Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: _____ MMM: _____ YYYY: _____

COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

☐ Ikiliniki *Clinic* ☐ Iziko lempilo loluntu *Community Health Centre (CHC)* ☐ Isibhedlele *Hospital* ☐ Ugqirha wesintu *Traditional Healer* ☐ Ugqirha *GP* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ukukhohlela *Cough* ☐ Ingwcine *Wheeze* ☐ Usuleleko lwesifuba *Chest Infection* ☐ Utyatyazo *Diarrhoea* ☐ Ukwehla emzimbeni *Poor weight gain* ☐ Akatyi ngendlela eyiyo *Poor feeding* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ iAntibiotics *Antibiotics* ☐ Iyeza lokukhohlela *Cough syrup* ☐ Impompo *Inhaler* ☐ iOxygen *Oxygen* ☐ Iincindi zomlomo *Oral fluids* ☐ Ukuthiwa incindi Ngedrip *Fluid by drip/ IV* ☐ Okunye *Other* *Specify*:_____ ☐ Andiqinisekanga *Unsure*	☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*	DD: _____ MMM: _____ YYYY: _____

23. Ukugqibela kwethu ukukubona, ukhona umntu owenza uvavanyo lwesifo se-TB(isifo sephepha) emntwaneni wakho? *Since we last spoke to you, has anyone tested your baby for TB?* .....

..... ☐ Ewe *Yes* ☐ Hayi *No* ☐ Andiqinisekanga *Unsure*

IF NO OR UNSURE, SKIP TO QUESTION 27

24. Ingaba lwenziwe nini na uvavanyo lwesifo se-TB emntwaneni wakho? *When was the baby tested for TB?*.....

..... ☐☐/☐☐☐/☐☐☐☐

25. Umntwana wavavanywa kweyiphi na ikliniki/isibhedlele? *At which clinic/hospital was the baby tested?*

☐ Ekliniki, cacisa *Clinic, specify*:_____	☐ Red Cross Hospital
☐ Groote Schuur Hospital	☐ New Somerset Hospital
☐ Okunye cacisa *Other specify*:_____	☐ Andiqinisekanga *Unsure*

COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

26. Ingaba ziye zathini na iziphumo zovavanyo? *What was the result of the tests?*

☐ Umntwana akana- TB kwaye akukho mfuneko yokuba atye amayeza *Baby does not have TB and does not need medicine*

☐ Umntwana akana- TB kodwa ikhona imfuneko yokuba afumane amayeza okukhusela i-TB *Baby does not have TB but needs medicine to prevent TB*

☐ Umntwana unayo iTB kwaye uyawadinga amayeza okunyanga i-TB *Baby does have TB and needs medicine to treat TB*

☐ Andiqinisekanga *Unsure*

☐ Okunye cacisa *Other specify*:_____

27. Ukugqibela kwethu ukukubona, umntwana wakho ukhe wanikwa amayeza e-TB? *Since we last saw you, has the baby been given any TB 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)

☐ Ewe, umntwana ebeyinikwa i-INH ethintela isifo seTB *Yes, the baby has been given INH TB prevention*

☐ Ewe, umntwana uwafumene amayeza okunya iTB *Yes, the baby has been given full TB treatment*

☐ Hayi, umntwana akazange afumane nawaphi na amayeza e-TB *No, the baby hasn't had ANY TB pills*

☐ Andiqinisekanga *Unsure*

☐ Okunye cacisa *Other specify*:_____

IF NO OR UNSURE, SKIP TO QUESTION 30

28. Umntwana wakho uwaqale nini amachiza e-TB, unyango olugcweleyo okanye amayeza athintela i-TB (INH)? *When was the TB medicine started? (Full treatment OR INH)* ..... ☐☐/☐☐☐/☐☐☐☐

29. Uwafumana phi umntwana wakho amachiza eTB, unyango olugcweleyo okanye amayeza athintela i-TB (INH)? *From where does your baby receive the TB medicine? (Full treatment OR INH)*

Igama lesibhedlele/ikliniki ***Name of hospital/clinic***:_____

COMPLETED BY: ☐☐☐

INFANT PID: ☐☐☐☐☐-☐-☐☐ Date: ☐☐/☐☐☐/☐☐☐☐

30. Ngawaphi amayeza aselwa ngumntwana wakho? Which of these medicines is your baby currently receiving: *Show the mother a range of possible medicines: multivitamins, iron drops, nevirapine, cotrimoxazole, TB treatment and antibiotics*

a.	Multivitamins (eg. Kiddievite)	☐ Ewe/*Yes* ☐ Hayi/*No*
b.	Iron drops	☐ Ewe/*Yes* ☐ Hayi/*No*
c.	Zinc syrup	☐ Ewe/*Yes* ☐ Hayi/*No*
d.	Nevirapine	☐ Ewe/*Yes* ☐ Hayi/*No*
e.	Zidovudine (AZT)	☐ Ewe/*Yes* ☐ Hayi/*No*
f.	Co-trimoxazole / Bactrim/Trimethoprim-Sulphamethoxazole / Resmed / Iantibiotic ukukhusela ulwasuleleko lwesifuba *Antibiotic to prevent chest infection*	☐ Ewe/*Yes* ☐ Hayi/*No*
g.	TB drugs	☐ Ewe/*Yes* ☐ Hayi/*No*
h.	Antibiotics	☐ Ewe/*Yes* ☐ Hayi/*No*
i.	Okunye *Other*	☐ Ewe/*Yes* ☐ Hayi/*No*
	Cacisa ***specify:***	_____

