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Travel and adherence to antiretroviral therapy among postpartum women living with HIV in South Africa: a cross-sectional study

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PREAMBLE

Declaration

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

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Date: 10/02/2020

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Abstract

In sub-Saharan Africa, women are disproportionately affected by HIV. Sustained adherence to lifelong antiretroviral therapy (ART) is needed to ensure their own health and prevent transmission of HIV to their partners and their children. However, non-adherence to ART remains a substantial challenge with many associated risk factors. Travel is often reported in the qualitative literature as a barrier to ART adherence among women living with HIV, but few quantitative studies have explored this association. This research aimed to describe travel in the past year among mothers living with HIV in the Long-term Adherence and Care Engagement (LACE) study, to explore factors associated with travel, and to investigate the associations between travel and i) self-reported adherence, and ii) HIV viral load.

Part A of this dissertation is the study protocol that introduces the need for this research and presents how the research will be carried out. Part B is a narrative literature review. The review summarises and synthesises existing research relating to HIV treatment and travel in sub-Saharan Africa, giving context to the dissertation. Part C is the journal "ready" manuscript. This section presents an analysis of data from the LACE study, a cross-sectional survey of women living with HIV approximately four years after they had started ART during pregnancy in Gugulethu, Cape Town.

At the LACE study visit, data on short-term travel patterns (stayed away from home for 3 or more nights) in the past year and self-reported adherence in the past 30 days (using a validated three-item scale) were collected through structured questionnaires, and a blood specimen was tested for HIV viral load. Poisson regression models with robust standard errors were used to explore factors associated with travel (any versus none), self-reported adherence (100% versus <100%), and viral suppression (≤50 copies/mL). Results were reported as crude risk ratios (RR) and adjusted risk ratios (aRR) with 95% confidence intervals (CI).

The results showed that among 353 women enrolled in the LACE study (mean age 32.6 years, 48% employed, 38% married/cohabiting, median 44 months postpartum) 23% (n=81) reported travelling in the past year. Of the women who travelled, most went to the Eastern Cape (90%) and travelled 1-2 times during the year (93%). Women who travelled were more likely to be married/cohabiting than women who had not travelled (aRR = 1.45; 95% Cl: 0.97 – 2.16). Only 9% of women who travelled (7 of 81) reported difficulty with ART adherence due to travel.

Overall, 59% of women reported 100% adherence in the past 30 days: 52% of women who had travelled in the past year versus 61% of those who had not travelled (aRR = 0.83; 95% Cl: 0.66-1.04). Only 56% of the cohort were virally suppressed: 60% and 55% of those who had and had not travelled in the past year, respectively (aRR = 1.10; 95% Cl: 0.89-1.36). Travel in the past year was not significantly associated with self-reported adherence or viral suppression in crude or adjusted analyses.

These results highlight that poor adherence and viremia were very common in this cohort of women, four years after starting ART in pregnancy. Almost a quarter of women reported travel in the past year but only a

few reported difficulties with adherence related to travel and we found no association between travel in the past year, self-reported adherence in the past 30 days or viremia. Further research is needed to understand adherence patterns during periods of travel and interventions are clearly needed to support women's long-term adherence to ART.

Keywords: antiretroviral therapy, women, travel, adherence, viral suppression, South Africa

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PART A: PROTOCOL

1. Protocol synopsis

Sustained antiretroviral therapy (ART) is essential to achieving and maintaining viral suppression in people living with HIV, which optimizes health and prevents HIV transmission. In pregnant and postpartum women in particular, lifelong ART has been essential to ongoing maternal health as well as prevention of mother-to-child HIV transmission.

Unfortunately, non-adherence to ART remains a challenge among postpartum women. Many factors affect a woman's ability to adhere to HIV treatment, including poverty, age, food security, and more recently travel has been proposed as a factor that may hinder adherence. Although the qualitative literature has shown that patients perceive travel as potentially disruptive to adherence, there are few quantitative data exploring travel patterns and the relationship between travel and adherence to ART.

The overall aim of this proposed research is to investigate the relationship between travel and ART adherence. The objectives of the proposed research are 1) to describe travel patterns of postpartum women over a one-year period, 2) to explore factors associated with travel, and 3) investigate whether travel is associated with poor adherence and HIV viremia. The proposed research is a secondary analysis of data collected during the Long-term Adherence and Care Engagement (LACE) study investigating the effect of HIV care service delivery on maternal ART outcomes during the postpartum period. The objectives will be addressed using an anonymised dataset and no additional data collection or contact with study participants will take place.

This research will provide further insight into the impact of travel on ART adherence and viral load (VL) in postpartum HIV-positive women.

2. Introduction

2.1 Background

Globally, there are 18.8 million women and girls living with HIV, and 25% of the world's HIV-positive women live in South Africa (1, 2). Women are at a higher risk of HIV infection with 63% of South African adults living with HIV being women of reproductive age (2). HIV/AIDS is the leading cause of death among women, making them an important population to focus antiretroviral therapy (ART) programmes on (3).

ART is important for all HIV-positive individuals. The World Health Organisation's (WHO) HIV treatment guidelines encourage ART initiation as soon as an individual has been diagnosed, to improve overall health and reduce the risk of transmitting the HIV infection (4). ART adherence is therefore important for the improvement of life expectancy and health. Women initiating and adhering to ART lowers the risk of HIV transmission to their partners and children by achieving and maintaining a suppressed HIV viral load (VL) (5).

Continuous ART adherence is essential to maintain good health outcomes. Unfortunately, adherence to HIV treatment is a major challenge for all people living with HIV and women are a high-risk group of inadequate ART adherence (6, 7).

Barriers to ART adherence in women living with HIV

When HIV-positive mothers are initiated on ART in pregnancy, optimal long-term ART adherence remains low, particularly in the postpartum period (6, 8). Buregyeya *et al*. found that women who are on ART have the highest motivation to adhere to HIV treatment during pregnancy, due to the desire to have an HIV-free baby and the desire to remain healthy for their children (9). However, ART adherence becomes more challenging for women during the postpartum period due to a multitude of barriers (9, 10) .

According to previous research, the most common factors associated with low ART adherence include poverty status, gender inequality, stigma, age, marital status, side effects from medication and food insecurity (10-12). Recently, research has identified travel as another potential barrier to ART adherence (9, 13, 14).

Travel, mobility and HIV

When investigating the barriers of non-adherence, there is limited literature focused on travel and mobility. What is currently known about travel is that it enables riskier sexual behaviour in men and women, and new HIV infections are associated with traveling and mobility (15). Traveling may also affect the ability to access HIV care and this barrier needs to be explored further (10, 14, 15). Travel and mobility are associated with patterns of accessing and receiving HIV care by complicating engagement and adherence to HIV care (13). Anecdotally, we know that many women travel postpartum, however, the level and patterns of geographic travel in this population needs further exploration.

Phillips *et al*. found that 34% of women who initiated ART during pregnancy in Gugulethu, Cape Town moved out of the area after delivery and 9% attended different ART clinics outside of the Western Cape province postpartum (14). Similarly, research on Gauteng-based women found that many women travelled back to family homes for childcare support after delivery (16). Travel appears to occur frequently in postpartum women, and current literature available on postpartum travel has suggested that this movement may be a risk factor for inadequate ART adherence.

Many qualitative studies have highlighted travel as a key risk factor that affects HIV-positive individual's ability to adhere to treatment. People living with HIV in Swaziland were interviewed to investigate reasons for discontinued ART adherence and many of them cited travel as a 'trigger' that leads to eventual non-adherence (17). Out-of-care women, in Malawi, also reported many barriers of

ART adherence which included high mobility, lack of emotional and financial support, and minimal ART education (18).

Mobility studies have explored the possibility of travel hindering ART adherence and have had self-reported accounts of travel leading to difficulties in treatment access, however, there is very little work that has characterised this relationship through quantitative work (13, 15). Hence, to better understand the patterns of travel and the relationship this travel has with ART adherence, more analyses of travel and ART adherence are needed.

2.2 Background to the proposed dissertation

Between April 2017 and May 2018, the Long-term Adherence and Care Engagement (LACE) study (HREC 866/2016) recruited 353 women previously enrolled in a larger maternal and child health-antiretroviral therapy (MCH-ART) cohort study (HREC 451/2012) (Appendix C). These women were invited to the Gugulethu Community Health Centre (CHC) for a single interview regarding their demographics and mother and child's health details. The LACE study assessed the potential impact of the MCH-ART intervention (co-located maternal and childcare postpartum versus standard of care stand-alone services) and evaluated women's HIV treatment outcomes 36-60 months postpartum (19).

Data collected during the LACE interview will provide data for this proposed research. The aim is to describe the travel patterns in postpartum women using the LACE questionnaires and to explore the relationship between travel and ART adherence. We will also investigate sociodemographic characteristics associated with travel.

2.3 Study rationale

Antiretroviral therapy (ART), through universal test and treat, is highly effective when individuals living with HIV initiate and adhere to treatment. We know that there are many facilitators of ART adherence, however, there are a plethora of potential barriers that need further exploration.

Postpartum women are thought to travel frequently, and this is a potential barrier for ART adherence that is poorly characterised. There is limited literature on the impact of travel on adherence to ART. The findings of this study will provide insight into the relationship between travel and ART adherence, and thus the need for ART counselling and interventions around travel.

3. Study aim and objectives

3.1 Study aim

The overall aim of this proposed study is to describe patterns of travel among women living with HIV between three and four years after starting ART in pregnancy, and to investigate whether there is an association between travel and adherence to ART.

3.2 Objectives

3.2.1 To describe the travel patterns over a one-year period (approximately 3-4 years postpartum) of HIV-positive mothers in the LACE study.

3.2.2 To explore factors associated with travel.

3.2.3 To investigate the associations between:

3.2.3.1 travel and self-reported ART adherence

3.2.3.2 travel and VL

3.3 Hypothesis

The primary hypothesis of this study is that travel patterns of HIV-positive women negatively affect their ART adherence and, in turn, worsen their viral suppression. Travel is suspected to disrupt the women's ability to adhere to treatment by disrupting schedules and access to HIV care.

Travel is potentially a step in a chain of events that negatively affects ART adherence and thus, the expectation is that those who travelled may have lower ART adherence and worse VL outcomes compared to those who did not travel.

4. Methodology

4.1 Study design

To address the proposed study objectives, the study design will be a cross-sectional secondary data analysis. The study will analyse data that were collected during questionnaires and VL measures taken from women enrolled in the LACE study which took place in 2017 at the Gugulethu Community Health Centre (CHC).

4.2 Research setting

This analysis will use data collected as part of the LACE study which was a continuation of the MCH-ART study. These studies took place at the Gugulethu CHC, a large primary healthcare facility in Gugulethu, Cape Town. Gugulethu is a low socioeconomic area with high levels of unemployment, and a high HIV burden. The Gugulethu Midwife Obstetrics Unit (MOU) at the CHC provides basic antenatal care (ANC) and delivery services for a large community that includes those in Philippi, Nyanga, Lower Crossroads, Heideveld, Gugulethu and women from the Eastern Cape (20). Over the time of the MCH-ART (2013-2014) study the MOU provided antenatal care for approximately 5000 women annually and the antenatal HIV prevalence was over 25%.

4.3 Study population and sampling

MCH-ART and LACE studies

The parent study, MCH-ART (HREF 451/2012), enrolled consecutive women, aged 18 and older, presenting for antenatal care (ANC) at the Gugulethu MOU who were eligible to start ART between April 2013 and June 2014 (Appendix C) (21). Overall, a total of 628 mothers were enrolled and initiated ART during pregnancy. These enrolled women were then followed prospectively through delivery where women with live births and who were breastfeeding were then enrolled into a postpartum randomized control trial and followed through 18 months postpartum. The postpartum trial aimed to compare different service delivery models to provide maternal HIV and child healthcare postpartum and 471 women were enrolled. As part of the MCH-ART study all women provided informed consent to be contacted in the future for other related research and they provided the study team with contact details.

Following closure of the MCH-ART study, all women enrolled in the postpartum trial were subsequently re-contacted and invited to participate in an additional follow-up visit, the LACE study (HREC REF 866/2016), between 36 and 60 months postpartum (Appendix C). In the LACE study, 353 of the 471 women enrolled in MCH-ART were successfully recruited and, following completion of informed consent, completed the LACE study visit. The primary aim of the LACE study was to investigate the impact of the MCH-ART intervention on outcomes of maternal viral suppression and retention in care at this later timepoint (22).

At the LACE visit, women completed a face-to-face interview including a battery of questionnaires. These included demographic characteristics and a questionnaire on travel in the previous 12 months. Women also completed a self-reported adherence questionnaire and maternal venous blood was drawn for real time VL testing (Abbott Molecular RealTime HIV-1 assay, Abbott Molecular, Illinois, USA) by the National Health Laboratory Services.

