Relationship between sexual partnerships, intimate partner violence and sexually transmitted infections in pregnant women living with HIV and not living with HIV in Cape Town, South Africa

by Yamkela Qayiya

Student Number: QYYYAM001

Submitted to the School of Public Health and Family Medicine

University of Cape Town

In fulfilment of the requirements for the degree of

Master of Public Health (MPH)

Faculty of health Sciences

UNIVERITY OF CAPE TOWN

31-January-2021

Thesis Supervisor:

Dr Dvora Joseph Davey

School of Public Health and Family Medicine

Table of Contents

Plagiarism Declaration

I, Yamkela Qayiya, hereby declare that the work on which this thesis is based is 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. I authorise the University to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 30- January-2021

PART A: PROTOCOL

1. Protocol Synopsis

According to the World Health Organisation (WHO), there are over 351 million global incident cases of *Trichomonas vaginalis* (TV), *Chlamydia trachomatis* (CT), and *Neisseria gonorrhoea* (NG) annually [1]. These sexually transmitted infections (STIs) are associated with poor reproductive health, sexual health, and several birth outcomes such as infertility, ectopic pregnancy, increased HIV risk, preterm labour, and intrauterine death [1-5]. Numerous studies have also shown these STIs increase the risk of HIV acquisition and vertical HIV transmission [6-10].

In low- and middle-income countries (LMICs) the prevalence of these STIs in pregnant women is as high as 25% [11]. Recent studies conducted on the prevalence of curable STIs among pregnant women in Southern Africa found a reported a high prevalence of CT (20%-37%), NG (1.3%-7%) and TV (5%-24%) particularly in women living with HIV [12-14]. A recent study conducted in South Africa reported that 32% of pregnant women tested positive for CT, NG and/or TV at their first antenatal visit, and most were asymptomatic cases [14]. Despite the known risks associated with STIs, the prevalence of CT, NG and TV and subsequent adverse outcomes are still largely unknown among pregnant women living in South Africa. Additionally, risk factors that are associated with STIs in pregnant women living in low- and middle-income countries still need to be explored.

The overall aim of the proposed research is to investigate the relationship between sexual relationships, intimate partner violence and STIs in pregnant women living with HIV (WLHIV) and not living with HIV. This proposed study is a secondary analysis of pregnant women enrolled in a prospective cohort study evaluating the incidence and prevalence of curable STIs. WLHIV and women not living with HIV were enrolled and followed for three visits; first visit was during the first antenatal care; second visit was during the 3rd trimester and final visit was within 1 week postpartum. The gestational age for enrolment was less than 28 weeks. All enrolled participants were attending antenatal care at the Gugulethu Midwife Obstetrics Unit (MOU) in Cape Town.

The proposed research will contribute to the growing literature impact of intimate partner violence on STIs and the association between relationship quality and STIs in pregnant women. Study findings will inform future research and programmatic interventions to promote STI testing and treatment for pregnant women and their partners.

2. Introduction

2.1. Background

The spread of sexually transmitted infections (STIs) results from a complex interaction of factors related to demography, socio-economic status, and sexual behaviours. Sexually transmitted infections (STIs) are among the most common acute conditions globally and when acquired can damage sexual and reproductive health later in life and, for pregnant women, the health of their babies. The World health Organisation (WHO) estimates that there are 351 million new cases of *Trichomonas vaginalis* (TV), *Chlamydia trachomatis* (CT), and *Neisseria gonorrhoea* (NG) annually [1]. The prevalence of STIs among young people and pregnant women is still unknown in many high HIV prevalence settings, especially in low- and middle-income settings [15,16].

Some STIs are asymptomatic and special resources are needed in order to detect the infection, and this is a difficult to do especially in low-income areas due to lack of resources and accessibility [16,17]. The standard of care in sub-Saharan Africa is to manage STIs based on symptoms, yet there is a dearth of research on the prevalence of asymptomatic STIs in pregnancy in WLHIV and women not living with HIV [15,17-18]. Despite the known risks associated with STIs, the prevalence of CT, NG and TV, risk factors and subsequent adverse outcomes are still largely unknown among pregnant women.

<u>STIs in Pregnancy</u>

There is growing literature which looks at correlates of STIs in adolescents and pregnant women. Various studies have shown that STIs increase the risk of HIV infection and vertical HIV transmission [6-10]. CT, NG and TV result in the disruption of the protective mucosal barrier which leads to the upregulation of

inflammatory cytokines that are associated with the acquisition of HIV [6-8]. Moreover, in pregnant WLHIV, STIs may increase the risk of vertical HIV transmission [9-10]. According to previous studies, STIs are also associated with various adverse birth outcomes which include conditions such as pneumonia, congenital infection, low birthweight, still birth, preterm delivery, and neonatal mortality [1-4,19-20]. Further emphasising the need for alternative strategies that aim at reducing STIs and its risk factors in low- and middle-income regions.

Intimate partner violence and STIs

Intimate partner violence (IPV) is defined as the physical, sexual or psychological harm by a partner(s). IPV is widely known as one of the causes of health-related issues which include depression, disability and death among reproductive age women. There is limited literature which focuses on the role of IPV in sexual health and reproduction in pregnant women living in LMICs. What is currently known is that women who reported experiencing IPV victimization were associated with increased risk of adverse birth outcomes, STIs and infertility [21]. Various studies have looked at the relationship between STI risk behaviours and IPV victimisation and found that women who experience IPV are at increased risk for unprotected sexual intercourse [21-23]. Additionally, women who reported a history of physical abuse are at higher risk for treatable STIs [24].

A study conducted in rural South Africa reported that IPV victimisation, low relationship equity is associated with an increased risk of HIV in pregnant women [25]. Research findings suggest that there is an association between IPV and STI acquisition [21-25], however there is limited literature on this in pregnant women living in South Africa. Therefore, more research is needed to understand the relationship between IPV in pregnant women and risk of HIV and curable STIs.

2.2. Background to the proposed dissertation

The proposed study is a secondary analysis study from a prospective cohort study conducted at a primary health care facility in Gugulethu. Between October 2017 and February 2019, the Sexually Transmitted

Infections in Pregnancy (STIP) study (UCT-HREC) (REC REF 454/2017) enrolled 250 pregnant women attending their first antenatal care from the Gugulethu Midwife Obstetric Unit in Cape Town. Half of the women were HIV-infected (n=107) and half will be HIV uninfected (n=135) to enable us to compare outcomes by serostatus. The STIP study mainly assessed the burden of STIs in pregnant women living in Gugulethu Cape Town [14].

We will conduct a secondary analysis of data collected from the STIP study via surveys and STI test results. The main aim of this study is to explore the relationship between IPV, relationship quality and STIs during pregnancy. This investigation will also include socio-demographic characteristics associated with STIs.

2.3. Study rationale

STIs continue being one of the most common acute conditions globally [1]. Although the prevalence of CT, NG and TV are known among pregnant women in South Africa, subsequent adverse consequences and risk factors are still also largely unknown. There is limited data investigating the risk factors or correlates associated with STIs among pregnant women living in low- and middle-income countries.

3. Study aim and Objectives

3.1. Study aim

The overall aim of the study is to investigate the relationship between sexual relationships, intimate partner violence and STIs in pregnant women living with HIV and not living with HIV.