QC COMPLETED BY: ☐☐☐ **QC DATE:** ☐☐/☐☐☐/☐☐☐☐

COMPLETED BY: ☐☐☐

PACART ethics approvals

Initial approval

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

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

17 April 2015

HREC REF: 194/2015

Prof L Myer
Epidemiology & Biostatistics
Public Health & Family Medicine
Falmouth Building

Dear Prof Myer

PROJECT TITLE: POSTPARTUM ADHERENCE CLUBS FOR ANTIRETROVIRAL THERAPY (PACART)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee 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 30th April 2016.

Please submit a progress form, using the standardised Annual Report Form 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)

Please quote the HREC REF in all your correspondence.

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

Yours sincerely

FAN YSLAMOOUMOOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
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 Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki guidelines.

ETHICS APPROVAL

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

E-52 – Room46, E-Floor, Old Main Building
Groote Schuur Hospital
Observatory 7925
Email: hrec-submissions@uct.ac.za
Website: https://health.uct.ac.za/home/human-research-ethics

30 July 2024

HREC REF: 424/2024

Dr J Odayar
Division of Epidemiology & Biostatistics
FHS
Email: 'asantha.oda ar uct.ac.za
Student: dnkrya001@myuct.ac.za

Dear Dr Odayar

PROJECT TITLE: COMPARING HEALTH OUTCOMES AMONG INFANTS OF WOMEN LIVING WITH HIV OBTAINING POSTPARTUM ART CARE AT ROUTINE PRIMARY HEALTH CARE SERVICES VERSUS ADHERENCE CLUBS IN CAPE TOWN, SOUTH AFRICA-SUB-STUDY LINKED TO 194/2015-
(MASTER CANDIDATE-IN PUBLIC HEALTH -DR RYAN DINKELE)

Thank you for your response letter dated 25 July 2024, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

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

Approval is only granted for one year until the 30 July 2025.

Please submit a progress report, using the standardised Annual Progress Report Forms (FHS016) **or** (FHS 017) if the study continues beyond the approval period. Please submit a Standard Closure form (FHS 010) when the study has been completed, this includes after publication or thesis submission and final completion.
(Forms can be found on our website: www.health.uct.ac.za fhs research humanethics forms)

The HREC acknowledge that the student: Dr Ryan Dinkele will also be involved in this study.

Please quote the HREC REF 424/2024 in all your correspondence.

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.

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

Yours sincerely
PROFESSOR MARC 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

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.

AUTHOR GUIDELINES AND SUBMISSION REQUIREMENTS

Snippet taken from the Journal of the Internation AIDS Society website (JIAS).

3. FREE FORMAT

JIAS offers Free Format submission for a simplified and streamlined submission process.

Before you submit, you will need:

- Your manuscript: this should be an editable file including text, figures, and tables, or separate files—whichever you prefer. All required sections should be contained in your manuscript, including abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. Figures should be uploaded in the highest resolution possible. If the figures are not of sufficiently high quality, your manuscript may be delayed. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. Supporting information should be submitted in separate files. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the editors and reviewers, and the editorial office will send it back to you for revision. Your manuscript may also be sent back to you for revision if the quality of English language is poor.
- An ORCID ID, freely available at https://orcid.org. (Why is this important? Your article, if accepted and published, will be attached to your ORCID profile. Institutions and funders are increasingly requiring authors to have ORCID IDs.)
- The title page of the manuscript, including:
    - Your co-author details, including affiliation and email address. (Why is this important? We need to keep all co-authors informed of the outcome of the peer review process.)
    - Statements relating to our ethics and integrity policies, which may include any of the following (*Why are these important? We need to uphold rigorous ethical standards for the research we consider for publication*):
        - data availability statement
        - funding statement
        - conflict of interest disclosure
        - ethics approval statement
        - patient consent statement
        - permission to reproduce material from other sources
        - clinical trial registration

4. MANUSCRIPT CATEGORIES AND REQUIREMENTS

The *JIAS* accepts submissions in the following categories:

- Research
- Short report
- Review
- Debate

- Commentary
- Letter to the Editor
- Viewpoint
- Field notes

Research - full reports of data from original research studies

Abstract:
Headings: Introduction, Methods, Results, Conclusions
Word limit: 350 words

Main text:
Headings: Introduction, Methods, Results, Discussion, Conclusions
Word limit (quantitative): 3500 words; tables do not contribute to the word count
Word limit (qualitative): 5000 words if the manuscript includes substantial quotes; tables with quotes contribute to the word count; mixed and multiple methods reports may be included if there is a qualitative component with quotes
Numbers of figures and tables: Unlimited
Additional files: Yes