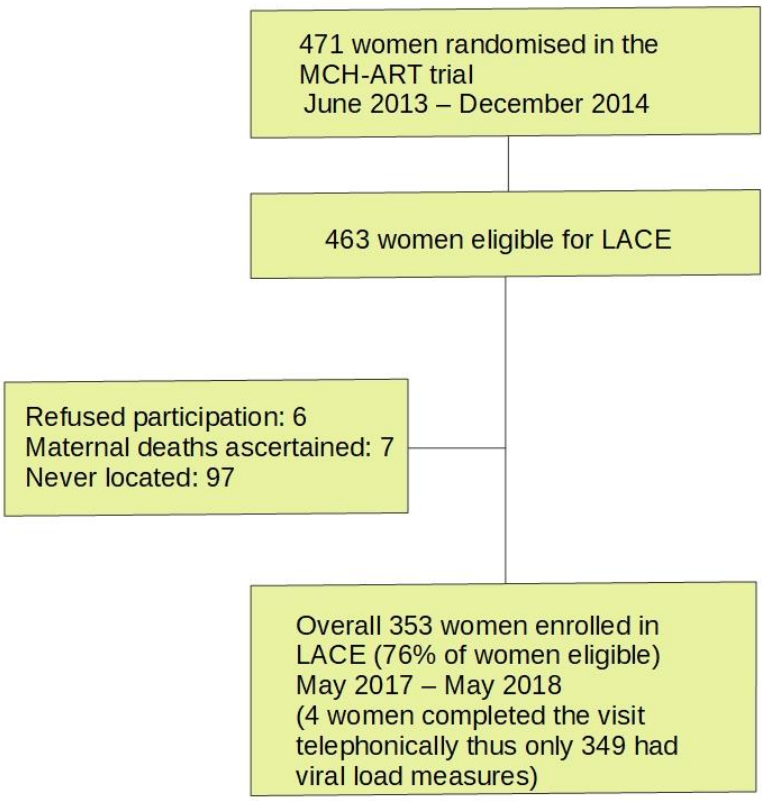

Figure A1: LACE study schematic showing situation of the proposed research analysis.

The proposed study

This proposed study will be a secondary data analysis including all women enrolled in the LACE study 36-60 months postpartum.

4.4 Data collection

The proposed study is a secondary analysis of existing data. All data to be used in these analyses were collected as part of the previous studies, as described above. The ART adherence and travel data will be from the LACE demographics, adherence and travel questionnaires which were administered through face-to-face interviews (Appendices A and B). VL results will be from the blood collected at the LACE visit.

4.5 Measurements

The LACE questionnaires included in this study include sociodemographic characteristics, self-reported adherence and travel patterns (Appendices A and B). Additional demographic and clinical characteristics from the time of enrolment into the MCH-ART study will be drawn from the existing MCH-ART data. VL was measured on all women who attended the LACE study and will also be included as an objective marker of treatment success. The main constructs of interest are summarised in Table A1.

Objective 1: To describe the travel patterns over a one-year period for HIV-positive mothers in the LACE study

To investigate the travel patterns for the participants, there will be an exploration of the main constructs that are defined as follows:

Travel – The travel questionnaire was informed by the available literature and travel will be explored through the questionnaire responses. The questionnaire asked whether the participants had travelled, where they had travelled, frequency of travel, and the nights away from home when travel occurred, therefore the following travel constructs will be used in this research:

- Any travel: "travelled" vs "did not travel"
    - Travelled: ≥3 nights away from home
    - Did not travel: <3 nights away from home
- Frequency of travel: "1-2 times" vs "3-5 times"
- Time spent away from home: "≤21 nights away" vs ">21 nights away"
- Where the participant travelled: description of geographic locations reported

Objective 2: To explore factors associated with travel

The primary outcome of interest for this objective will be travel. The factors potentially associated with travel will be assessed based on the travel and demographic questionnaire responses. The constructs are as follows:

- Any travel: "travelled" vs "did not travel"
- Demographic and behavioural characteristics which include age, marital status, employment status, socioeconomic status, parity, and time of MCH-ART antenatal care (ANC) presentation will be explored. ANC presentation will be considered a proxy for general healthcare seeking behaviours in these women (23).

Objective 3: To investigate the associations between travel and ART adherence

The third objective's primary exposure is travel and the main outcomes of interest are ART adherence and viral suppression. Travel and ART adherence will be explored through the questionnaire responses which will include a qualitative reported impact travel had on ART adherence. ART adherence will be explored through surrogate end points defined as follows:

Self-reported adherence – This construct is defined in two ways:

- no missed ART dose for previous 7 days

- A three-item scale score (0-100) for adherence in the past 30 days. A threshold of 100% adherence and less than 100% adherence will be used based on the following three questions:
    - "In the last 30 days, on how many days did you miss at least one dose of any of your HIV medicines?"
    - "In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?" (Likert scale 1: very poor – 6: excellent)
    - "In the last 30 days how often did you take your HIV medicines in the way that you were supposed to?" (Likert scale 1: never – 6: always)

VL – This construct will be explored in terms of viral suppression. Viral suppression will be defined by VL thresholds of ≤50 copies/mL. VL ≤1000 copies/mL will also be examined in sensitivity analyses. VL will be considered an objective marker of adherence, although it is important to keep in mind that poor adherence is the main reason for unsuppressed VL but there could be other factors responsible, such as drug resistance (24).

Self-reported impact – Participants who reported travel were asked whether there was difficulty adhering to ART during travel. The construct will be a binary variable defined as "difficult" vs "not difficult". Their descriptions of adherence difficulties will also be included.

Table A1: Variables of interest for cross-sectional study.

Variable	Type
Travel patterns	
Travel	Categorical – binary (travelled/did not travel)
Travel frequency	Categorical – binary (1-2 times/3-5 times)
Nights away from home	Categorical – binary (≤21 nights/>21 nights)
Relocation	Categorical – binary (relocated/did not relocate)
Association between travel and ART adherence	
HIV viral load (VL)	Categorical – binary (viral suppression/viremia)
Self-reported ART adherence (30 days)	Categorical – binary (100%/<100%)
Self-reported ART adherence (7 days)	Categorical – binary (yes/no)
Self-reported impact on ART adherence	Categorical – binary (difficult/not difficult)
Additional covariates	
Mean age (in years)	Continuous - numerical
Level of education	Categorical – binary (primary/secondary+)
Employment status	Categorical – binary (employed/unemployed)
Socioeconomic status (SES)	Categorical – ordinal (low/moderate/high)
Housing	Categorical – binary (formal/informal)
Relationship status	Categorical – binary (married/unmarried)
Disclosure status	Categorical – binary (disclosed/undisclosed)
Parity	Categorical – binary (≤2 children/≥3 children)
Presentation to ANC	Categorical – binary (early/late)

4.6 Data management and analysis plan

The completed questionnaire data will be exported to Stata Version 15.0 (Stata Corporation, College Station, Texas, USA) for data cleaning, exploration and analysis. The electronic data will be stored in secure, password-protected compressed files, accessible only to the researchers. The data are anonymous. Study participants will only be identified by a unique study ID and no personal identifiers in all study datasets. The data will not be shared with other parties nor be used for any purpose other than specific objectives of this study.

4.6.1 Univariate and bivariate analysis

In Stata, all the variables of interest will be explored to detect any missing data. The data will be reviewed for any capturing errors. The univariate analysis will be a summary of the participants' baseline characteristics using descriptive statistics. The data exploration will include scatterplots, histograms, and box and whisker plots, along with medians and interquartile ranges (IQR) for continuous variables, and frequencies and proportions for categorical variables, to examine patterns in the data.

The bivariate analysis will include descriptive statistics of baseline characteristics, grouped by travel categories and the adherence outcomes, with appropriate statistical tests for each variable. The Wilcoxon rank-sum test will be used for continuous variables and the Fischer's exact test will be used for categorical variables. These tests will be carried out to explore potential differences in characteristics of women who did and did not travel, and women with and without adequate adherence/viral suppression.

4.6.2 Description of the travel patterns over a one-year period for HIV-positive mothers in the LACE study

In order to address objective one, percentage of women who travelled, frequency of travel and travel destinations will be described through descriptive statistics. Visits to other ART clinics while travelling, self-reported impact on ART adherence, and retrieval of a transfer letter will also be described. Frequencies and proportions of the travel constructs will be used to describe the patterns of travel in these postpartum women.

4.6.3 Exploration of factors associated with travel

In order to address objective two, Poisson regression models with robust standard errors will be generated to explore factors that may be associated with travel. The main outcome of interest will be the 'any travel' variable. Analyses will report crude risk ratios (RR) and adjusted risk ratios (aRR) with 95% confidence intervals (CIs). An α-level of 0.05 for statistical significance will be used in all evaluations.

4.6.4 Investigation of the associations between travel and ART adherence

The main outcome explored in this proposed study will be ART adherence. This will be defined by two main constructs: Self-reported adherence (three-item scale score) “100% adherence” vs “<100% adherence” and HIV viral suppression, “viral suppression (≤50copies/mL)” vs “viremia (>50copies/mL)”.

In order to address objective three, Poisson regression models with robust standard errors will be carried out to estimate the association between travel and ART adherence. Other potential risk factors based on literature review and available data will be included in these models as a secondary objective. The Poisson regression will be done to investigate the relationship between travel and each main outcome. All analyses will report RR and aRR with 95% confidence intervals. An α-level of 0.05 for statistical significance evaluations. Two models will be explored: one using self-reported adherence as the outcome and another with viral suppression as the outcome.

The self-reported impact travel has on ART adherence will also be described for more context on the relationship between the exposure and outcome.

4.7 Potential limitations

All the data for this study is based on the parent study’s questionnaires. The available variables collected and explored in the study will be limited to what the parent study initially collected.

Questionnaires are self-reported measurement tools, thus, the study’s primary exposure and outcome, will be vulnerable to recall and social desirability biases. These biases can lead to overestimation of adherence to care and make the identification of risk factors for the study outcome more difficult. The inclusion of VL is a strength as this presents on objective marker of treatment success, however VL is not a direct measure of treatment adherence.

The definition of travel in adherence literature is highly variable, ranging from day to day mobility to more permanent migration. For this study, simple definitions of travel e.g. travel as a binary variable (travelled/did not travel), may obscure more nuanced travel patterns and associations with adherence. Although women reported on travel in the previous 12 months, we were only able to examine adherence and VL at the study visit and thus short-term impacts of travel more distal from the study visit may not be detected.

Lastly, investigating the effects of travel on ART adherence is limited to the participants’ travel status. Without the participants’ reasons for travelling and without the data for the women lost to follow-up, the findings of this study are restricted. These variables would help to better differentiate the source of inadequate ART adherence between travel and the individual’s behaviours.

4.8 Logistics and timetable

The expected timeline for the completion of this proposed study is summarised in Table A2.

Table A2: Schedule for completion of study.

	Aug '19	Sept '19	Oct '19	Nov '19	Dec '19	Jan '20	Feb '20
Lit Review							
Data Management							
Data Analysis							
Results							
Write-up							

5. Ethical considerations

The parent-study's on-going ethics approval from the University of Cape Town's human research ethics committee (UCT-HREC) and Columbia University, has been available since 2012. The UCT-HREC annually renews this ethics approval and this proposed study was also approved by the UCT-HREC (HREC REF 864/2019) (Appendix C).

5.1 Informed consent

There will be no direct contact with any of the study participants, however, women eligible for this proposed study must have signed the LACE study's informed consent form (Appendix D).

5.2 Risks

Given that this secondary analysis has no direct involvement by participants, there is minimal risk to participants enrolled. The major risk in this study is the potential loss of confidentiality during the data collection and management process. This risk will be removed as only anonymised data will be used. Study participants will only be identified by a unique study ID and no personal identifiers are included in the study datasets.

The electronic data will be stored in secure, password-protected compressed files.

5.3 Benefits

There are no direct benefits to any of the study participants, however, the proposed study aims to add information to the limited literature regarding the relationship between travel and ART adherence.

Insights on the effects of travel on ART adherence will contribute to our understanding on whether additional counselling or support is needed to prepare for times of travel.

6. Budget

This cross-sectional study is undertaken for the completion of a Master's in Public Health degree, and thus does not require a budget.

7. Stakeholders and dissemination

The objectives of this study will generate evidence that is valuable to ART programmes. Stakeholders most interested in this research would be the South African Department of Health, prevention of mother-to-child transmission (PMTCT) programmes, women in South Africa who will attend HIV care, and research teams exploring methods to improve ART adherence in women. The findings of this study will be made available to these stakeholders through local and international conferences and publication in a peer-reviewed journal.

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PART B: LITERATURE REVIEW

1. Introduction and objectives

Burden of HIV and the importance of antiretroviral therapy

The human immunodeficiency virus (HIV) is a major global health burden. It is one of the leading causes of death in Africa, where 470 000 deaths were reported in 2018 (1, 2). African women are disproportionately affected by the burden of HIV, particularly in sub-Saharan Africa (SSA) where 80% of women living with HIV reside (3).

HIV-positive populations require antiretroviral therapy (ART) for good health outcomes such as high CD4 count and low HIV viral load (VL) (4). Continued adherence to ART is essential to ensure effective viral suppression and immune recovery, which in turn reduces the risk of disease progression and transmission (5). HIV treatment is a combination of antiretroviral (ARV) medications which work together to stop the virus from multiplying (4). Since 2015, the World Health Organisation (WHO) recommends initiating ART on the same day of, or soon after, HIV diagnosis regardless of CD4 count(s) and disease stage (5). To date, there has been a 43% decrease in HIV/AIDS-related deaths since 2003 (4, 6).

By decreasing VL in the infected individual, the risk of HIV transmission is reduced by 96% if ART is adhered to (4). However, in Africa, a reduction of this magnitude is unlikely because ART adherence levels remain low. In 2018 only 16.3 million of the 25.7 million (63%) people living with HIV were receiving their necessary ARV medication (1) and postpartum women seem to be a particular challenge. (7, 8). Disruptions in ART adherence can lead to increased risk of drug resistance and treatment failure; thus, it is important to explore factors that enable and hinder ART adherence in HIV patients to help improve health outcomes.