3.2. Objectives

1. To identify risk factors associated with intimate partner violence during pregnancy.
2. To identify risk factors associated with prevalent STIs in pregnant women.
3. To investigate the relationship between relationship quality, IPV and STI diagnosis at first ANC in pregnant women.

3.3. Hypothesis

The study hypothesis is that women who experience intimate partner violence and low relationship quality will have higher risk of STI acquisition compared to those who do not experience any intimate partner violence and have a high relationship quality.

4. Methodology

4.1. Study design

This is a secondary study analysis of data from a prospective cohort study conducted at a primary health care facility in Gugulethu, Cape town from October 2017 to February 2019. The proposed study is a cross sectional study of women living with HIV, and those who are not, attending their first antenatal care visit at the Gugulethu Midwife Obstretic Unit (MOU) in Cape Town.

4.2. Study population and sampling

Pregnant women who attended their antenatal care at Gugulethu MOU between October 2017 and February 2019 are included. Since this is a secondary analysis, there is no direct contact with any participants of this study.

Inclusion criteria

The inclusion criteria for the study is as follows:

- Pregnant women who are 18 or older
- Confirmed HIV test
- Attending their first antenatal care visit
- Willing to participant in the study and have not withdrawn consent from the parent (STIP) study.

Exclusion criteria

Participants who meet any of the following exclusion criteria were excluded:

- Any medical, psychiatric, or social condition which in the opinion of the investigators would affect the ability to consent and/or participate in the study.
- Antibiotic usage in the last 30 days

4.3. Study Setting

The study was conducted in Gugulethu Midwife Obstetric Unit (MOU) in Cape Town. The Gugulethu MOU has been providing services to women in Gugulethu, and surrounding areas which include Nyanga, Khayelitsha, Phillipi, Crossroaads and Heideveld. All women enrolled in the study were tested for STIs (CT, NG and TV) using GeneXpert/Cepheid tests in the health facility. HIV testing was done by the Department of health staff and STI testing was conducted by the study staff.

4.4. Data collection

The data used for this secondary analysis were taken from the STIP study. The data were taken from medical case report forms (CRF) and demographic questionnaire (Appendix A), the interviews were conducted between October 2017 and February 2019. The questionnaires were administrated through face-to-face interviews at the first antenatal care visit of the participants. STI and HIV testing was also conducted at the time of enrolment. Where there is missing data on records or data, the National Health Laboratory Service (NHLS) database will be searched in an attempt to complete the missing data. Table 1A shows the list of variables that will be collected for this analysis.

Table 1A: List of the variables of interest for analysis

Variables	**Type**	**Categorical**
Maternal age (years)	Continuous – numerical	n/a
Gestational age at first antenatal care (weeks)	Continuous – numerical	n/a
Level of education	Categorical – binary	Primary/secondary

Relationship status	Categorical – binary	Married and (or) cohabiting / Not married
HIV status	Categorical – binary	Positive / Negative
STI result	Categorical – binary	Positive / Negative
IPV experience during pregnancy	Categorical – binary	Yes / No
IPV experience in the past 12 months	Categorical – binary	Yes / No
Relationship quality	Categorical	Very low /Low / medium /High / very High

5. Data Management and Analysis plan

The completed questionnaires from the parent study were captured in real time on Research Electronic Data Capture (REDCap) database which has limited access and protected by a password. The data is only available to the study investigators. The relevant data for this dissertation have been transferred to an external hard drive that is also password protected. The external hard drive is kept safe in a locked area at the University of Cape Town study offices. Data processing, cleaning and analyses will be performed using STATA version 14 (STATA for Windows, version 14, Stata Corp; College Station, TX). The data will be cleaned, and efforts will be made to complete any missing data by going back to the source medical records and NHLS database were applicable.

Univariate and bivariate analysis

After the data has been exported from REDCap it will be transferred and imported into the analysis software (STATA 14). The data will be explored using visual diagrams which include scatter plots, box and whisker plots and bar graphs. Baseline characteristics will be presented and summarised using descriptive statistics which include proportions, median and interquartile range (IQR) or means with standard deviations to describe the continuous covariates depending on the distribution of the data. Categorical variables will be

described using frequency and proportions. Correlation between variables will be evaluated using the relevant diagrams and plots.

Model building

The main outcome of the study is STI diagnosis at first antenatal visit in pregnant women which is a binary variable; women who tested positive for any STI (CT, NG and TV) (Yes-STI) and those who tested negative (No-STI). The secondary outcome is intimate partner violence, which is also a binary variable, women who reported experiencing any IPV (Yes-IPV) and those who have not (No-IPV). A few models will be explored one is a multivariable logistic regression used to describe correlates of STI acquisition and IPV, adjusted for relevant variables such as gestational age, maternal age, and relationship status, and the other will be a multivariate logistic regression to describe relationship between relationship status, IPV and STI acquisition. Additionally, we will use logistic regression model to evaluate social demographic and sexual behaviours that are associated with our outcome of interest (STI diagnosis). In order to understand the relationship between the variables and reduce bias in our models we will create directed acyclic graphs (DAGs).

Covariates will be investigated as potential confounders or mediators prior to building the models. Confounders found will be adjusted for accordingly. All covariates that have a significant effect on the outcome will be included in our multivariate models. Model outputs will be presented as ratios (odds ratio or risk ratio) with 95% confidence intervals, and statistical significance for all the analyses will be assessed using the significance level of 0.05.

6. Potential limitations

This study relies on data that is largely self-reported except for STI and HIV results, the primary exposure and outcome of the analysis are subject to biases, mainly recall and social desirability biases. There may be underreporting of certain behaviours such as risky sexual behaviours and intimate partner violence due to social desirability biases. The data used is also collected from one health facility which may limit the

generalisability to other populations. Baseline characteristics were collected and adjusted for however there may be other unmeasured variables that could introduce bias or confounding into this analysis.

7. Ethical considerations

7.1. Ethical review

The study protocol, informed consent form, data collection tools and other requested documents has been reviewed and approved by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (UCT-HREC: REC REF 454/2017) (Appendix C). UCT-HREC reviews progress of the study at least annually (Appendix D).

7.2. Informed consent

The parent study has on-going approval from the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee. The annual renewal of the year 2020 to 2021 which this dissertation is being conducted can be found in the (Appendix C). There is no direct contact with the study participants. Participants who are eligible for this secondary analysis have signed relevant informed consent forms allowing for secondary data use of the data. Informed consent form for the STI testing and questionnaire were delivered in participants' home language (isiXhosa) by trained interviewers. The informed consent form (ICF) detailed the purpose of the study, study procedures, and the risks and benefits to mothers that participants may encounter at the additional study measurement visit.

7.3. Risks

This study is working with secondary data, and therefore there is no direct contact with the study participants. The study has minimal risk to participants enrolled in the parental study. All individuals working with the data will sign a confidentiality agreement with the supervisor and the principal investigator of the parent study, and will undergo training in ethics and confidentiality prior to accessing any of the data. The dataset used in this research is anonymous there are no identifiers. Every effort will be made to ensure maintenance of confidentiality.

7.4. Benefits

Since this is secondary analysis with no direct interaction with the study participants, this analysis will not have direct benefits to the participants enrolled in the parent study. However, this study does have indirect benefits which include identifying the optimal strategy for delivering STI diagnostics to pregnant women. This study also aims to provide further understanding and knowledge regarding STIs in LMICs, IPV and sexual health and this information has the potential to improve maternal services for HIV-infected and uninfected women in Cape Town, the Western Cape Province, and across South Africa.