Barriers to retention and adherence of antiretroviral therapy

There are a multitude of barriers associated with non-adherence to ART and attrition from HIV care. The fear of social discrimination (stigma) through the disclosure of one's HIV status is a key barrier to lowered retention in care (9). Previous research also provides evidence that late ART initiation, poverty, gender inequality, age, employment, marital status, religion, fear of side effects from medication, and food insecurity can all be barriers to ART adherence and retention (10-14). These barriers are universal in individuals living with HIV, but women have added adherence challenges that arise during and post-pregnancy where they are often too busy taking care of their child and are feeling overwhelmed engaging in further reproductive and ART care (11, 15, 16). Buregyeya *et al*. found that the transition from antenatal care (ANC) to HIV care clinics in Uganda was difficult for women due to fear of stigma and discrimination. Another challenge for women was shifting to a

different environment from their ANC, where they were motivated to adhere to HIV treatment during pregnancy in order to ensure births to HIV-free children (15).

Travel has also been identified as a potential barrier to ART adherence for people living with HIV (17), yet when investigating the barriers to ART adherence, there is limited literature focused on travel and mobility.

Why is there a need to explore mobility and travel as barriers to retention and adherence?

The current data available shows that travel enables riskier sexual behaviour in adults, and new HIV infections may be associated with traveling and mobility (18). More recently, qualitative research has identified travel as a barrier to ART adherence but very few quantitative studies have investigated this association (14, 15, 19-21). Particularly, the mobility of postpartum women has been flagged as a disruption to ART adherence (13, 15, 21, 22).

Objective

This dissertation explores travel among women living with HIV approximately four years after starting ART in pregnancy. It also investigates the relationship between travel and ART adherence.

To inform this research, the objective of this literature review is to discuss the available evidence on travel and its relationship to ART adherence among people living with HIV including:

- Definitions of travel and mobility in the HIV literature
- Travel patterns and reasons for travel among people living with HIV
- The relationship between travel and ART adherence

2. Search method

PubMed and Google Scholar were used to identify relevant publications for this literature review. The search terms and their synonyms used are listed in Table B1. The literature was restricted to English language publications, and no time period or continent restrictions were applied due to the dearth of research on the topic. Titles and abstracts of the articles were reviewed for inclusion or exclusion in this literature review. Literature available up until November 2019 were included in this review.

Inclusion criteria for publications:

- The study population was HIV-positive adults
- Study participants must have initiated ART
- Outcomes of interest were retention, ART adherence, VL and travel
- Must have reported on travel or mobility

Studies focusing on short-term ARV prophylaxis or child treatment and outcomes were excluded from this review. The search found 264 papers, 233 articles were excluded from this review because they did not meet the criteria stated above, 30 relevant articles plus 1 policy document were identified and included in this review.

Table B1: Literature review search terms.

HIV – human immunodeficiency virus, prevention of mother-to-child transmission (PMTCT)
Travel – mobility, travel, migration
Antiretroviral treatment - antiretroviral therapy (ART), antiretroviral medication (ARV/ARVs)
Adherence - adhere, adherence, adherent; comply, compliant, compliance; retention, retained

3. Definitions of travel and mobility in the HIV literature

The growing body of knowledge linking travel and HIV is contradictory, highly nuanced and indeterminate. Much of this could be due to the varying definitions of travel and mobility in the literature (18). The heterogeneity of travel definitions is often attributed to the different travel patterns of HIV-positive populations. Travel patterns can range from commuting to work or HIV clinics, to urbanisation, circulatory migration, internal and international migration, and mobility due to sexual behaviour, which is often documented in polygamous males (13, 18, 23).

Travel, mobility and migration

The terms commonly used are “travel”, “mobility”, and “migration”. Travel is often defined as short-term movement e.g. sleeping away from one’s home/city of residence for at least one or more nights with no intention of changing their place of residence (18, 24). While mobility is defined as overall movement done by individuals, encompassing travel between one’s home and the ART clinic (23), or clinic switching, where individuals move from their original ART initiation clinic to a new one either close to the original or further away (13). The term ‘travel’ has repeatedly been used to define mobility and these terms are often used interchangeably in research (25), which adds to the complication of interpreting literature.

The definition of migration also varies in the HIV literature. In some cases, it is described as internal, local relocation to a new city, or external migration, where one permanently relocates to a new country (18, 26). In other situations, migration refers to travel from one’s town of residence to their town of employment, i.e. “circular migration” (25, 27).

The impact of varying definitions of travel

These varying definitions of travel complicate the interpretation of the association between travel and ART adherence in research. Travel is evidently a multifaceted variable with behavioural, social, political, and economic elements, resulting in its many definitions (23). Understanding travel’s impact

on HIV care requires a nuanced understanding of why travel occurs and what it changes in the barriers and facilitators of HIV infection and ART adherence (14, 18).

4. Travel patterns & reasons for travel among people living with HIV

SSA has a highly mobile population. Their travel patterns are diverse and complicated, in part due to the varying reasons for travel in this region. Common reasons for travel include employment, marriage and postpartum childcare support. Travel patterns also vary by type of travel, travel destination, and demographics.

Patterns of movement can be both long-term and short-term ranging from one night to many months away from home (27). In rural areas of SSA, community members travel for short periods of time, for employment (27, 28). Travel and migration patterns are often varied depending on their destination. Many rural community members travel to neighbouring provinces and/or their country's capital city. A migration flow was observed in Manicaland, Zimbabwe, where most of the travel by both men and women was to neighbouring provinces and the capital city, Harare (27, 28).

Studies from across SSA document circular migration as a common travel pattern among people living with HIV. Migration from rural to urban areas is popular among men and women for employment opportunities (27-29). This type of movement is very important for development of a country, however, the search for employment in urban areas is a legacy of colonial and apartheid rule in many SSA countries (30). In South Africa, the apartheid era drove cheap labour into mining and urban industrial locations thus leading many men to migrate, leaving their families in rural settlements (30). This pattern has had lasting effects on temporary labour migration, and population mobility to this day.

People in SSA also experience travel patterns that vary by gender. Gender is considered an important element to understanding travel patterns, reasons and impact. Men and women have been shown to travel differently, and while it has always been suggested that mobility is highest in males, there is growing knowledge that shows women's rates of travel are increasing (29). A study in KwaZulu-Natal exploring travel patterns between sexes and age, found that women were more likely to travel compared to men. They also found that women were more likely to in-migrate from other communities, while men were more likely to out-migrate (28, 31). It is common that men migrate for work and to start a home, while women migrate for marriage, employment, and for social support (26, 31).

Among women, key reasons for mobility are marriage and childcare support. Women often migrate into new cities or countries to move into their partner's home. This travel is mostly based on customary practices where sending a female member of the family to a new area is beneficial for poor families in SSA (29). In Uganda and Zimbabwe, women living in rural areas tend to be migrants that

moved into the area to join their partners (27, 28). Women also tend to travel postpartum for childcare support. When women deliver their babies, they may travel long distances to their families' homes for social support with postpartum recovery and assistance with their new-born (13, 26). The postpartum travel can be long distance travel from urban to rural areas for support from family members, to traveling approximately 1km to clinics (21, 26).

Other characteristics that influence travel patterns include age, education and marital status. In most cases 20 to 30-year olds, people with a tertiary education, and married persons are more likely to travel and migrate away from their place of origin (27, 28, 31). However, in Uganda, the median age of those who travelled was different between men and women (28). Women in-migrants and permanent residents were of similar age, but in-migrant men are significantly older than residents (28).

5. The relationship between travel and ART adherence/retention

Regardless of variation in definitions and patterns of mobility, it seems clear that there is a relationship between population mobility and the HIV epidemic. Studies have extensively reviewed the relationship between travel and HIV transmission, stating increased sexual behaviour as a contributor to this association and the UNAIDS highlighted that this interaction can affect a mobile population's ability to access HIV care and that a relationship between mobility and HIV can be disadvantageous (18, 23, 32). The literature on travel in relation to HIV transmission as well as ART adherence and retention is discussed here. The studies included in this section of the review are summarised in Table B2.

Travel and HIV transmission

Travel and mobility are considered a key driver of the HIV epidemic. The current literature available has shown that travel increases human interactions which enables riskier sexual behaviour in adults and results in new HIV infections (18, 28). When investigating this relationship, Palk *et al* found that adults are more likely to have multiple sexual partners the more frequently they travel, and men's frequent mobility is associated with an increased risk of HIV infection (25).

It is important to note that there have also been papers with conflicting results regarding travel and the risk of HIV acquisition. Studies exploring the relationship between mobility and HIV prevalence in rural Zimbabwe have found no association between rural to urban migration and risk of HIV infection (27, 33). There are no differences observed between HIV incidence among migrants and residents observed and HIV incidence is similar between genders (27, 33). However, migration from one rural area to another is associated with increased risk of HIV infection in Zimbabwe. This suggests that the level of development in an area can affect the risk of HIV infection, rather than mobility (27). For example, in Tanzania, rural residents have significantly higher risky sexual behaviour than rural-urban

migrants and migrant populations engage in more preventative sexual activities, suggesting that migration does not affect the risk of HIV transmission (33).

The "proximate determinants framework" is a theoretical epidemiological framework that maps out the causal pathways between broader, upstream variables and the more direct downstream factors (e.g. biological mechanisms) that affect an outcome of interest (18, 34). The framework has been used to explore travel as an influencing factor through the causal pathway rather than as directly affecting HIV transmission which may help to explain some of the conflicting literature on the association between travel and HIV transmission (18, 34).

Travel and ART adherence and retention

There are still significant knowledge gaps concerning mobility effects in SSA, and their relationship with HIV care access and adherence to ART. The "proximate determinants framework" is also a useful way to think about the relationship between travel and ART adherence.

The general consensus in travel and ART adherence research is that it is difficult to produce accurate estimations of ART adherence and retention in HIV care when studying the mobility and travel of HIV-positive people. It may be effective to look at travel as an upstream factor that acts along a causal pathway down to more direct and immediate determinants of ART adherence.

As an upstream factor, traveling may act as a catalyst of non-adherence to ART by affecting risk factors that lower the ability to access HIV care (14, 18, 21). A study looking at the mobility of Dominicans from the Dominican Republic and New York City found that travel and mobility are associated with treatment interruptions (17). The associations explored so far suggest that the effects of travel may extend to HIV care accessibility and ART adherence (14, 18, 21).

Many qualitative studies have emphasised the potential for travel to indirectly affect adherence to treatment. These studies have had self-reported accounts of travel leading to difficulties in treatment access for people living with HIV. In 2003, Weiser *et al* interviewed patients and their health care providers in Botswana and found that restricted finances, forgetting to take their ARV medication, and running out of medications were associated with non-adherence. Along with that, 13% of patients reported frequent travel or relocation as a reason for poor ART adherence and many patients had to travel distances as far as 1000km for HIV care (23, 35).

In Swaziland, adults living with HIV were interviewed to investigate reasons for discontinued ART adherence and many cited travel as a 'first step' in a series of events that led to eventual non-adherence (14). According to the individuals, the pathway to non-adherence involved interconnecting decisions that occur one after the other, leading to the negative outcome (14). Malawian out-of-care women also reported many barriers of ART adherence which included high mobility, lack of

emotional and financial support, and minimal ART education (22). In this context, travel caused difficulties in accessing treatment in new areas.

According to current literature, travel's upstream effects on non-adherence occur by removing an individual from a comfortable environment where they have more privacy to take their antiretroviral medication. By leaving your place of residence, it becomes more difficult for one to take their medication in a "safe space" and fear of disclosing their HIV status may cause the lack of ART adherence. Travel disrupts daily schedules/routines and removes individuals from their social support system back home, thus affecting the ability to adhere (23, 29, 36, 37). Traveling also requires individuals to collect extra medication in advance to account for their trip and if not, a new clinic must be found to receive ART. However, individuals may not be able to find another clinic, or they may feel uncomfortable seeking alternative ART clinics due to fears of HIV status disclosure in a new area.

While we have self-reported accounts of travel as a barrier of ART adherence, there are few studies which have characterised this relationship quantitatively (17, 18). The few studies that have done quantitative analyses have found that travel and migration are associated with poor health outcomes, and high levels of mobility are linked to the risk of acquiring and living with poorly controlled HIV/AIDS (17). Two studies on postpartum women living with HIV in South Africa found that clinic-switching was associated with increased risk of poor health outcomes. In Cape Town, clinic-switching women were at a higher risk of viremia (21), and women in Gauteng who switched clinics within their province were out-of-care for longer periods compared to those who switched to a different clinic outside their province, as indicated by their CD4 counts (13). The travel effects of these women suggest that we need to better understand the relationship travel patterns have with ART adherence.

6. Discussion

This review highlights that travel is a prevalent theme in the HIV literature, although definitions are variable. Travel has been associated with an increased risk of acquiring HIV in SSA and patterns of travel, particularly migration, are quite well documented. However, there is scant literature on short-term travel and mobility patterns, especially regarding ART adherence. Travel's relationship to HIV care adherence is still relatively unexplored. With evidence of a high frequency of travel among sub-Saharan Africans, particularly those living with HIV, it is essential to understand how this movement affects their treatment.

Antiretroviral therapy (ART) through universal test and treat is highly effective given that HIV-positive individuals initiate and adhere to treatment, but we know that there is a plethora of barriers to ART adherence that needs further exploration. This literature review highlights the need for further

research to better understand the association between travel and ART adherence, as well as mechanisms through which travel influences adherence. Thus, the study aims to explore the travel among a cohort of South African women living with HIV who are approximately four years postpartum, and to investigate the relationship between their travels and ART adherence.

Table B2: Summary of literature included in review.

In-text citation	Author, year	Setting	Study design	Population	Definition of travel	Definition of adherence	Key findings
				Observational studies			
(20)	Abgrall, 2013	France and sub-Saharan Africa	Cohort study	Sub-Saharan African migrants living with HIV in France	Travel: Visiting native country for 2 weeks to 6 months	Self-reported adherence with a three-item score: highly adherent (100%), moderately adherent (between 99% and 80%), or nonadherent (<80%)	Travelling led to increased risk of non-adherence to ART. Main predictors of non-adherence were mistrust of African healthcare, prolonged stay, and unexpected events during visit.
(13)	Clouse, 2017	South Africa	Cohort study	Postpartum women living with HIV thought to be lost to follow-up (LTFU)	Mobility: clinic switching - moving from origin clinic to destination clinic	Continued HIV care: any access to a new ART clinic during follow-up period	Women were mobile and thus out of care for median 373 days. ART non-adherence was due to financial constraints, stigma, and a perception that sustained ART use was not needed. Loss to follow-up (LTFU) can be overestimated due to clinic-switching.

In-text citation	Author, year	Setting	Study design	Population	Definition of travel	Definition of adherence	Key findings
(27)	Coffee, 2005	Zimbabwe	Cross-sectional study	Adults in rural communities	Migration: living outside own community ≥1 month in the year Short-term movement: living outside own community for ≥1 night for the past month	Not applicable (N/A)	No association between rural-urban migration and HIV transmission. However, rural-rural travel increases rate of HIV infection.
(33)	Mundandi, 2006	Zimbabwe	Cohort study	Adult out-migrants and residents	Out migration: Relocating to the capital city of Zimbabwe or surrounding Manicaland areas	N/A	No association between migration and HIV incidence.
(25)	Palk, 2015	Lesotho	Quantitative study	Mobile adults of Lesotho	Travel: Being away from home for at least one night	N/A	Travel is most common in urban areas near job opportunities such as areas bordering South Africa. Mobility leads to an increased level of risky sexual behaviour and only men's mobility was associated with an increased risk of HIV incidence.

In-text citation	Author, year	Setting	Study design	Population	Definition of travel	Definition of adherence	Key findings
(21)	Phillips, 2018	South Africa	Cohort study	Postpartum women living with HIV	Mobility: clinic switching - moving from origin clinic to destination clinic	Viral suppression: ≤50 copies/mL and ≤1000 copies/mL	A substantial number of postpartum women do not link to ART care. Movement caused by clinic switching may result in non-adherence to ART and poor linkage to care. Linkage to care was more likely in older, married, employed women who planned their pregnancies and presented for ANC early. This was seen to be beneficial for retention and viral suppression as well. The vulnerable women were younger mothers who were primigravid.
(35)	Weiser, 2003	Botswana	Cross-sectional study	Adults living with HIV	Travel: moving long distances to clinics	Taking prescribed ART 95% of one year	Financial constraints are a key driver of non-adherence to ART. Other key barriers to ART adherence found were stigma, travel/migration, and medication side effects.
				Qualitative studies			
(22)	Gugsa, 2017	Malawi	Qualitative study	Pregnant and lactating women initiating ART (Option B+)	Mobility: being away from one's residence	In-care: attending routine ARV refill visits	Many factors are associated with ART adherence. ART adherence barriers include lack of support from male partners, poor ART counselling, and mobility. Having a good support system is an enabler of ART adherence.
(14)	Shabalala, 2018	Swaziland	Qualitative study	ART-naïve adults living with HIV	Mobility: relocation from place of residence	LTFU: not attending ART refill for three months or more	Mobility is a trigger for a multitude of barriers to ART adherence. These barriers include side effects, employment uncertainty, fear of HIV status and food insecurity.

In-text citation	Author, year	Setting	Study design	Population	Definition of travel	Definition of adherence	Key findings
(17)	Taylor, 2014	Dominican Republic and United States of America	Ethnographic qualitative study	Mobile adult Dominicans living with HIV	Travel: spending ≥3 nights at a different location ≥50km from home	Self-reported adherence: had received ART continuously for over 6 months	Travel patterns of mobile Dominicans are very complex and are dependent on distance, destination and duration. Travel appeared to be a barrier to HIV care along with stigma and fear of disclosure of HIV status in a new area. Both leading to treatment interruptions.
				Systematic Reviews			
(36)	Shubber, 2016	Worldwide	Systematic Review and Meta-Analysis	Adults, adolescents and children living with HIV	Travel: Commuting and being away from home	Varied. Self-reported ART adherence and objective adherence measures e.g. pill count	There are a multitude of barriers of ART adherence that people living with HIV encounter. Barriers include forgetting to take medication, travelling, distance to clinic, change of routine, stigma, depression and substance use. Health care should provide better support.
				Opinion or commentary			
(29)	Camlin, 2018	Sub-Saharan Africa	Commentary	Mobile adults living with HIV	Varied. Mobility, migration, counter-urbanisation	N/A	Mobility is varied in definition and patterns. There are differences in travel among populations, genders and age. It is important to explore these patterns to better understand their effects on HIV prevention.
(18)	Deane, 2010	Tanzania	Review	Mobile adults living with HIV	Varied. Short-term travel, migration, commuting, circular migration	N/A	Mobility has been identified as an important driver of the spread of HIV. Studies focused on travel and the risk of HIV are contradictory primarily due to the heterogeneity of definitions of travel. Future research needs to incorporate more nuanced definitions of travel to better understand its role in the HIV epidemic.

In-text citation	Author, year	Setting	Study design	Population	Definition of travel	Definition of adherence	Key findings
(37)	Tanser, 2015	Worldwide	Review	Migrants and mobile adults living with HIV	Migration: relocating to a new city or country	Varied. Self-reported ART adherence, LTFU, CD4 count	Migrants have been shown to have poor ART adherence due to a wide range of factors such as stigma, poor healthcare system logistics, language barrier and legal documentation issues. It is important for the health system to keep migrants in mind when offering HIV services to reach UNAIDS' 90 90 90 goals.
(23)	Taylor, 2011	Worldwide	Review	Mobile adults living with HIV	Varied. Short-term travel, migration, commuting to ART facilities, circular migration	Accessing antiretroviral medication	Few studies have explored mobility's impact on HIV treatment adherence and access. Migration particularly hinders ART adherence by making HIV services difficult to access and navigating stigma in new areas.
(34)	Boerma, 2005	Worldwide	Supplement article	Mobile adults living with HIV	N/A	N/A	The proximate-determinants framework may be useful in study designs to analyse and interpret the upstream factors that lead to biological and behavioural outcomes.

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PART C: JOURNAL “READY” MANUSCRIPT

Travel and adherence to antiretroviral therapy among postpartum women living with HIV in South Africa: a cross-sectional study

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Abstract

Objectives: Travel may be an influencer of poor antiretroviral therapy (ART) adherence. We describe travel over one year among mothers living with HIV in Cape Town, South Africa, and explore associations between travel and i) self-reported adherence, and ii) HIV viral load.

Methods: A cross-sectional survey was conducted of women four years after ART initiation during pregnancy. Travel (≥3 nights away from home) in the past year and self-reported adherence in the past 30 days were collected through structured questionnaires, and a viral load test was completed. Poisson regression with robust standard errors was used to explore factors associated with any travel, self-reported adherence (100% versus <100%), and viral suppression (≤50 copies/mL).

Results: Among 353 women, 23% (n=81) reported travelling in the past year, mostly to the Eastern Cape (90%). Being married was associated with travelling (aRR = 1.45; 95% CI: 0.97 – 2.16), while those in formal housing were less likely to travel (aRR = 0.63; 95% CI: 0.42 – 0.96). Overall, 59% of women reported 100% adherence; 52% of travellers versus 61% of non-travellers (aRR = 0.83; 95% Cl: 0.66 – 1.04). Sixty percent of travelling women were virally suppressed compared to 55% of non-travellers (aRR = 1.10; 95% Cl: 0.89 – 1.36).

Conclusion: Poor adherence and viremia were common four years after starting ART in pregnancy. We found no association between travel in the past year and self-reported adherence or viremia. Further research is needed to understand adherence while travelling and interventions are needed to support long-term ART adherence.

Keywords: antiretroviral therapy, women, travel, adherence, viral suppression, South Africa

1. Introduction

HIV is a major health burden in sub-Saharan Africa (SSA), particularly for women who are disproportionately affected by HIV. In South Africa, 4.7 million of 7.5 million people living with HIV (63%) are women (1, 2). There is a global concern regarding women and HIV because of the burden of new HIV transmissions in this group as well as concern about transmission to their partners and their potential children (2, 3).

Women living with HIV require lifelong antiretroviral therapy (ART) for good health outcomes (4). Sustained ART adherence is necessary to guarantee effective viral suppression and immune recovery, which reduces the risk of HIV progression and transmission (5). However, long-term ART adherence continues to be a challenge and women in SSA are a high-risk group for inadequate adherence (6, 7).

Many risk factors have been shown to affect a person's ability to adhere to ART. These risk factors include forgetting to take medication, poverty, stigma, age, employment status, and marital status (8-11). Recently, it has been suggested that travel may also be a barrier to ART adherence and engagement in ongoing HIV care (12-14).

Travel has been shown to be one of the drivers of the HIV epidemic as it is thought to increase human interactions that lead to 'riskier' sexual behaviour, such as having multiple sexual partners (15, 16). This risky sexual behaviour then leads to an increased risk of HIV acquisition. While the connection between travel and the spread of HIV has been established, few papers have focussed on travel patterns of people living with HIV, and how these travel patterns affect ART adherence and access to HIV care.

In the qualitative literature, people living with HIV frequently report travel as a barrier to their ART adherence (11, 14, 17), but only a few studies have quantified this relationship (18-22). These few studies have shown that travel patterns can affect access to HIV care (18-22). In certain cases, travel, migration, and general mobility are associated with poor health outcomes, disengagement from care or poor ART adherence (23).

Studies from South Africa have observed that women tend to travel long distances postpartum, mainly for employment purposes and for assistance with childcare (24). Postpartum women have also been shown to frequently switch ART clinics and those who switch have lower CD4 counts and viremia, suggesting that certain travel patterns may result in poor health outcomes (21, 22). Migration has also been associated with loss to follow-up (LTFU) and the longer one travels for, the worse the rate of LTFU and ART adherence is (18-20).

Travel patterns may affect ART adherence by removing an individual from their daily routine. By leaving their home, challenges arise where one lacks privacy to take their antiretroviral medication

and there is a fear of disclosing one's HIV status in new areas (23, 25). Being away from their home means parting from their support system which may affect the ability to adhere (25, 26).

Although we know that travel is relatively common among women in SSA, there is need for further research to examine the association between travel and adherence to ART. To address this, we aimed to describe travel and ART adherence in women who were enrolled in a cross-sectional study approximately four years after starting ART in pregnancy in Cape Town, South Africa. The objectives of this study are to describe the travel patterns of mothers living with HIV over a one-year period preceding the study visit, to explore factors associated with travel, and to investigate the associations between travel and i) self-reported adherence, and ii) HIV viral load (VL).

2. Methodology

2.1 Research setting

We conducted a secondary analysis of data collected during the Long-term Adherence and Care Engagement (LACE) study. The LACE study was a cross-sectional study aimed at evaluating long-term outcomes of women living with HIV. These women were enrolled in a larger prospective cohort study, the Maternal & Child Health – Antiretroviral Therapy (MCH-ART) study, where they started ART in pregnancy at a large clinic in Gugulethu, Cape Town (27-29). Gugulethu is a low socioeconomic area of Cape Town with high levels of unemployment, and a high HIV burden. The Gugulethu Midwife Obstetrics Unit (MOU) provides basic antenatal care (ANC) and services for a large community that includes those in Philippi, Nyanga, Lower Crossroads, Heideveld, Gugulethu and surrounding areas from as far out as the Eastern Cape (30).

Overall, 628 consecutive women, aged 18 and older, presenting for ANC, and who were eligible to start ART between April 2013 and June 2014 were recruited into the MCH-ART study and followed prospectively through delivery (27). Women who were breastfeeding were then randomised into a postpartum trial which aimed to compare different service delivery models to provide maternal HIV care and routine childcare postpartum (n = 471) (27). Women enrolled in the postpartum cohort were followed through 18 months postpartum and were then invited back to participate in the LACE study in 2017, between 36 and 60 months postpartum (28, 29). Of the 471 women enrolled in MCH-ART, 353 were recruited into the LACE study. The recruitment has been described in detail elsewhere (28).

2.2 Data collection

The data for this analysis was collected during a single face-to-face interview, which included detailed questionnaires and VL testing (Abbott Molecular RealTime HIV-1 assay, Abbott Molecular, Illinois, USA) by the National Health Laboratory Services. The questionnaires included demographic characteristics, travel in the previous 12 months, and self-reported ART adherence in the past 30 days using a three-item scale that has been validated in the United States and in South Africa (31, 32).

2.3 Data analysis

Study data were analysed using Stata Version 15.0 (Stata Corporation, College Station, Texas, USA). The characteristics of the study cohort were described using univariate analyses. Characteristics included demographic information such as age, level of education and socioeconomic status, and behavioural information such as timing of presentation to ANC at start of MCH-ART, which was used as a proxy for health-seeking behaviour (33). Medians and interquartile ranges (IQR) were reported for continuous variables, and frequencies and proportions for categorical variables. The Wilcoxon rank-sum test (for continuous variables) and the Fischer's exact test (for categorical variables) were used to explore potential differences in characteristics of the women's travel status, ART adherence and viral suppression. These associations were further investigated using crude and adjusted Poisson regression models with robust standard errors (34). Log-binomial models were also attempted, and these results are presented in supplementary tables. In all models, covariates with an α-level of 0.10 from bivariate analyses were included in the model along with the demographic characteristics age, employment status, education, presentation to ANC and parity based on prior literature (16, 22). All model results are presented as crude and adjusted relative risks (RR or aRR) with 95% confidence intervals (CIs).