7.5 Confidentiality

Efforts have been made to minimize the risk of any loss of confidentiality throughout the study design and conduct of the parent study. Steps are taken to ensure that confidentiality is always maintained. The data used in this study has no point identifiers. All data, electronic or hardcopy, will be kept in secure locked area and will be accessed only by the study investigators.

8. Logistics and timetable

Table 2A: Time schedule for the dissertation

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7
Literature review	X	X	X				
Data Collection			X				
Data Management			X	X			
Data Analysis			X	X	X	X	
Results				X	X	X	
Write up					X	X	X

9. Budget

There is no budget for this study. This work is part of the completion of the master's in public health degree.

10. Stakeholders and Dissemination

Publication or presentation of the results of the study will be agreed on in collaboration with the study investigators. The findings of the study will be available to stakeholders by publication of a peer-reviewed journal and by presentation of the study findings in research conferences.

11. References

1. World Health Organization. Global Health Sector Strategy on Sexually Transmitted Infections, 2016–2021. Geneva, Switzerland: WHO Document Production Services, 2016.
2. Adachi K, Klausner JD, Xu J, et al. Chlamydia trachomatis and Neisseria gonorrhoeae in HIV-infected pregnant women and adverse infant outcomes. Pediatr Infect Dis J 2016; 35:894–900.
3. Cotch MF, Pastorek JG 2nd, Nugent RP, et al. Trichomonas vaginalis associated with low birth weight and preterm delivery. The Vaginal Infections and Prematurity Study Group. Sex Transm Dis 1997; 24:353–360.
4. Silver BJ, Guy RJ, Kaldor JM, et al. Trichomonas vaginalis as a cause of perinatal morbidity: A systematic review and meta-analysis. Sex Transm Dis 2014; 41:369–376.
5. Francis SC, Mthiyane TN, Baisley K, Mchunu SL, Ferguson JB, Smit T, Crucitti T, Gareta D, Dlamini S, Mutevedzi T, Seeley J. Prevalence of sexually transmitted infections among young people in South Africa: A nested survey in a health and demographic surveillance site. PLoS medicine. 2018 Feb 27;15(2):e1002512.
6. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. The Lancet. 1998 Jun 1;351:S5-7.
7. Masson L, Mlisana K, Little F, Werner L, Mkhize NN, Ronacher K, Gamieldien H, Williamson C, Mckinnon LR, Walzl G, Karim QA. Defining genital tract cytokine signatures of sexually transmitted infections and bacterial vaginosis in women at high risk of HIV infection: a cross-sectional study. Sexually transmitted infections. 2014 Dec 1;90(8):580-7.
8. Wasserheit JN. Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. Sexually transmitted diseases. 1992;19(2):61-77.
9. C King C, R Ellington S, P Kourtis A. The role of co-infections in mother-to-child transmission of HIV. Current HIV research. 2013 Jan 1;11(1):10-23.

10. Adachi K, Xu J, Yeganeh N, Camarca M, Morgado MG, Watts DH, Mofenson LM, Veloso VG, Pilotto JH, Joao E, Gray G. Combined evaluation of sexually transmitted infections in HIV-infected pregnant women and infant HIV transmission. PloS one. 2018;13(1).
11. Davey DJ, Shull HI, Billings JD, Wang D, Adachi K, Klausner JD. Prevalence of curable sexually transmitted infections in pregnant women in low-and middle-income countries from 2010 to 2015: a systematic review. Sexually transmitted diseases. 2016 Jul;43(7):450
12. Mudau M, Peters RP, De Vos L, Olivier DH, J Davey D, Mkwanazi ES, McIntyre JA, Klausner JD, Medina-Marino A. High prevalence of asymptomatic sexually transmitted infections among human immunodeficiency virus-infected pregnant women in a low-income South African community. International journal of STD & AIDS. 2018 Mar;29(4):324-33.
13. Wynn A, Ramogola-Masire D, Gaolebale P, Moshashane N, Sickboy O, Duque S, Williams E, Doherty K, Klausner JD, Morroni C. Prevalence and treatment outcomes of routine Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis testing during antenatal care, Gaborone, Botswana. Sex Transm Infect. 2018 May 1;94(3):230-5.
14. Davey DL, Nyemba DC, Gomba Y, Bekker LG, Taleghani S, DiTullio DJ, Shabsovich D, Gorbach PM, Coates TJ, Klausner JD, Myer L. Prevalence and correlates of sexually transmitted infections in pregnancy in HIV-infected and-uninfected women in Cape Town, South Africa. PloS one. 2019;14(7)
15. Francis SC, Mthiyane TN, Baisley K, Mchunu SL, Ferguson JB, Smit T, Crucitti T, Gareta D, Dlamini S, Mutevedzi T, Seeley J. Prevalence of sexually transmitted infections among young people in South Africa: A nested survey in a health and demographic surveillance site. PLoS medicine. 2018 Feb 27;15(2):e1002512.
16. Passey M. Issues in the management of sexually transmitted diseases in Papua New Guinea. Papua and New Guinea medical journal. 1996 Sep;39(3):252-60.

17. Wilkinson D, Karim SA, Harrison A, Lurie M, Colvin M, Connolly C, Sturm AW. Unrecognized sexually transmitted infections in rural South African women: a hidden epidemic. Bulletin of the World health Organization. 1999;77(1):22.
18. Wilkinson D, Sach M, Connolly C. Epidemiology of syphilis in pregnancy in rural South Africa: opportunities for control. Tropical Medicine & International Health. 1997 Jan;2(1):57-62.
19. Wangnapi RA, Soso S, Unger HW, Sawera C, Ome M, Umbers AJ, Ndrewei N, Siba P, Suen CL, Vallely A, Wapling J. Prevalence and risk factors for Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis infection in pregnant women in Papua New Guinea. Sex Transm Infect. 2015 May 1;91(3):194-200.
20. Warr AJ, Pintye J, Kinuthia J, Drake AL, Unger JA, McClelland RS, Matemo D, Osborn L, John-Stewart G. Sexually transmitted infections during pregnancy and subsequent risk of stillbirth and infant mortality in Kenya: a prospective study. Sexually transmitted infections. 2019 Feb 1;95(1):60-6.
21. Coker AL. Does physical intimate partner violence affect sexual health? A systematic review. Trauma, Violence, & Abuse. 2007 Apr;8(2):149-77.
22. Mittal M, Senn TE, Carey MP. Mediators of the relation between partner violence and sexual risk behavior among women attending a sexually transmitted disease clinic. Sexually transmitted diseases. 2011 Jun;38(6):510.
23. Roberts TA, Auinger P, Klein JD. Intimate partner abuse and the reproductive health of sexually active female adolescents. Journal of adolescent health. 2005 May 1;36(5):380-5.
24. Allsworth JE, Anand M, Redding CA, Peipert JF. Physical and sexual violence and incident sexually transmitted infections. Journal of Women's Health. 2009 Apr 1;18(4):529-34.
25. Jewkes RK, Dunkle K, Nduna M, Shai N. Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. The lancet. 2010 Jul 3;376(9734):41-8.

PART B: Journal Manuscript

Relationship between sexual partnerships, intimate partner violence and sexually transmitted infections in pregnant women living with HIV and not living with HIV in Cape Town, South Africa

Abstract

Background

Women are at high risk of HIV and sexually transmitted infections (STIs) prior to and during pregnancy. There is limited research on the link between quality of sexual relationships, intimate partner violence (IPV) and STIs in pregnancy. This study aims to evaluate the association between relationship type and quality, IPV, and STI diagnosis in pregnant women.