Travel patterns

The proportion of women who travelled in the past year was described as any travel (spending ≥3 nights away from home) versus no travel. The frequency of travel (1-2 times or 3-5 times in the past year), time spent away from home (spending either more or less than 21 nights away from home), and where women travelled to, were also described. Attendance to other clinics while away, self-reported impact on ART adherence, and receiving a transfer letter were also explored through descriptive statistics. Poisson regression models with robust standard errors were used to explore factors associated with any travel away from home in the past year (34).

ART adherence

The main outcome of interest was ART adherence. This construct was defined using the surrogate endpoints, self-reported adherence in the past 30 days and VL on the day of the study visit. Self-reported adherence was characterised using a three-item scale score (31). The three-item adherence scale used the number of days ART doses were missed in the past 30 days, how good of a job the women did taking their ART (Likert scale 1: very poor – 6: excellent), and how often they took their ART as directed (Likert scale 1: never – 6: always). The responses to each item were averaged to obtain an overall adherence score between 0 and 100% (32). The final ART adherence variable was explored as a binary outcome: adherent = 100% versus non-adherent <100% in past 30 days. Sensitivity analyses were carried out for ART adherence using a 95% adherence score threshold for the past 30-days, and no reported missed ART doses in the past 7 days.

Viral suppression was defined as VL ≤50 copies/mL, with sensitivity analyses using a VL threshold of ≤1000 copies/mL. Here, VL was considered an objective marker of adherence, although it is important to keep in mind that while poor adherence is the main reason for unsuppressed VL, there could be other factors responsible, such as drug resistance (4).

We investigated the factors associated with any travel and adherence outcomes by using multivariable Poisson regression models with robust standard errors to estimate the relative risk of each outcome (34). Among women who reported traveling, we also explored their self-report of adherence difficulties while traveling based on the questionnaire responses.

2.4 Ethics

Both the MCH-ART and LACE studies were approved by the University of Cape Town Human Research Ethics Committee and the Columbia University Institutional Review Board. As part of the MCH-ART and LACE study enrolment, all women signed informed consent forms for use of questionnaire data and blood test results. The women also consented to be contacted in the future for other related research and provided the study team with their contact details. Ethical approval to conduct this analysis was provided by the University of Cape Town Faculty of Health Sciences' Human Research Ethics Committee.

3. Results

Participant characteristics

Overall, 353 of the 471 women enrolled in the postpartum MCH-ART cohort were successfully recruited into the LACE study and included in this analysis. Four of the eligible women conducted their LACE interview telephonically and therefore did not provide blood samples for VL results. These women were excluded from the VL analyses. The descriptive characteristics of the cohort are shown in Table C1.

Women enrolled in the LACE study were a median of 44 months postpartum (IQR 42-46 months), and their mean age was 32.6 years (SD 5.43). The majority of women only completed primary education (69%), 52% were unemployed, and 53% lived in formal housing such as hostels, flats, and houses. Overall, 52% of women initially presented late (>20 weeks gestation) for ANC in the MCH-ART study and 55% had ≤ 2 children. Most of the cohort was unmarried (62%) and almost all women had disclosed their HIV status to someone close to them (98%).

Table C1: Descriptive characteristics of 353 LACE postpartum women, grouped by their travel status. Presented as n (%) unless specified.

Variable	**Travelled (n = 81)** n (%)	**Did not travelled (n = 272)** n (%)	**Overall women (N = 353)** n (%)	**p-value**
Mean age in years (±SD)	32.8 (±5.33)	32.6 (±5.48)	32.6 (±5.43)	0.679
Level of education				
Primary	52 (64.2)	191 (70.2)	243 (68.8)	0.304
Secondary/Tertiary	29 (35.8)	81 (29.8)	110 (31.2)	
Employment Status				
Employed	38 (46.9)	132 (48.5)	170 (48.2)	0.798
Unemployed	43 (53.1)	140 (51.5)	183 (51.8)	
Socioeconomic Status (SES)				
Lowest SES	26 (32.1)	78 (28.7)	104 (29.5)	0.106
Moderate SES	28 (34.6)	69 (25.4)	97 (27.5)	
Highest SES	27 (33.3)	125 (45.9)	152 (43.0)	
Housing				
Informal (shack)	49 (60.5)	118 (43.4)	167 (47.3)	0.007
Formal (house/hostel)	32 (39.5)	157 (56.6)	186 (52.7)	
Marital status				
Married/cohabiting	40 (49.4)	94 (34.6)	134 (38.0)	0.016
Unmarried	41 (50.6)	178 (65.4)	219 (62.0)	
Disclosure Status				
Disclosed	77 (95.1)	268 (98.5)	345 (97.7)	0.066
Undisclosed	4 (4.9)	4 (1.5)	8 (2.3)	
Parity				
2 or less children	42 (51.9)	153 (56.2)	195 (55.2)	0.485
3 or more children	39 (48.1)	119 (43.8)	158 (44.8)	
Presentation to ANC at enrolment into MCH-ART				
Early	40 (49.4)	129 (47.4)	169 (47.9)	0.757
Late	41 (50.6)	143 (52.6)	184 (52.1)	

Travel patterns

Eighty-one women reported travelling in the year preceding the LACE visit (Table C2). Only one woman permanently relocated. Most women only travelled 1-2 times (93%) and women travelled mostly to the Eastern Cape (90%). One woman travelled out of South Africa to Mozambique. Most women who travelled had received a transfer letter to attend a new clinic if needed (91%) and only seven women (9%) reported travel impacting their ability to adhere to their ART regimen.

Predictors of travel

In bivariate analyses comparing women who had travelled to those who had not, women who had travelled were more likely to live in informal housing than women who did not travel (61% versus 43%, p = 0.007) (Table C1). Women who travelled were also more likely to be married compared to the non-travellers (49% versus 35%, p = 0.016). In multivariable models adjusted for age,

employment, and marital status, women who lived in formal housing were 37% less likely to travel (aRR = 0.63; 95% CI: 0.42 – 0.96). Women who were married or cohabiting with a partner were 45% more likely to travel compared to the unmarried women but this was not statistically significant (aRR = 1.45; 95% CI: 0.97 – 2.16) (Table C3).

Table C2: Travel patterns of 81 women who reported ever traveling over a one-year period.

Variable	**HIV-positive women** n (%)
Travel Frequency	
1-2 times	75 (92.6)
3-5 times	6 (7.4)
Nights away from home	
≤21 nights	45 (55.6)
>21 nights	36 (44.4)
Travelled to:	
The same place	77 (95.1)
Different places	4 (4.9)
Destination	
Eastern Cape	73 (90.1)
Free State	1 (1.23)
Gauteng	3 (3.70)
Western Cape	3 (3.70)
Outside South Africa	1 (1.23)
Self-reported impact on ART adherence	
Difficult	7 (8.6)
Not difficult	74 (91.4)
Attendance to other clinics while away	
Yes	12 (14.8)
No	69 (85.2)
Received a transfer letter	
Yes	74 (91.4)
No	7 (8.6)

30-day ART adherence

Overall, 59% (n = 208) of women reported 100% adherence to their ART regimen based on the three-item self-reported adherence scale (median 100%, IQR 94.4 – 100%) in the 30 days prior to the LACE visit. Women who reported 100% adherence were more likely to be employed than non-adherent women (53% versus 41%, p = 0.019) (Table S1). Adherent women were also more likely to be married/cohabiting (43% versus 31%, p = 0.025). Only 20% of women who reported 100% adherence had travelled in the past 12 months compared to 27% of women with <100% adherence (p=0.141).

In multivariable models adjusted for travel, age, education, housing, and timing of presentation to ANC, employment and marital status remained associated with adherence. Employed women were 24% more likely to adhere to their ART regimen than the unemployed women (aRR = 1.24; 95% CI: 1.04-1.49) (Table C4). Married/cohabitating women were 25% more likely to have 100% adherence

than women who were not married/cohabiting (aRR = 1.25; 95% CI: 1.04-1.50). Travelling in the past year was not associated with 30-day ART adherence in crude or adjusted analyses (aRR = 0.83; 95% CI: 0.66-1.04) and this lack of an association continued in sensitivity analyses using a 95%-threshold for the three-item 30-day ART adherence score (Table S6) and no missed ART doses in the past 7-days (Table S7).

Table C3: Poisson regression model (n = 353) of factors associated with travel in postpartum women. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.00 [0.97 – 1.04]	0.99 [0.96 – 1.03]
Completed secondary education	1.23 [0.83 – 1.83]	
Employed	0.95 [0.65 – 1.40]	0.93 [0.63 – 1.35]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	1.15 [0.73 – 1.82]	
Highest SES	0.71 [0.44 – 1.15]	
Formal house	0.59 [0.40 – 0.87]	0.63 [0.42 – 0.96]
Married/cohabiting	1.59 [1.09 – 2.33]	1.45 [0.97 – 2.16]
Has 3 or more children	1.15 [0.78 – 1.68]	
Late presentation to ANC	0.94 [0.64 – 1.38]	

Viral suppression

Among 349 women with viral loads available, 56% (n = 196) were virally suppressed: 60% and 55% of those who had and had not travelled in the past year, respectively (Table S2). There was a very small difference in age between suppressed and non-suppressed women, 33.2 years old (SD 5.19) and 32.8 years old (SD 5.72), respectively (p = 0.03). Virally suppressed women were more likely to be married/cohabiting than unsuppressed women (44% versus 30%, p = 0.008), and were more likely to be 100% adherent to their ART regimen than women who had viremia (72% versus 43%, p <0.001). Women who were viraemic were more likely to have presented for ANC late when they enrolled in the MCH-ART study, compared to women who were virally suppressed (61% versus 45%, p = 0.004).

In multivariable models adjusted for age, employment status, housing, marital status and travel, 100% self-reported adherence on the three-item scale and early presentation for ANC at enrolment into the MCH-ART cohort were significant predictors of being virally suppressed at the LACE visit (Table C5). Women who were 100% adherent to their ART had a 71% increased likelihood of being virally suppressed than non-adherent women (aRR = 1.71; 95% CI: 1.36-2.14). Women who had presented late to ANC at enrolment into MCH-ART (>20 weeks gestation) were less likely to be suppressed compared to early presenters (aRR = 0.78; 95% CI: 0.65-0.93). Travel in the past year was not associated with viral suppression in crude or adjusted analyses (aRR = 1.10; 95% CI: 0.89-1.36) and

this lack of an association persisted in sensitivity analyses of a VL threshold of ≤1000 copies/mL (Table S8).

Table C4: Poisson regression model (n = 353) of factors associated with 100% ART adherence in the past 30 days. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.01 [0.99 – 1.02]	1.00 [0.98 – 1.02]
Completed secondary education	1.00 [0.83 – 1.21]	0.96 [0.79 – 1.16]
Employed	1.23 [1.03 – 1.47]	1.24 [1.04 – 1.49]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	1.04 [0.81 – 1.32]	
Highest SES	1.11 [0.90 – 1.37]	
Formal house	0.93 [0.78 – 1.11]	0.98 [0.82 – 1.17]
Married/cohabiting	1.22 [1.03 – 1.45]	1.25 [1.04 – 1.50]
Has 3 or more children	1.08 [0.91 – 1.28]	
Late presentation to ANC	0.94 [0.79 – 1.11]	0.96 [0.81 – 1.14]
Travelled	0.84 [0.67 -1.07]	0.83 [0.66 – 1.04]

Table C5: Poisson regression model (n = 349) of factors associated with viral suppression (≤50copies/mL), restricted to women with VL results available. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.02 [1.00 – 1.03]	1.01 [1.00 – 1.03]
Completed secondary education	0.97 [0.79 – 1.19]	
Employed	1.16 [0.96 – 1.39]	1.06 [0.89 – 1.27]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	1.04 [0.82 – 1.33]	
Highest SES	1.00 [0.80 – 1.26]	
Formal house	0.85 [0.70 – 1.02]	0.89 [0.74 – 1.06]
Married/cohabiting	1.29 [1.07 – 1.54]	1.12 [0.93 – 1.33]
Has 3 or more children	0.94 [0.78 – 1.13]	
Late presentation to ANC	0.76 [0.63 – 0.92]	0.78 [0.65 – 0.93]
Travelled	1.09 [0.88 – 1.34]	1.10 [0.89 – 1.36]
Adhered to ART in last 30-days	1.76 [1.40 – 2.21]	1.71 [1.36 – 2.14]

4. Discussion

This study found that 23% (81 of 353) of women reported travelling at least once in the past year but no association was observed between travel and self-reported adherence in the past 30 days, or with viral suppression at the LACE visit. A large proportion of women reported <100% adherence and

44% were viraemic, highlighting concerns of disengagement from HIV care in the long-term among women who initiate ART in pregnancy.

Among the women who travelled, more than half were away from their homes for more than 21 nights at a time, mostly to the Eastern Cape. This is in line with our expectations as we know that the Gugulethu clinic has a wide catchment area (30). Many people living in the Gugulethu area have family in the Eastern Cape and women are known to travel to the Western Cape for economic opportunities and health services. Similar cross province travel has been shown to be common in Gauteng, where women travel postpartum to the surrounding province, Limpopo (24).