Methods

We conducted a cohort study of 242 pregnant women ≥18 years attending their first antenatal care visit in Cape Town, South Africa between February 2017 and February 2019. We conducted interviews and tested pregnant women for three different STIs: *Chlamydia trachomatis* (CT), *Neisseria gonorrhoea* (NG) and *Trichomonas vaginalis* (TV) using point-of-care PCR testing (GeneXpert, Cepheid, USA). We used multivariable logistic regression to evaluate the association between relationship quality, STI, and IPV during pregnancy, adjusting for maternal age, gestational age and relationship status.

Results

In 242 pregnant women (median age 29 years [IQR = 24–34], and median gestational age 19 weeks [IQR= 14-24]), 78 (32%) were diagnosed with CT, NT, and/or TV at baseline. Unmarried, non-cohabiting women had almost 2-times the odds of having an STI during pregnancy (aOR=1.92, 95% CI=1.06-3.48); women living with HIV had increased odds of having an STI (aOR=1.97, 95% CI=1.07-3.62) adjusting for covariates. Overall, 5% of women who had an STI reported experiencing IPV during the past year (n=4) and 2% of the women who tested STI-negative (n=4). Women who reported having high relationship quality in their primary relationship had decreased odds of experiencing IPV (aOR=0.11, 95% CI=0.017-0.073) compared to those

who reported low relationship quality, adjusting for covariates, but this was not associated with STI diagnosis. Reporting recent IPV was not associated with STI acquisition (aOR=2.41, 95% CI=0.55-10.45).

Conclusion

We found a high prevalence of STIs among pregnant women. Women who were unmarried or non-cohabiting with the father of the baby or were living with HIV had increased odds of having a STI during pregnancy. Women who reported better relationship quality were associated with decreased odds of experiencing IPV. Experiencing IPV was not associated with STI acquisition.

Introduction

The burden of morbidity and mortality worldwide caused by sexually transmitted pathogens reduces the quality of life, reproductive health, and child health. Sexually transmitted infections (STIs) are among the most common acute conditions globally [1]. *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV) are the most common curable STIs, with over a quarter of a billion of new cases reported annually among individuals aged 15-49 years [1,2]. In low- and middle-income countries (LMICs) the prevalence of these STIs in pregnant women is as high as 25% [3]. The sequelae of untreated STIs in pregnancies and infant outcomes have been reported by various studies and it includes conditions such as pneumonia, congenital infection, low birthweight, preterm delivery, and neonatal mortality [1,4,5].

Numerous studies have shown that STIs increase the risk of maternal HIV acquisition and vertical HIV transmission [6-10]. CT, NG and TV result in the disruption of the protective mucosal barrier which leads to the upregulation of inflammatory cytokines that are associated with the acquisition of HIV [6-8]. Further, in pregnant women living with HIV (WLHIV), STIs may increase the risk of vertical HIV transmission [9]. Another study reported that the risk of vertical HIV transmission nearly doubled amongst WLHIV co-infected with other STIs [10].

The high prevalence of curable STIs, and high proportion of asymptomatic infections and adverse pregnancy outcomes makes STI control and treatment a major public health concern especially in low- and middle-income countries [2]. According to the World Health Organisation (WHO), it is essential to evaluate risk factors associated with STIs particularly the impact of STIs on vertical HIV transmission [1]. Studies conducted on the burden of curable STIs among pregnant women in Southern Africa reported a high prevalence of CT (20%-37%), NG (1.3%-7%) and TV (5%-24%), particularly in WLHIV [11-14]. In another study conducted among pregnant WLHIV from multiple sites in sub-Saharan Africa and Asia 20% of the women were positive for CT and NG which was associated with adverse pregnancy or infant outcomes [5].

Women who experience intimate partner violence (IPV) may be at increased risk of adverse birth outcomes, STIs and infertility [15]. A recent study done in young adult women showed that IPV victims had a higher STI

prevalence compared to women in non-violent relationships [16]. Another study reported that women with history of physical abuse are at a higher risk for curable STIs [17]. In rural South Africa, a study demonstrated that physical and sexual IPV, and low relationship power equity increased incidence of HIV in young women. [18] Young women living in rural South Africa who reported IPV had higher HIV seropositivity, suggesting that HIV and IPV share underlying risk factors [19]. Despite the current evidence that suggests a significant association between IPV and STIs in women [15-20], there has been limited research on this relationship in South Africa, especially in pregnant women. Our study explores the association between relationship status, relationship quality, reported recent IPV and STI diagnosis among pregnant WLHIV and not living with HIV in antenatal care in Cape Town, South Africa.

Method

Study design

We conducted a cohort study of pregnant women attending their first antenatal care (ANC) visit at a public sector in Gugulethu, Cape Town, South Africa, from October 2017 to February 2019. We sought to evaluate the prevalence and incidence of STIs, and risk factors that are associated with STIs in pregnant WLHIV and women without HIV. The population in Gugulethu of 400,000 is predominantly of low socioeconomic status, therefore majority of the people use the local public-sector health services that are provided free of charge. The setting, eligibility criteria, data collection, specimen collection, testing and primary study outcomes have been previously documented [13]. Briefly, women ≥ 18 years of age and currently pregnant (<34 weeks) who reside in the Gugulethu community were invited to participate in the study at their first antenatal care. Trained staff members were instructed to recruit a sample of pregnant women who came for their ANC visit, by employing a recruitment strategy that will accommodate normal clinic procedures. Women were invited to participate in three visits throughout their pregnancy: first ANC, during the third trimester and post-partum (within 10 days after delivery).

Study procedures

During each study visit, trained research staff members administrated a questionnaire verbally, which collected socio-demographic background, partner's STI status, relationship status and sexual history data. Participants, with the assistance of the staff members, self-collected vulo-vaginal swab specimen during each visit. Research staff members tested the specimens using Xpert CT/NG assays (Cepheid, Sunnyvale, California) for STIs (CT, NG and TV). In compliance with the South African National Guidelines, women who tested positive for any of the STIs were treated [22]. NG infections were treated with 250 mg intramuscular injection and 1g of azithromycin orally, CT infections were treated with 1g azithromycin orally and TV with 400mg metronidazole 2 times a day for a week. Each participant also collected a second vaginal swab which was frozen and stored. Women who were found to be positive for any STI were also counselled on the importance of testing and asked to notify their partner with a referral letter to attend the clinic for STI treatment. Data on HIV status was determined from maternal health records based on rapid HIV antibody testing administered at women's first ANC visit as part of routine care. We purposefully over-recruited pregnant WLHIV to achieve 50/50 ratio of WLHIV to those who are HIV uninfected. Interviewers entered the data into a tablet during the interview using Research Electronic Data Capture (REDCap).

Statistical Analysis

We used univariate and bivariate analyses to describe participant characteristics. We used medians and interquartile ranges to describe continuous data, and frequencies and percentages to present categorical variables. We present unadjusted and adjusted odds ratios, and 95% confidence intervals adjusted for *a priori* confounders including gestational age, maternal age, and relationship status for all models except the relationship status model. In order to understand the relationship between the variables and reduce bias in our models we created directed acyclic graphs (DAGs). We used a logistic regression model to investigate the association between relationship status, intimate partner violence and STIs. All data analyses were performed in STATA v14 (StataCorp. 2015).