Only housing and marital status were associated with traveling in the past year. Living in informal housing was associated with increased risk of travel. It is possible that the mechanism for this association relates to socioeconomic status and the search for employment that leads to more travel (35). Marriage as a predictor was an unexpected finding, because the assumption was that married women might be more stable. However, these findings align with Palk and Blower's research and perhaps the travel amongst married women is connected to visits to relatives or moving in with their partner (16).

Surprisingly, age, education and employment status had no association with travel in this study. Multiple travel related papers have cited these factors as common reasons for travelling. Young people have been shown to be more likely to clinic switch or migrate for employment, and employment is a key driver of travel (16, 22, 35, 36). Most women in this cohort were over 25 years of age so we were unable to describe travel in younger women. Travel definitions vary in the literature which may explain some of the differences in findings. Studies on postpartum women have defined travel as clinic-switching (visiting more than two clinics) and this travel pattern was associated with younger women (<24 years old) and travelling for employment purposes, while our study defines mobility as leaving home for more than three days (21, 22). However, a study in Lesotho defining travel as "being away from home for at least one night" found associations between age, education and employment, where travellers are more likely to be older, employed and having at least a secondary education (16).

No association was observed between travel and either self-reported adherence or viral suppression in this study. The lack of significant association between any travel patterns and ART adherence contrasts with prior research that has suggested that travel can disrupt ART adherence and create difficulty accessing HIV care (12, 14, 17, 18, 37). Multiple qualitative studies have cited that people living with HIV report travel as a barrier to their ART adherence (11, 12, 14). The few quantitative studies on travel and ART adherence contradict our findings. A study in Canada, where travel was defined as migration during HIV treatment, observed a positive and statistically significant association between travel and non-adherence where those who frequently travelled were 79% more likely to not

adhere to ART compared to those who did not travel (18). Abgrall *et* al investigated ART adherence in SSA migrants living in France and found that their visits to their home country increased the risk of non-adherence, and this association was stronger, the longer the migrants travelled (19).

Almost all the women who travelled in our cohort reported receiving a transfer letter to help them link to a new clinic if needed and only 7 of the 81 women reported any adherence difficulty related to travel. This suggests that this cohort was proactive and perhaps much of the travel was planned. The fact that we were not able to measure adherence at the same time as travel means that temporality is a concern. We were only able to look at the association between reported travel in the past 12 months and self-reported adherence and viral load at the end of that 12-month period. It is possible that adherence disruptions did occur during times of travel, but we could not observe them.

What is concerning is that only 59% of women reported 100% adherence in the past 30 days and only 56% were virally suppressed. So, while travel was not associated with adherence in this analysis, women are still not optimally adhering to their HIV care. Given the need to raise ART adherence in populations living with HIV to reach UNAIDS' 90 90 90 goals (4), our study shows that there are still gaps in maternal and postpartum ART adherence support.

A few significant predictors for ART adherence were identified in this study. First, being employed was associated with a 24% increased likelihood of being adherent to ART. It is possible that being employed and having a steady income results in accessibility to HIV care, and a daily routine may help to take ART medication as prescribed. Second, women who were married were 25% more likely to be adherent to ART. Many papers have highlighted social support as a facilitator of ART adherence, thus being married or cohabiting may provide a good support system and environment to adhere to care (9, 14, 37). Lastly, early presentation to ANC was associated with better virologic outcomes, which is consistent with previous literature. This association is unsurprising because timing of ANC presentation can often be used as a proxy to health-seeking behaviours (8, 33).

There are several limitations of this study that should be considered. The use of the parent study's questionnaires for data collection means that alternative travel and adherence definitions could not be explored. All the key constructs of the study were self-reported which may introduce recall bias and social desirability bias, these biases can lead to overestimation of ART adherence. However, 100% 30-day ART adherence was measured using a scale validated in South Africa and was associated with viral suppression in this cohort (31) and the inclusion of HIV viral load as an objective marker of ART adherence is a strength to this study. The sample size for this study was 353 women and only 23% reported any travel. This may have limited the detection of small associations. The simplification of the travel definition in this study into a binary variable of any travel in the past year, also limits our ability to understand the scope of travel and the nuances of the women's reasons for travelling. Finally, we measured travel in the past year but were only able to assess adherence and viral load at

the LACE visit at the end of the one-year period, hence temporality is a major concern. Producing estimations of ART adherence and retention in HIV care when studying the mobility and travel of HIV-positive people is particularly difficult. Measuring adherence in mobile populations and defining travel is a challenge due to the variations in definitions of both constructs. This may contribute to the contradictory results of research on travel and ART adherence (11, 15). These complexities may also contribute to the limited number of studies focusing on the association between travel and ART adherence, despite the prevalence of qualitative studies reporting on travel as a barrier to adherence (9, 12-14, 38).

In conclusion, these findings highlight that women are still at high risk for non-adherence to ART, years after initiating ART during pregnancy. In this study, a large proportion of women were not virologically suppressed and had inadequate self-reported ART adherence. Almost a quarter of women travelled in the past year but only a few reported difficulties with adherence related to travel and we found no association between travel in the past year and self-reported adherence in the past 30 days or viremia.

In the context of women's health postpartum, these numbers imply there are persistent gaps in postpartum HIV care. Further research is needed to understand adherence patterns during periods of travel and to determine the best way to proactively monitor and support long-term adherence to ART.

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PART D: APPENDICES

1. Appendix A: LACE Demographics and Travel Questionnaires

(Note: Questions used in this study's analyses are highlighted in yellow)

LACE: Demographics & Medical History
V2.0 22 February 2017

PID: L - __ __ __ __ - __ __

			Visit Date: __ __/__ __ __/__ __ __ __
1.	Have you moved to a different home since we last spoke to you?		No = 0 Yes = 1
2.	Have you changed your cell phone number(s) since we last spoke to you?		No = 0 Yes = 1
3.	Is there anyone else that we can contact if we are looking for you in the event of an emergency?		No = 0 Yes = 1
Interviewer - Please remember to update locator information for ALL participants			
We are now going to ask you a few questions:			
4.	What is the highest level of schooling/education that you have completed?		Grade:_____/ Standard:_____ Postsecondary:_____
5.	Are you currently working and or studying?		No = 0 → **SKIP to Q7** Yes = 1
6.	If yes, which of one the following best describes what you do? Choose one only		Employed full-time = 1 Employed part-time = 2 Informal job/hawker = 3 Attending school/learner = 4 Attending tertiary education facility = 5
7.	What is the MAJOR source of income for your household? Choose one only		None = 0 Full-time employment = 1 Part-time employment = 2 Informal employment = 3 Disability grant = 4 Social grant = 5 Pension = 6 Other grant = 7, specify type: _____ Other = 8, specify:_____ Don't know = 9
8.	What kind of home do you live in?		Shack/informal dwelling = 1 Formal house = 2 Flat/council home = 3 Other = 4, specify: _____
9.	Does your house have the following: Read and answer for all	a. A toilet inside	No = 0 Yes = 1
		b. Running water inside	No = 0 Yes = 1
		c. Electricity inside	No = 0 Yes = 1
		d. A refrigerator	No = 0 Yes = 1
		e. A telephone	No = 0 Yes = 1
		f. A television	No = 0 Yes = 1

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Initials of counsellor: _____

10.	Including yourself, how many people (adults and children) live in your house?	# of people: _____
11.	How many adults (aged 16 or older), including you, live in your house?	# of adults:_____
12.	How many children (aged 15 and under) live in your house?	# of children: _____
13.	How many times have you been pregnant (including current pregnancy if pregnant)?	# of pregnancies: _____
14.	How many children have you given birth to?	# of children: _____ **If 0, SKIP to Q19**
15.	How many of these children are living?	# of children: _____
16.	How many of these children currently live with you?	# of children: _____
17.	How many of your children have tested HIV-positive?	# of HIV-positive children: _____
18.	How many of these children who have tested HIV-positive are currently living?	# of HIV-positive children currently alive: ___
19.	In the past 12 months, have you been referred to any health facility for medical care other than your routine HIV/ART care (eg. GF Jooste or Groote Schuur)?	No = 0 → SKIP to Q20 Yes = 1

	a) Where were you referred?	b) What was the diagnosis?	c) Did you sleep in the hospital	d) How many nights were you in hospital?	e) When was this? Please give approximate date
i.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
ii.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
iii.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
iv.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
v.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
vi.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
vii.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _

Initials of counsellor: _____

viii.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
ix.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _
x.			No = 0 Yes = 1		Day: _ _ Month: _ _ _ Year: _ _ _ _

20.	In the past 12 months, has a doctor or nurse told you that you have TB?	No = 0 → SKIP to Q25 Yes = 1
21.	When did you receive this diagnosis?	Day: _ _ Month: _ _ _ Year: _ _ _ _
22.	Where did you receive this diagnosis?	Name of clinic:
23.	Where in your body was the TB (eg, lungs, other location)?	Place in body:
24.	Did you receive treatment for TB?	No = 0 Yes = 1
25.	Since you were diagnosed with HIV, have you told anyone about your HIV-status?	No = 0→ SKIP to Q28 Yes = 1

26.	Please answer this question for each of the family members listed below.	i. Do they live with you? If NA selected, do not answer i and ii for that person	ii. Do they know you are HIV positive?	iii. Do they know if you are taking ART?
a.	Husband/partner	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
b.	Mother	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
c.	Father	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
d.	Sister	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
e.	Brother	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
f.	Daughter	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
g.	Son	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
h.	Uncle	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
i.	Aunt	No = 0 Yes = 1	No = 0 Yes = 1	No = 0 Yes = 1

Initials of counsellor: _____

		N/A = 9		
j.	Male cousin	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
k.	Female cousin	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
l.	Other male family member	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
m.	Other female family member	No = 0 Yes = 1 N/A = 9	No = 0 Yes = 1	No = 0 Yes = 1
27.	Aside from family members listed above, who else have you told about your HIV status since your HIV diagnosis? (read and answer for all)		i. Do they know you are HIV positive?	ii. Do they know if you are taking ART?
a.	Health professionals		No = 0 Yes = 1	No = 0 Yes = 1
b.	Support group		No = 0 Yes = 1	No = 0 Yes = 1
c.	A sexual partner who does not live with you		No = 0 Yes = 1	No = 0 Yes = 1
d.	Friends		No = 0 Yes = 1	No = 0 Yes = 1
e.	Spiritual leader		No = 0 Yes = 1	No = 0 Yes = 1
f.	Current or former employer		No = 0 Yes = 1	No = 0 Yes = 1
g.	Public disclosure/ community		No = 0 Yes = 1	No = 0 Yes = 1
h.	Other, specify _____		No = 0 Yes = 1	No = 0 Yes = 1
28.	Are you currently in a relationship?		No = 0→ SKIP to Q33 Yes = 1	
29.	How would you describe your current relationship?		Married = 1 Not married, living together = 2 Married, not living together = 3 Not married, not living together = 4 Other = 5, specify:	
30.	How long have you been in this relationship?		Duration in: Months_____ Years _____	
31.	Is your current partner the parent of any of your children? (including current pregnancy if pregnant)		No = 0 Yes = 1	
32.	Is your current partner the same partner you had when you delivered your baby in the MCHART study?		No = 0 Yes = 1	
33.	Do you have relationships/sexual partners with any other people (even if you are not currently in a relationship)?		No = 0→ SKIP to Q35 Yes = 1	
34.	What is the nature of your other relationship(s)? Mark all that apply.		a. Spouse/ married b. Boyfriend c. Casual Partner/One Night Stands	

		Other, specify:_____
35.	How many relationships have you had since your baby was born during the MCH-ART study? (Including your current partner if you are in a relationship)	# of relationships: _____ Still in the same relationship: 999
36.	Are you currently taking ART?	No = 0 Yes = 1
37.	When was the last day and time you took ART?	Day: __ __ Month: __ __ __ Year: __ __ __ __ time: __ __ h __ __ *please use a 24 hour clock 09h30 (morning) 21h30(evening)
a.	Have you taken ART at all in the last 7days?	No = 0 Yes = 1→ SKIP to Q38
b.	If No, why not?	Reason
38.	Are you currently enrolled in an ART Clinic? *attended a clinic in the last 3 months	No = 0 Yes = 1→ SKIP to Q40
39.	If no, what is the reason that you are no longer enrolled in an ART clinic? You can list more than one reason.	1._____ 2._____ 3._____ 4._____ 5._____ → SKIP to Q47
40.	If yes, which clinic do you currently attend?	Clinic name: _____
41.	How do you usually travel to the clinic for routine care	Hired car=1 My own car=2 Taxi =3 Bus=4 Walk =5 Other=6 , specify
42.	How long does it usually take you to get to the clinic?	Minutes: _____ Hours: _____
43.	How much do you usually pay for transport?	Rand: _____
44.	Do you have to take time off work to go to the clinic?	No = 0 Yes = 1

45.	Do you have to make special arrangements for people to watch your child/children?	No = 0 → SKIP to Q47 Yes = 1 Don't have any children =2 → SKIP to Q47
46.	Do you pay someone to watch your child so you can go to the clinic?	No = 0 Yes = 1
47.	In the past 12 months have you spoken to a counsellor at the clinic/ hospital about your HIV care?	No = 0→ SKIP to Q48 Yes = 1
a.	If Yes, where did you go?	Clinic name: _____
b.	In the past 12 months how many times have you been counselled?	# of times: _____
c.	Who did you speak to during this counselling? (counsellor, nurse, doctor)	
d.	What did you talk about during this counselling?	
48.	When you attend your routine ART care visit, does a health care provider ask you about:	
	a) Medication adherence	No = 0 Yes = 1
	b) Your health	No = 0 Yes = 1
	c) Child health	No = 0 Yes = 1
	d) Child feeding	No = 0 Yes = 1
	e) Family planning	No = 0 Yes = 1
49.	Is your child attending a clinic for immunizations/routine well baby care?	No = 0→ SKIP to Q51 Yes = 1
50.	If yes, which clinic?	Clinic name: →SKIP to Q52
51.	If no, why not? You can list more than one reason.	1._____ 2._____ 3._____ 4._____ 5._____
52.	Does your child currently live with you?	No = 0 Yes = 1→ SKIP to Q55
53.	If no, who does the child stay with? (relationship to child eg: grandmother, aunt)	