Ethical considerations

Authorisation to conduct the study was provided by the Faculty of Health Science Human Research Ethics Committee at the University of Cape Town (#454/2017) in partnership with University of California Los Angeles (#19-000237). A written informed consent form was reviewed and signed by all participants before being enrolled in the study.

Results

Population characteristics of pregnant women attending first antenatal visit

A total of 242 pregnant women were enrolled at first ANC visit. The median age was 29 years (IQR= 24-34 years); median gestational age was 19 weeks (IQR= 14-24 weeks) at enrolment. Overall, 48% of the participants reported being married or cohabiting with the father of the unborn baby. Half of the participants reported being unmarried and/or not cohabitating with the father of the unborn baby, and approximately 3% of the participants reported to have no relationship with the father of the unborn baby. Almost half (47%) were HIV infected at their first ANC (n=107), and 33% of them reported being newly diagnosed with HIV (n=35). Most participants reported vaginal sex during pregnancy (93%, n=225). Overall, 3% of women reported that they have experienced IPV during the past year (n=8), and 2% reported experiencing IPV during pregnancy. Almost a third of pregnant women in the study were diagnosed with an STI (n=78, 32%). The most common infection that we diagnosed was CT (20%) followed by TV (15%) then NG (6%) (Table 1).

Relationship quality during and prior to pregnancy

Almost all women in the study reported having a partner and being in a relationship (n=235, 97%), but fewer than half were married or cohabiting with their partner. Approximately three-fourths of women (78%) reported being very satisfied with their sexual relationships, and that their partner met the original expectations of the relationship (n=181, 77%). Overall, 77% of women also indicated that their partners met their needs in the relationship (n=181). Most women (80%) reported that their relationships are good compared to most relationships (n=193). And 84% of women reported that they do not wish to be in any

other relationship (n=204). Finally, 88% of the women reported that they love their partners very much (n=211), and 70% of them reported that they are little to no problems in the relationship (n=167) (Table 1).

Table 1: Demographic, relationship factors and behavioural characteristics of pregnant women attending first antenatal visit, Cape Town, November 2017- July 2018 (n=242)

Characteristic	n=242	%
Age		
Maternal age in years (Med, IQR)	29	(24-34)
Gestational age in weeks (Med, IQR)	19	(14-24)
Relationship status with the partner		
Married/cohabiting	115	47.5%
Not married and not cohabiting	120	49.5%
No relationship	7	3%
HIV status		
Negative	135	56%
Positive	107	44%
STI diagnosis in study		
STI Negative	164	68%
STI Positive (any)	78	32%
CT	49	20%
NG	14	6%
TV	37	15%
How well does your partner meet your needs?		
Very low	5	2%
Low	7	3%
Medium	42	17%
High	43	18%
Very High	138	57%
Do not have a partner	7	3%
How satisfied are you with your relationship?		
Very low	6	2%
Low	9	4%
Medium	30	12%
High	42	17%
Very High	148	61%
Do not have a partner	7	3%
How good is your relationship compared to most?		
Very low	6	2%
Low	6	2%
Medium	30	12%
High	48	20%
Very High	145	60%
Do not have a partner	7	3%
How often do you wish you had not been into this relationship?		
Very low	186	77%

Low	18	7%
Medium	11	5%
High	7	3%
Very High	13	5%
Do not have a partner	7	3%
To what extent has your relationship met your original expectations?		
Very low	11	5%
Low	5	2%
Medium	31	13%
High	41	17%
Very High	147	61%
Do not have a partner	7	3%
How much do you love your partner?		
Very low	6	2%
Low	4	2%
Medium	14	6%
High	23	10%
Very High	188	78%
Do not have a partner	7	3%
How many problems are there in your relationship?		
Very low	145	60%
Low	25	10%
Medium	40	17%
High	7	3%
Very High	17	7%
Do not have a partner	7	3%
Has your partner insulted/hurt you in the 12 months before pregnancy?		
No	235	97%
Yes	7	3%
Has your partner insulted you, humiliated you, after finding out you were pregnant?		
No	233	98%
Yes	4	2%
How often did partner abuse happen?		
More than 3 times	4	100%
Has your partner physically hurt you or used a weapon in the 12 months before pregnancy?		
No	237	98%
Yes	5	2%
Has your partner physically hurt you after finding out you pregnant?		
No	234	99%
Yes	3	1%
How often did it happen?		
1 time	1	33%
2 times	1	33%
3 times	1	33%

Data are n (%) or mean (95% CI). IQR- interquartile range. *n=242. n=5 missing responses for women who reported being insulted or humiliated by their partner. N=5 missing responses for women who experienced IPV during pregnancy.

Relationship factors associated with STIs at first ANC visit

We evaluated if any relationship factors were associated with STI diagnosis (CT, NG and/or TV) in pregnant women attending their first ANC visit. We found that being unmarried and/or not cohabiting with the father of the baby was associated with increased odds of STIs diagnosis in crude analysis (OR=2.10, 95% CI= 1.19-3.70), which persisted when we adjusted for maternal age and gestational age (aOR=1.92, 95% CI=1.06- 3.48) (Table 2). Women who reported that their partner meets their needs had lower odds of having an STI compared to those who reported that needs were not met (OR = 0.31, 95% CI: 0.09-1.00), however, when adjusted for age and relationship status the association attenuates (aOR= 0.39, 95% CI: 0.11-1.36). We did not find an association between women's reported relationship satisfaction and STI diagnosis. Relationship quality was also not associated with acquiring an STI. No association was found between IPV and STI diagnosis (OR=2.16, 95% CI= 0.55-3.62), including after adjusting for maternal age, gestational age, and relationship status (aOR=2.41, 95% CI=0.55-10.45).

Table 2: Factors associated with sexually transmitted infection diagnosis in pregnant women attending first antenatal care visit (n = 242), Cape Town.

	Total	**STI detected (n, %)**	**No STI detected (n, %)**	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
Total	242 (100%)	78 (32%)	164 (68%)		
Age					
Maternal age in years (Med, IQR)	**29 (24-34)**	**28 (24-33)**	**30 (25-35)**	**0.95 (0.91-1.00)**	
Gestational age in weeks (Med, IQR)	19 (13-24)	20(14-24)	18(13-23)	1.03 (0.98- 1.08)	
Relationship status with the partner					
Married/cohabiting	115 (48)	27 (35)	88 (54)		
Not married and not cohabiting	**120 (50)**	**47 (60)**	**73 (45)**	**2.10 (1.19-3.70)**	**1.92 (1.06-3.48) ***
No relationship	7 (3)	4 (5)	3 (2)	4.35 (0.92-20.64)	3.80 (0.79-18.23) *
HIV status					
Negative	135 (56)	37 (47)	98 (60)		
Positive	107 (44)	41 (53)	66 (40)	1.64 (0.96-2.83)	**1.97 (1.07-3.62) ***
Ever experienced IPV					
No	234 (97)	74 (95)	160 (98)		
Yes	8 (3)	4 (5)	4 (2)	2.16 (0.52-8.88)	2.41 (0.55-10.45) *
IPV during pregnancy					
No	234 (99)	74 (99)	160 (99)		
Yes	3 (1)	1 (1)	2 (1)	1.08 (0.10-12.11)	1.30 (0.11-15.52) *