Initials of counsellor: _____

54.	Where does the child live?	Name of town & province:
55.	When was your last menstrual period?	Day: __ __ Month: __ __ __ Year: __ __ __ __ Unsure = 9
56.	Are you pregnant at the moment?	No = 0 →SKIP to Q58 Yes = 1 Not sure = 2 →SKIP to Q58
57.	Has the pregnancy been confirmed?	No = 0 →DO PREGNANCY TEST NOW Yes = 1
We will now ask you a few questions about any times you have travelled away from your home in Cape Town.		
58.	In the past 12 months, have you ever spent three or more nights traveling away from your usual house?	No = 0→ END Yes = 1
59.	In the past 12 months, how many times have you travelled away from your usual home for at least three nights?	1. 1-2 times 2. 3-5 times 3. More than 5 times
60.	What was the longest period of time you were away from home?	a) _____ days b) _____ weeks c) _____ months OR d) Relocated permanently
61.	a) When you have travelled, did you travel to:	1. Always the same place/town 2. More than one place/town/province
	b) Where did you travel to, list as many places as apply? (Town, Province)	i. _____ ii. _____ iii. _____ iv. _____
62.	a) Some people find it difficult to take their treatment while away from home, when you were away the last time, did you have any difficulties taking your treatment?	No = 0→ SKIP to Q63 Yes = 1
	b) What things made it difficult? (Circle all the apply)	i. I forgot to carry my pills ii. I was busy and forgot to take my pills iii. I stayed with people who did not know my status iv. I ran out of medication v. My length of stay extended unexpectedly vi. Any other things? _____ _____ _____
63.	Have you ever attended an ART clinic other than your usual clinic while you were away from home?	No = 0 Yes = 1

64.	a) Did you ever receive an ART top up while you were away from home?	No = 0→ SKIP to Q65 Yes = 1
	b) If yes, where did you get the treatment from?	a) Clinic name_____ b) Friend/family member c) Other_____
65.	a) Did you ever receive a transfer letter from your routine ART clinic to receive care at another clinic when you went away?	No = 0 Yes = 1→ END
	b) If no, why not (circle all that apply)?	i. I had enough treatment for the time I was going to be away ii. I did not know I would need a transfer letter to receive ART from another clinic iii. I left unexpectedly and did not have time to go to the clinic for a letter iv. My usual clinic gave me enough ART to see me through the time I was away v. I went to the clinic to try to get a letter but was not able to get a transfer letter vi. Any other reason you did not get a transfer letter:_____ ___ _____ _____ _____

Date completed: __ __/__ __ __/ __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __/__ __ __/ __ __ __ __ Signed measurement nurse: _____

2. Appendix B: LACE Maternal Adherence Questionnaire

(Note: Questions used in this study's analyses are highlighted in yellow)

LACE: Maternal Adherence
V2.0 22 February 2017

PID: L - __ __ __ __ - __ __

Visit Date: __ __/__ __ __/__ __ __ __

We are going to ask you some questions about your HIV medicine.

1.	Have you taken ART in the last 30 days?	No =0 → SKIP to Q10 Yes =1				
2.	i) In the past 30 days, have you experienced any of the following:		ii) If yes, please rate the severity of the symptom here.			
			It doesn't bother me	It bothers me a little	It bothers me	It bothers me a lot
a.	Nausea	No =0 Yes =1	1	2	3	4
b.	Vomiting	No =0 Yes =1	1	2	3	4
c.	Diarrhoea	No =0 Yes =1	1	2	3	4
d.	Appetite Change	No =0 Yes =1	1	2	3	4
e.	Headache	No =0 Yes =1	1	2	3	4
f.	Rash	No =0 Yes =1	1	2	3	4
g.	Fevers	No =0 Yes =1	1	2	3	4
h.	Other Pain	No =0 Yes =1	1	2	3	4
i.	Sweats	No =0 Yes =1	1	2	3	4
j.	Fatigue	No =0 Yes =1	1	2	3	4
k.	Dizziness	No =0 Yes =1	1	2	3	4
l.	Unusual Dreaming	No =0 Yes =1	1	2	3	4
m.	Other, specify _____ _____	No =0 Yes =1	1	2	3	4
3.	How many times a day do you take your ART pills?	# of times: _____				
4.	How many pills do you take each time?	# of pills:_____				
5.	How many different HIV medicines do you take?	# of medicines:_____				
6.	In the last 30 days, on how many days did you miss at least one dose of any of your HIV medicines?	# of days: _____ (0-30)				
7.	In the last 30 days, how good a job did you do at taking your HIV medicines in the way that you were supposed to?	Very poor =1 Poor=2 Fair =3 Good=4 Very good=5 Excellent=6				

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Initials of counsellor: _____

8.	In the last 30 days how often did you take your HIV medicines in the way that you were supposed to?	Never=1 Rarely=2 Sometimes=3 Usually = 4 Almost always=5 Always=6
9.	What are the names of the ARVs you are taking? *ask to show the bottles if possible	1._____ 2._____ 3._____ 4._____ 5._____
10.	In the past 30 days which of the following things made you **miss a pill or made it hard for you to take your pills**? Read all. Circle as many as apply.	a) Was away from home? b) Lost your pills? c) Was busy with other things? d) Simply forgot? e) Had too many pills to take? f) Was getting side effects? g) Wanted to avoid side effects or were feeling bad? h) Wanted to take a break from the pills? i) Did not want others to notice you taking medication? j) Had a change in daily routine or work schedule? k) Thought that the pills would still work even if a few were missed? l) Felt the drugs were toxic/ harmful? m) Slept through dose time? n) Felt sick or ill? o) Felt overwhelmed? p) Felt depressed? q) Other reason. Specify:_____ r) I never missed a pill and I had no difficulty taking my pills

Date completed: __ __/__ __ __/ __ __ __ __ Signed counsellor completing CRF: _____

Date of QC: __ __/__ __ __/ __ __ __ __ Signed measurement nurse: _____

Initials of counsellor: _____

3. Appendix C: Human Research and Ethics Council Approval

3.1. HREC REF 864/2019 Ethics approval

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

Room G 50 Old Main Building
Groote Schuur Hospital
Observatory 7925
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

15 January 2020

HREC REF: 864/2019

Dr Tamsin Phillips
School of Public Health & Family Medicine
Room 5.38, Level 5
Falmouth Building

Dear Dr Phillips

PROJECT TITLE: TRAVEL AND ADHERENCE TO ANTIRETOVIRAL THERAPY (ART) AMONG POSTPARTUM WOMEN LIVING WITH HIV IN SOUTH AFRICA (SUB-STUDY 866/2016) (MASTER DEGREE - MS RUFARO MVUDUDU)

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

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

Approval is granted for one year until the 30 January 2021.

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)

The HREC acknowledges that the student: Ms Rufaro Mvududu will also be involved in this study.

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.

Please quote the HREC REF in all your correspondence

Yours sincerely

Signature removed to avoid exposure online

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HRECREF 811/2019
OL

3.2. HREC REF 866/2016 Ethics approval

HUMAN RESEARCH ETHICS COMMITTEE
21 MAY 2019
HEALTH SCIENCES FACULTY UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.04.2020
☐ Not approved	See attached comments		
Signature Chairperson of the HREC		Date Signed	22/5/2019

Comments to PI from the HREC
Ph to go for re deviation document

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	17 May 2019		
HREC REF Number	866/2016	Current Ethics Approval was granted until	30 Jan 2019
Protocol title	Long-term Adherence and Care Engagement (LACE): A supplement to the MCH-ART protocol		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes ✓ No		
If yes, could you please provide the HREC Ref's for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study			
Principal Investigator	Prof Landon Myer		
Department / Office Internal Mail Address	Office 5.43 Level 5 Falmouth Building		

1.1 Does this protocol receive US Federal funding?	✓ Yes	☐ No

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

3.3. HREC REF 451/2012 Ethics approval

HUMAN RESEARCH ETHICS COMMITTEE
09 NOV 2018
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN
FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30/11/2019
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	Signature removed	Date Signed	1/11/2018

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	30 October 2017 2018		
HREC REF Number	451/2012	Current Ethics Approval was granted until	30 October 2018
Protocol title	Strategies to optimize antiretroviral therapy services for maternal & child health: the MCH-ART study		
Protocol number (if applicable)	NA		
Are there any sub-studies linked to this study?	✓ Yes ☐ No		
If yes, could you please provide the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.	HREC REF 194/2013: Estimation of delivery dates using obstetric ultrasound in the MCH-ART study HREC 550/2015: Childbearing, family planning and relationships among women living with HIV in Gugulethu, Cape Town		
Principal Investigator	Prof Landon Myer		

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

4. Appendix D: LACE Study Informed Consent Form (ICF)

TITLE OF RESEARCH: Long-term Adherence and Care Engagement (LACE) Study

WHAT IS THE PURPOSE OF THIS STUDY?

We are from the University of Cape Town and ICAP at Columbia University. Previously, you took part in the MCH-ART study where we followed you and your baby (who was born in 2013-2014) until the baby was 12-18 months old.

At this time, you are being asked to take part in an additional follow-up visit for this same study.

The purpose of this additional study visit is to learn more about your health and the health of your child as well as the HIV care and treatment you have received since the last MCH-ART study visit. We would like to understand how the HIV care you received when you were still in the MCH-ART study has impacted your HIV care now that your child is older.

The purpose of this consent form is to give you information to help you decide if you want to take part in this additional study visit.

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

If you agree to take part, you will be asked to complete one additional study visit with your child, if possible.

As in the MCH-ART study, this visit is separate from the usual clinic visits that you have for HIV care. This visit will take 2-3 hours and will include the following:

- Answer questions about your recent HIV-related health care, HIV disclosure, and use of HIV drugs (including side effects and adherence). We will ask you additional questions about HIV, stigma, and mental health (including drug and alcohol use), family planning, child feeding practices, partner violence, child health and health care and how you feel about the HIV care that you have received.
- Have approximately 15mLs (3 teaspoons) of blood drawn from your arm
- Measurement of weight, length and mid-upper arm circumference of your child

- Measurement of your height, weight and mid-upper arm circumference
- Neurodevelopmental assessment of your child

NOTE: The blood that is drawn at this visit will be used to check your viral load (this is the amount of HIV in your blood) and if necessary, to check whether the HIV in your blood is resistant to any HIV medicines. Results from these tests will be made available to you. It will also be used to check for levels of HIV medicines in your blood. Results from these tests will not be made available.

Review of medical records

As part of this study, we will also be looking at and taking information from your routine medical records, and the records of your child born in the MCH-ART study. This will including obstetric, ART clinic, laboratory and pharmacy records. Since clinics use many types of patient files, we would like your permission to access all your records: paper files, pharmacy records and electronic databases at the facilities you and your child may visit. From these records, we are interested in learning about the HIV care and treatment that you received after you delivered your baby in the MCH-Art study. Finally, we want to learn about your child's health status after delivery as well. We will use your and your child's provincial folder number to find these medical records in the clinic or electronic database. All data that we review and abstract is confidential and no participant names are recorded on study documents.

Verbal Autopsy

In the event that your child born while you were in the MCH-ART study has passed away, we may ask you to complete a questionnaire with a trained interviewer to help us to understand how the child died. If you feel uncomfortable and would prefer not to complete the questionnaire, you can refuse to do so

Contact for future study

After the completion of this visit, it is possible that we will contact you again at your next clinic visit or at another time in the future to take part in additional research studies. At that time, you would be asked to review and sign another consent form. If you are asked to take part in any future studies, you can choose not to. You will be asked to provide contact information so that we may get in touch with you regarding additional research studies. Study staff will talk with you about the best way to contact you.

WHAT ARE THE POTENTIAL RISKS?

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

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.

WHAT ARE THE POTENTIAL BENEFITS?

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 child during the course of the study, we will make sure 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 and postpartum women in Cape Town, the Western Cape Province, and across South Africa.

WHAT ARE THE ALTERNATIVES TO TAKING PART?

There is no alternative to taking part in this study. If you decide not to take part you will continue your routine care as usual.

WHAT ABOUT CONFIDENTIALITY?

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

Only study staff and personnel involved in routine audits will have access to these materials. The following individuals and/or agencies will be able to look at and copy your research records:

- The investigators, study staff and other professionals who may be evaluating the study

- Authorities from Columbia University and the University of Cape Town, including the IRB or Ethics Committee. An IRB is a committee organized to protect the rights and welfare of people involved in research.
- The Office of Human Research Protection (OHRP)
- The study sponsor, National Institutes of Health (NIH), including persons or organizations working with NIH may review your data for accuracy but may not copy information with your name on it.

All staff involved in data collection and management will get specific training in confidentiality.

This research is also covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use any information that may identify you in any US-based federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence unless you have consented for this use. Study information protected by this Certificate cannot be disclosed to anyone else who is not involved in this research except, if there is a US-federal, state, or local law that requires disclosure; if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Even with these procedures as well as the Certificate of Confidentiality in place, 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.

WHAT HAPPENS IF I GET HURT TAKING PART IN THIS STUDY?

There are no experimental medicines being used in this study and risk of injury due to study participation is very low. However this research study is covered by an insurance policy taken out by the University of Cape Town if you suffer a bodily injury because you are taking part in the study.

The insurer will pay for all reasonable medical costs required to treat your bodily injury, according to the SA Good Clinical Practice Guidelines 2006. The insurer will pay without you having to prove that the research was responsible for your bodily injury. You may ask the study doctor for a copy of these guidelines.

The insurer will *not* pay for harm if, during the study, you:

- Do not follow the study nurses' instructions
- Do not take reasonable care of yourself

If you are harmed and the insurer pays for the necessary medical costs, usually you will be asked to accept that insurance payment as full settlement of the claim for medical costs. However, accepting this offer of insurance cover does not mean you give up your right to make a separate claim for other losses based on negligence, in a South African court.

It is important to follow the study nurses' instructions and to report straightaway if you suspect study related bodily harm.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

At the end of this visit, you will be given R150 in grocery vouchers to thank you for your time and contribution to this study as well as money to cover your transport cost. Refreshments for you and your child will be provided. A small gift for your child will also be given to you.

ARE THERE ANY COSTS?

There is no cost for being in this study.

CAN I LEAVE THE STUDY?

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

FUTURE USE OF SPECIMENS:

If you agree, an additional 5mLs of blood will be taken for future HIV and maternal and child health related research (making it 20mLs in total). At this time, we cannot provide details of when this testing may be conducted, or exactly what tests we would like to do. However, additional testing will not be done using these stored samples without the approval of the appropriate research ethics committees involved in this research.

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

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

Consent for storage of your blood:

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

_____ (initial) I do **NOT** agree to the storage of my blood for future use.

DO YOU HAVE ANY QUESTIONS?

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

Do you have any questions?

FOR ADDITIONAL INFORMATION:

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

Dr 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

Dr Elaine Abrams

ICAP, Columbia University

Mailman School of Public Health

College of Physicians and Surgeons

Tel: +1 212 342 0543

Email: eja1@cumc.columbia.edu

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

Columbia University Medical Center IRB

Tel: +1 212 305 5883

CONSENT STATEMENT:

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.

Please indicate your consent with your signature.

Volunteer's name _____

_____

Signature of Volunteer Date

Staff member's name_____

_____

Signature of study staff Date

If the volunteer is unable to read or write the entire counselling process must be observed by an independent witness who can then confirm the procedure once the she has given consent.

Fingerprint of volunteer:

Witness:

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

Name: _____

Signature: _____

Date: _____

Thank you.

5. Appendix E: Supplementary Manuscript Data Analyses Tables

5.1. Descriptive characteristics tables

Table S1: Descriptive characteristics of 353 LACE postpartum women, grouped by their 30-day ART adherence. Presented as n (%) unless specified.

Variable	**Adherent, 100% (n = 208)** n (%)	**Nonadherent, <100% (n = 145)** n (%)	**Overall women (N = 353)** n (%)	**p-value**
Mean age in years (±SD)	32.8 (±5.52)	32.4 (±5.32)	32.6 (±5.43)	0.528
Level of education				
Primary	143 (68.8)	100 (69.0)	243 (68.8)	0.966
Secondary/Tertiary	65 (31.2)	45 (31.0)	110 (31.2)	
Employment Status				
Employed	111 (53.4)	59 (40.7)	170 (48.2)	0.019
Unemployed	97 (46.6)	86 (59.3)	183 (51.8)	
Socioeconomic Status (SES)				
Lowest SES	58 (27.9)	46 (31.7)	104 (29.5)	0.601
Moderate SES	56 (26.9)	41 (28.3)	97 (27.5)	
Highest SES	94 (45.2)	58 (40.0)	152 (43.0)	
Housing				
Informal (shack)	102 (49.0)	65 (44.8)	167 (47.3)	0.436
Formal (house/hostel)	106 (51.0)	80 (55.2)	186 (52.7)	
Marital status				
Married/cohabiting	89 (42.8)	45 (31.0)	134 (38.0)	0.025
Unmarried	119 (57.2)	100 (69.0)	219 (62.0)	
Disclosure Status				
Disclosed	207 (99.5)	138 (95.2)	345 (97.7)	0.007
Undisclosed	1 (0.5)	7 (4.8)	8 (2.3)	
Parity				
2 or less children	111 (53.4)	84 (57.9)	195 (55.2)	0.396
3 or more children	97 (46.6)	61 (42.1)	158 (44.8)	
Presentation to ANC at enrolment into MCH-ART				
Early	103 (49.5)	66 (45.5)	169 (47.9)	0.459
Late	105 (50.5)	79 (54.5)	184 (52.1)	
Travel Status				
Travelled	42 (20.2)	39 (26.9)	81 (23.0)	0.141
Did not travel	166 (79.8)	106 (73.1)	272 (77.0)	

Table S2: Descriptive characteristics of 349 LACE postpartum women, grouped by their VL. Presented as n (%) unless specified. *Excluding four women who had telephonic interviews and no blood drawn for viral load results.*

Variable	**Viral suppression, ≤50copies/mL (n = 196)** n (%)	**Viremia, >50copies/mL (n = 153)** n (%)	**Overall women (N = 353)** n (%)	**p-value**
Median age in years (±SD)	33.2 (±5.19)	32.8 (±5.72)	32.6 (±5.43)	0.030
Level of education				
Primary	136 (39.4)	104 (68.0)	240 (38.8)	0.777
Secondary/Tertiary	60 (30.6)	49 (32.0)	109 (31.2)	
Employment Status				
Employed	94 (48.0)	86 (56.2)	169 (48.4)	0.126
Unemployed	102 (52.0)	67 (43.8)	180 (51.6)	
Socioeconomic Status (SES)				
Lowest SES	56 (28.6)	45 (29.4)	101 (29.9)	0.934
Moderate SES	56 (28.6)	41 (26.8)	97 (27.8)	
Highest SES	84 (42.9)	67 (43.8)	151 (43.3)	
Housing				
Informal (shack)	102 (52.0)	65 (42.5)	167 (47.8)	0.076
Formal (house/hostel)	94 (48.0)	88 (57.5)	182 (52.2)	
Marital status				
Married/cohabiting	86 (43.9)	46 (30.0)	132 (32.8)	0.008
Unmarried	110 (56.1)	107 (70.0)	217 (62.2)	
Disclosure Status				
Disclosed	191 (97.5)	150 (98.0)	341 (97.7)	0.715
Undisclosed	5 (2.5)	3 (2.0)	8 (2.3)	
Parity				
2 or less children	112 (57.1)	82 (53.6)	194 (55.6)	0.508
3 or more children	84 (42.9)	71 (46.4)	155 (44.4)	
Presentation to ANC at enrolment into MCH-ART				
Early	107 (54.6)	60 (39.2)	167 (47.9)	0.004
Late	89 (45.4)	93 (60.8)	182 (52.1)	
Travel Status				
Travelled	48 (24.5)	32 (20.9)	80 (22.9)	0.430
Did not travel	148 (75.5)	121 (79.1)	269 (77.1)	
30-day ART adherence				
100% adherence	141 (71.9)	66 (43.1)	207 (59.3)	<0.001
<100% adherence	55 (28.1)	87 (56.9)	142 (40.7)	
Self-reported travel impact on ART adherence				
Difficult	1 (2.1)	5 (15.6)	6 (7.5)	0.024
Not difficult	47 (97.9)	27 (83.4)	74 (92.5)	

5.2. Log-binomial regression models

Table S3: Log-binomial regression model (n = 353) of factors associated with travel in postpartum women. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.00 [0.97 – 1.04]	1.00 [0.96 – 1.03]
Completed secondary education	1.23 [0.83 – 1.83]	
Employed	0.95 [0.65 – 1.40]	0.90 [0.57 – 1.43]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	1 (ref)
Moderate SES	1.15 [0.73 – 1.82]	1.29 [0.79 – 2.09]
Highest SES	0.71 [0.44 – 1.15]	0.98 [0.52 – 1.85]
Formal house	0.59 [0.40 – 0.87]	0.65 [0.40 – 1.07]
Married/cohabiting	1.59 [1.09 – 2.33]	1.41 [0.95 – 2.10]
Has 3 or more children	1.15 [0.78 – 1.68]	
Late presentation to ANC	0.94 [0.64 – 1.38]	

Table S4: Log-binomial regression model (n =353) of factors associated with 100% ART adherence in the past 30 days. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.01 [0.99 – 1.02]	1.00 [0.98 – 1.01]
Completed secondary education	1.00 [0.83 – 1.21]	0.94 [0.78 – 1.13]
Employed	1.23 [1.03 – 1.47]	1.24 [1.04 – 1.48]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	1.04 [0.81 – 1.32]	
Highest SES	1.11 [0.90 – 1.37]	
Formal house	0.93 [0.78 – 1.11]	1.00 [0.84 – 1.19]
Married/cohabiting	1.22 [1.03 – 1.45]	1.24 [1.03 -1.48]
Has 3 or more children	1.08 [0.91 – 1.28]	
Late presentation to ANC	0.94 [0.79 – 1.11]	
Travelled	0.85 [0.67 – 1.07]	0.84 [0.67 – 1.05]

Table S5: Log-binomial regression model (n = 349) of factors associated with viral suppression (≤50copies/mL), restricted to women with VL results available. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]
Age in years	1.02 [1.00 – 1.03]
Completed secondary education	0.97 [0.79 – 1.19]
Employed	1.16 [0.96 – 1.39]
Socioeconomic Status (SES)	
Lowest SES	1 (ref)
Moderate SES	1.04 [0.82 – 1.33]
Highest SES	1.00 [0.80 – 1.26]
Formal house	0.85 [0.70 – 1.02]
Married/cohabiting	1.29 [1.07 – 1.54]
Has 3 or more children	0.94 [0.78 – 1.13]
Late presentation to ANC	0.76 [0.63 – 0.92]
Travelled	1.09 [0.88 – 1.34]
Adhered to ART in last 30 days	1.76 [1.40 – 2.21]

This analysis was attempted but the multivariable analysis did not converge.

5.3. Sensitivity analyses

Table S6: Poisson regression model (n= 353) of factors associated with 95% adherence in the past 30 days. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.01 [0.99 – 1.02]	1.00 [0.98 – 1.02]
Completed secondary education	0.98 [0.82 – 1.17]	0.93 [0.78 – 1.12]
Employed	1.22 [1.03 – 1.43]	1.23 [1.04 – 1.46]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	1.04 [0.82 – 1.31]	
Highest SES	1.11 [0.90 – 1.36]	
Formal house	0.92 [0.78 – 1.09]	0.98 [0.82 – 1.16]
Married/cohabiting	1.25 [1.06 – 1.47]	1.27 [1.07 – 1.50]
Has 3 or more children	1.05 [0.89 – 1.25]	
Late presentation to ANC	0.91 [0.77 – 1.08]	0.93 [0.79 – 1.10]
Travelled	0.89 [0.72 – 1.10]	0.86 [0.70 – 1.07]

Table S7: Poisson regression model (n = 353) of factors associated with no missed ART doses in the past 7-days. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.00 [0.99 – 1.01]	1.00 [0.99 – 1.00]
Completed secondary education	1.01 [0.91 – 1.11]	0.99 [0.89 – 1.09]
Employed	1.06 [0.97 – 1.17]	1.07 [0.97 – 1.17]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	0.98 [0.86 – 1.12]	
Highest SES	1.05 [0.94 – 1.18]	
Formal house	1.01 [0.92 – 1.11]	1.03 [0.93 – 1.15]
Married/cohabiting	1.08 [0.99 – 1.18]	1.11 [1.00 – 1.22]
Has 3 or more children	0.96 [0.88 – 1.06]	
Late presentation to ANC	0.91 [0.83 – 0.99]	0.92 [0.83 – 1.00]
Travelled	0.97 [0.87 – 1.09]	0.96 [0.86 – 1.08]

Table S8: Poisson regression model (n=349) of factors associated with viral suppression (≤1000 copies/mL), restricted to women with VL results available. Presented as unadjusted (RR) and adjusted (aRR) risk ratios with 95% confidence intervals (CI).

	Crude Risk Ratio (RR) [95% Confidence Interval]	**Adjusted Risk Ratio (aRR) [95% Confidence Interval]**
Age in years	1.01 [1.00 – 1.02]	1.01 [0.99 – 1.02]
Completed secondary education	0.95 [0.80 – 1.13]	
Employed	1.14 [0.98 – 1.34]	1.08 [0.92 – 1.25]
Socioeconomic Status (SES)		
Lowest SES	1 (ref)	
Moderate SES	1.04 [0.85 – 1.28]	
Highest SES	1.02 [0.85 – 1.24]	
Formal house	0.89 [0.76 – 1.03]	0.92 [0.79 – 1.07]
Married/cohabiting	1.19 [1.02 – 1.39]	1.08 [0.93 – 1.26]
Has 3 or more children	0.96 [0.82 – 1.12]	
Late presentation to ANC	0.83 [0.71 – 0.96]	0.84 [0.72 – 0.98]
Travelled	1.06 [0.88 – 1.26]	1.06 [0.89 – 1.27]
Adhered to ART in last 30-days	1.50 [1.25 – 1.80]	1.46 [1.22 – 1.75]

6. Appendix F: Journal Submission Guidelines

Author Guidelines

GENERAL POINTS

We welcome original research papers, reviews and editorials.

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