Relationship quality					
Low	17 (7)	7 (9)	10 (6)		
High	225(9)	71 (91)	154 (94)	0.66 (0.24-1.80)	0.72 (0.25-2.03)
How well does your partner meet your needs					
Low	12 (5)	7 (9)	5 (3)		
High	223 (95)	**67 (91)**	**156 (97)**	**0.31 (0.09-1.00)**	**0.27 (0.082-0.91)** ¥
How satisfied are you with your relationship?					
Low	15 (6)	6 (8)	9(5)		
High	220 (94)	68 (92)	158 (95)	0.67 (0.23-1.96)	0.85 (0.28-2.59) *
How good is your relationship compared to most?					
Low	12 (5)	5 (7)	7 (4)		
High	223 (95)	69 (93)	154 (96)	0.62 (0.19-2.05)	0.92 (0.27-3.14) *
How often do you wish you had not been into this relationship?					
Low (Not Often)	204 (87)	64 (86)	140 (87)		
High (very often)	31 (13)	10 (14)	21 (13)	1.04 (0.46-2.34)	0.81 (0.35-1.89) *
To what extent has your relationship met your original expectations?					
Low	16 (7)	6 (8)	10 (6)		
High	219 (93)	68 (92)	151 (94)	0.75 (0.26-2.15)	0.98 (0.33-2.89) *
How much do you love your partner?					
Low	10 (4)	4 (5)	6 (4)		
High	225 (96)	70 (95)	155 (96)	0.68 (0.19-2.48)	0.80 (0.21-3.08) *
How many problems are there in your relationship?					
Low	170 (73)	53 (72)	117 (73)		
High	64 (27)	21 (28)	43 (27)	1.08(0.58-1.99)	0.98(0.52-1.85) *

Confidence intervals in bold symbolises statistical significance.
*Model adjusted for maternal age, gestational age and relationship status.
¥ Model adjusted for age

Factors associated with IPV at first ANC

Reported recent IPV was associated with decreased odds in women who reported being in a relationship that meets their needs adjusting for maternal age, gestational age and relationship status (aOR=0.081, 95% CI: 0.01-0.53). IPV was also independently associated with women who reported being satisfied with their relationship adjusting for maternal age, gestational age and relationship status (aOR=0.073, 95% CI: 0.011-0.46). Women who reported having less problems in their relationship were associated with decreased odds of experiencing IPV adjusting for age and relationship status (aOR = 0.32, 95% CI: 0.16-0.63). Women who reported loving their partner were also associated with decreased odds of experiencing IPV (aOR=0.09, 95% CI: 0.015-0.48). IPV was also associated with decreased odds in women who reported not wishing to be in

another relationship (aOR=0.41, 95% CI: 0.24-0.69). There was no association detected between relationship expectations and IPV. (Table 3)

Table 3: Factors associated with intimate partner violence during pregnancy in pregnant women attending first antenatal care visit (n = 242), Cape Town.

	Total	**IPV (n, %)**	**No IPV (n, %)**	**Odds ratio (95% CI)**	**Adjusted** OR (95% CI)
	242 (100%)	8 (3%)	234 (97%)		
Age					
Maternal age in years (Med, IQR)	29 (24-34)	30 (24-37)	29 (18-45)	1.00 (0.89-1.13)	
Gestational age in weeks (Med, IQR)	19 (13-24)	17 (12-25)	19 (14-24)	0.99 (0.88-1.11)	
Relationship status with the partner					
Married/cohabitating	115 (48)	5 (71%)	115 (49%)		
Not married and not cohabitating	120 (50)	2 (29%)	120 (51%)	0.35 (0.07-1.78)	
HIV status					
Negative	135 (56)	3 (43)	132 (56)		
Positive	107 (44)	5 (57)	102 (44)	2.16 (0.37-7.80)	2.37 (0.50-11.31) *€
How well does your partner meet your needs					
Low	54 (23)	4 (67)	50 (22)		
High	181 (77)	**2 (33)**	**179 (78)**	**0.14 (0.35-0.79)**	**0.081 (0.01-0.53) *¥**
How satisfied are you with your relationship?					
Low	45 (19)	4 (67)	41 (18)		
High	190 (81)	**2 (33)**	**188 (82)**	**0.11 (0.019-0.62)**	**0.07 (0.01-0.46) *¥**
How good is your relationship compared to most?					
Low	45 (19)	4 (67)	38 (17)		
High	190 (81)	**2 (33)**	**191 (83)**	**0.10 (0.02-0.56)**	**0.07 (0.01-0.43) *¥**
How often do you wish you had not been into this relationship?					
Low	215 (91)	3 (50)	212 (93)		
High	**20 (9)**	**3 (50)**	**17 (7)**	**0.47 (0.29-0.76)**	**0.41 (0.24-0.69) *¥**
To what extent has your relationship meet your original expectations?					
Low	47 (20)	3 (50)	44 (19)		
High	188 (80)	3 (50)	185 (81)	0.24 (0.05-1.22)	0.18 (0.03-1.03) *¥
How much do you love your partner?					
Low	24 (10)	3 (50)	21 (9)		
High	211 (90)	**3 (50)**	**208 (91)**	**0.10 (0.019-0.53)**	**0.09 (0.02-0.48) *¥**
How many problems are there in your relationship?					
Low	210 (90)	2 (33)	208 (91)		
High	**24 (10)**	**4 (67)**	**20 (9)**	**0.35 (0.19-0.66)**	**0.32 (0.16-0.63) *¥**
Relationship quality					
Low	17 (7)	2 (29)	15 (6)		
High	225 (93)	5 (71)	220 (94)	**0.17 (0.03-0.95)**	**0.11 (0.017-0.073) *€**

Confidence intervals in bold had p<0.05.
*Model adjusted for maternal age, gestational age and relationship status
¥ n=2 missing responses
€ n=1 missing response

Discussion

Our study investigated the association between relationship quality, intimate partner violence and STIs among pregnant WLHIV and women without HIV attending antenatal care in a public clinic in Cape Town, South Africa. Overall, one third of the women screened at first ANC visit were diagnosed with a positive STI (CT, NG and/or TV). Pregnant WLHIV and women who were unmarried and/or not cohabiting had increased odds of STI diagnosis. Relationship quality was not associated with STI acquisition, however women who reported that their needs were met had decreased odds of STI acquisition. Women in the study reported low IPV experiences prior to and during pregnancy. Women with a higher reported relationship quality had decreased odds of experiencing IPV. However, STI diagnosis was not associated with experiencing IPV.

Our study found a high STI prevalence (37%) in both pregnant WLHIV and women without HIV women attending their first antenatal visit at a public clinic in Cape Town. These findings are similar to results found in other studies of pregnant women in other sub-Saharan African countries [11, 23, 24]. Our study had low reporting of IPV victimization during pregnancy (3%), which is different from a study conducted among adolescent mothers in Durban which found that 41% of pregnant women experienced IPV [25], this may suggest that IPV is more prevalent in younger women. Furthermore, our low reporting of IPV during pregnancy (3%) was also vastly different to IPV prevalence estimates of similar studies conducted in sub-Saharan Africa (20%-38%) [26-32]. These reports of IPV during pregnancy are a public health concern especially in low-middle income countries. IPV during pregnancy was not associated with STI (CT, NG and/or TV) diagnosis, and this finding is inconsistent with other studies done in a similar setting which found an association between IPV and STI risk [18,25,29 & 33-36]. Our findings also confirm that HIV was significantly associated with STI acquisition [18,25,26,33 & 37].

In terms of prevention implications, our study strengthens evidence for an increase in STI testing and treatment especially in vulnerable populations. Given the impact of HIV infection in young women across South Africa [38], HIV prevention interventions that aim to reduce STI acquisition in women are necessary, and the inclusion of discussions about IPV in HIV counselling and testing programs. The low level of IPV

reported in our study during pregnancy warrants for better measures of reporting IPV to reduce biases (i.e. underreporting, social desirability and recall bias). Additionally, more research is needed to replicate findings, and the development of better antenatal IPV screening protocols that allow for a better identification of women experiencing different patterns of IPV and provide support and services. Furthermore, study findings show that women who experienced IPV reported a low relationship quality, thus when considering future interventions, it is important to implement strategies or treatments that can target both partners in the relationship, with the intention of minimizing IPV in relationships and improve the quality of relationship.

Strengths of this study are the inclusion of data on three forms of violence (physical, verbal and sexual) and relevant confounders and mediators. HIV and other STI testing were done and captured in real time at the facility. However, these findings should be considered in light of several limitations. This study relies heavily on self-reporting data for IPV, which is subject to several biases that include recall bias and interviewer bias. Underreporting of IPV is very likely due to social desirability biases. Our research only accounted for recent IPV experiences with current partner. More research is needed to explore association between sexual health of couples and both past and current IPV experiences, as past experiences of IPV may impact current health behaviours. The data was only collected from one health facility which may affect generalizability to other populations. However, the setting was similar to others within neighbouring regions and the country. The study has a small sample size which limits our results and makes it difficult to identify associations or relationships from the data. Additionally, the lack of data from male partners prevents us from understanding some of the partner behaviours that may contribute to IPV perpetration and STI acquisition.

This present study is one of the first studies to examine the association between relationship quality, IPV and STI in pregnant women living and not living with HIV in South Africa. Although it remains unclear whether IPV is associated with HIV and STI acquisition, the data does demonstrate potential IPV underreporting, and that there is need for additional research with a larger sample size and different settings in order to investigate the true relationship between these variables.

In conclusion, we found a high prevalence of curable STIs during pregnancy in pregnant women. Women who were living with HIV, and/or unmarried, not cohabiting had increased odds of having an STI at first ANC visit. Self-reported IPV during pregnancy was not associated with STI diagnosis, but relationship quality was associated with reporting IPV. Future studies with new measures of IPV are needed to investigate the relationship between IPV and STIs in pregnancy.

References

1. World Health Organization. Global health sector strategy on sexually transmitted infections 2016-2021: toward ending STIs. World Health Organization; 2016.

2. Newman L, Rowley J, Vander Hoorn S, Wijesooriya NS, Unemo M, Low N, Stevens G, Gottlieb S, Kiarie J, Temmerman M. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. PloS one. 2015;10(12).

3. Davey DJ, Shull HI, Billings JD, Wang D, Adachi K, Klausner JD. Prevalence of curable sexually transmitted infections in pregnant women in low-and middle-income countries from 2010 to 2015: a systematic review. Sexually transmitted diseases. 2016 Jul;43(7):450.

4. Wangnapi RA, Soso S, Unger HW, Sawera C, Ome M, Umbers AJ, Ndrewei N, Siba P, Suen CL, Vallely A, Wapling J. Prevalence and risk factors for Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis infection in pregnant women in Papua New Guinea. Sex Transm Infect. 2015 May 1;91(3):194-200.

5. Adachi K, Nielsen-Saines K, Klausner JD. Chlamydia trachomatis infection in pregnancy: the global challenge of preventing adverse pregnancy and infant outcomes in Sub-Saharan Africa and Asia. BioMed research international. 2016;2016.

6. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. The Lancet. 1998 Jun 1;351:S5-7.

7. Masson L, Mlisana K, Little F, Werner L, Mkhize NN, Ronacher K, Gamieldien H, Williamson C, Mckinnon LR, Walzl G, Karim QA. Defining genital tract cytokine signatures of sexually transmitted infections and bacterial vaginosis in women at high risk of HIV infection: a cross-sectional study. Sexually transmitted infections. 2014 Dec 1;90(8):580-7.

8. Wasserheit JN. Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. Sexually transmitted diseases. 1992;19(2):61-77.

9. C King C, R Ellington S, P Kourtis A. The role of co-infections in mother-to-child transmission of HIV. Current HIV research. 2013 Jan 1;11(1):10-23.

10. Adachi K, Xu J, Yeganeh N, Camarca M, Morgado MG, Watts DH, Mofenson LM, Veloso VG, Pilotto JH, Joao E, Gray G. Combined evaluation of sexually transmitted infections in HIV-infected pregnant women and infant HIV transmission. PloS one. 2018;13(1).

11. Mudau M, Peters RP, De Vos L, Olivier DH, J Davey D, Mkwanazi ES, McIntyre JA, Klausner JD, Medina-Marino A. High prevalence of asymptomatic sexually transmitted infections among human immunodeficiency virus-infected pregnant women in a low-income South African community. International journal of STD & AIDS. 2018 Mar;29(4):324-33.

12. Wynn A, Ramogola-Masire D, Gaolebale P, Moshashane N, Sickboy O, Duque S, Williams E, Doherty K, Klausner JD, Morroni C. Prevalence and treatment outcomes of routine Chlamydia trachomatis, Neisseria gonorrhoeae and Trichomonas vaginalis testing during antenatal care, Gaborone, Botswana. Sex Transm Infect. 2018 May 1;94(3):230-5.

13. Davey DL, Nyemba DC, Gomba Y, Bekker LG, Taleghani S, DiTullio DJ, Shabsovich D, Gorbach PM, Coates TJ, Klausner JD, Myer L. Prevalence and correlates of sexually transmitted infections in pregnancy in HIV-infected and-uninfected women in Cape Town, South Africa. PloS one. 2019;14(7).

14. Johnson HL, Ghanem KG, Zenilman JM, Erbelding EJ. Sexually transmitted infections and adverse pregnancy outcomes among women attending inner city public sexually transmitted diseases clinics. Sexually transmitted diseases. 2011 Mar 1;38(3):167-71.

15. Coker AL. Does physical intimate partner violence affect sexual health? A systematic review. Trauma, Violence, & Abuse. 2007 Apr;8(2):149-77.

16. Hess KL, Javanbakht M, Brown JM, Weiss RE, Hsu P, Gorbach PM. Intimate partner violence and sexually transmitted infections among young adult women. Sexually transmitted diseases. 2012 May;39(5).

17. Allsworth JE, Anand M, Redding CA, Peipert JF. Physical and sexual violence and incident sexually transmitted infections. Journal of Women's Health. 2009 Apr 1;18(4):529-34.

18. Jewkes RK, Dunkle K, Nduna M, Shai N. Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. The lancet. 2010 Jul 3;376(9734):41-8.

19. Jewkes R, Dunkle K, Nduna M, Levin J, Jama N, Khuzwayo N, Koss M, Puren A, Duvvury N. Factors associated with HIV sero-status in young rural South African women: connections between intimate partner violence and HIV. International journal of epidemiology. 2006 Dec 1;35(6):1461-8.

20. Maman S, Campbell J, Sweat MD, Gielen AC. The intersections of HIV and violence: directions for future research and interventions. Social science & medicine. 2000 Feb 1;50(4):459-78.

21. Davey DL, Nyemba DC, Gomba Y, Bekker LG, Taleghani S, DiTullio DJ, Shabsovich D, Gorbach PM, Coates TJ, Klausner JD, Myer L. Prevalence and correlates of sexually transmitted infections in pregnancy in HIV-infected and-uninfected women in Cape Town, South Africa. PloS one. 2019;14(7).

22. Department of Health, Republic of South Africa. Sexually Transmitted Infection Management Guidelines 2015. Pretoria: Department of Health, Republic of South Africa 2015. Health SANDo. "Sexually Transmitted Infections Management Guidelines." 2015. Shrier, Ian, and Robert W. Platt. "Reducing bias through directed acyclic graphs." BMC medical research methodology 8.1 (2008): 70.

23. Mayaud P, Grosskurth H, Changalucha J, Todd J, West B, Gabone R, Senkoro K, Rusizoka M, Laga M, Hayes R. Risk assessment and other screening options for gonorrhoea and chlamydial infections in women attending rural Tanzanian antenatal clinics. Bulletin of the World Health Organization. 1995;73(5):621.

24. Davey, D.J., Shull, H.I., Billings, J.D., Wang, D., Adachi, K. and Klausner, J.D., 2016. Prevalence of curable sexually transmitted infections in pregnant women in low-and middle-income countries from 2010 to 2015: a systematic review. Sexually transmitted diseases, 43(7), p.450.

25. Gebrekristos LT, Groves AK, McNaughton Reyes L, Maman S, Moodley D. IPV victimization in pregnancy increases postpartum STI incidence among adolescent mothers in Durban, South Africa. AIDS care.2020 May 13;32(sup2):193-7.

26. Bernstein M, Phillips T, Zerbe A, McIntyre JA, Brittain K, Petro G, Abrams EJ, Myer L. Intimate partner violence experienced by HIV-infected pregnant women in South Africa: a cross-sectional study. BMJ open. 2016 Aug 1;6(8).

27. Groves AK, Kagee A, Maman S, Moodley D, Rouse P. Associations between intimate partner violence and emotional distress among pregnant women in Durban, South Africa. Journal of interpersonal violence. 2012 May;27(7):1341-56.

28. Ikeako LC, Nnagbo JE, Ezegwui HU, Chigbu C, Enebe T, Umeh UA, Ajah L. Prevalence and predictors of intimate partner violence among antenatal clinic attendees in a tertiary health institution in Nigeria. Journal of Advances in Medicine and Medical Research. 2017 Jan 2:1-8.

29. Kouyoumdjian FG, Calzavara LM, Bondy SJ, O'campo P, Serwadda D, Nalugoda F, Kagaayi J, Kigozi G, Wawer M, Gray R. Intimate partner violence is associated with incident HIV infection in women in Uganda. Aids. 2013 May 15;27(8):1331-8.

30. Makayoto LA, Omolo J, Kamweya AM, Harder VS, Mutai J. Prevalence and associated factors of intimate partner violence among pregnant women attending Kisumu District Hospital, Kenya. Maternal and child health journal. 2013 Apr 1;17(3):441-7.

31. Mbokota M, Moodley J. Domestic abuse-an antenatal survey at King Edward VIII Hospital, Durban. South African Medical Journal. 2003;93(6):455-7.

32. Reyes HL, Maman S, Groves AK, Moodley D, Chen MS. A longitudinal study of the relationship between intimate partner violence and postpartum unsafe sex among newly diagnosed HIV-infected South African women. AIDS care. 2019 Jun 3;31(6):707-13.

33. Li Y, Marshall CM, Rees HC, Nunez A, Ezeanolue EE, Ehiri JE. Intimate partner violence and HIV infection among women: a systematic review and meta-analysis. Journal of the international AIDS society. 2014 Jan;17(1):18845.

34. Shamu S, Abrahams N, Zarowsky C, Shefer T, Temmerman M. Intimate partner violence during pregnancy in Z imbabwe: a cross-sectional study of prevalence, predictors and associations with HIV. Tropical Medicine & International Health. 2013 Jun;18(6):696-711.

35. Willie TC, Callands TA, Kershaw TS. Intimate partner violence, sexual autonomy and postpartum STD prevention among young couples: A mediation analysis. Perspectives on sexual and reproductive health. 2018 Mar;50(1):25-32.

36. Decker MR, Miller E, McCauley HL, Tancredi DJ, Anderson H, Levenson RR, Silverman JG. Recent partner violence and sexual and drug related STI/HIV risk among adolescent and young adult women attending family planning clinics. Sexually transmitted infections. 2014 Mar 1;90(2):145-9.

37. Dunkle KL, Jewkes RK, Brown HC, Gray GE, McIntryre JA, Harlow SD. Gender-based violence, relationship power, and risk of HIV infection in women attending antenatal clinics in South Africa. The lancet. 2004 May 1;363(9419):1415-21.

38. Global HIV. AIDS statistics–2019 fact sheet (2019).

PART C: Appendices

Acknowledgements

I would like to extend my sincere gratitude to the following individuals and groups:

Dr Dvora Joseph Davey- my UCT Thesis supervisor for always being supportive and encouraging, thank you for always responding expeditiously to my emails and questions, and always giving great suggestions. Her guidance helped me in all the time of this research and writing of this dissertation.

Centre for Infectious Disease and Epidemiological Research (CIDER), University of Cape Town– Green clinic staff, and particularly; Yolanda Gomba and Snowy Mocha for the on the ground details and support with any information I needed.

Dorothy Nyemba- For always supporting and giving me advice throughout this process. Thank you for your valuable guidance and support in completion of this project.

Sandisiwe and Sinazo Noholoza - for the love, laughter, and support.

Rufaro Mvududu- for always dedicated your time and giving me useful advice and support. Thank your sharing your knowledge and words of wisdom.

I also acknowledge my parents; Zoliswa Qayiya and Sonwabo Ngqengqa, and my aunt; Vuyelwa Grey for the love, support, and encouragements. My sisters: Akhanye Qayiya and Nosipho Bukuqekile for the encouragement and love, none of this is possible without you.

My thankfulness is also to the staff of the Division of Epidemiology and Biostatistics, Faculty of Health Sciences, University of Cape Town, especially Prof Landon Myer and Prof Maia Lesosky for their support.

Any omission in this brief acknowledgement does not mean lack of gratitude.

Thank you.

Appendix A: Sexual Transmitted Infections Addendum Case Report Form (ENGLISH)

Questions applicable to this project: Section A, C and D

STI Addendum CRF (ENGLISH)

To be completed by **ALL** enrolled STIP participants

Patient ID _____

Visit Code _____

Visit Date							
D	D	M	M	Y	Y	Y	Y

We are now going to ask you some questions about your sex life. There are no right or wrong answers, please tell us about your personal experience.

A: Recent Sexual History	
1. How many sex partners have you had within the last three months?	_____
2. How many sex partners do you have <u>now</u>?	_____ ***If 0 partners* -> SKIP to Q4**
3. What is your relationship status with the father of your child?	1. Married, living together 2. Married, not living together 3. Not married, living together 4. Not married, not living together
4. Is your <u>most recent</u> sex partner the father of your child?	1. Yes 2. No 3. Don't Know/Unsure
5. Have you had vaginal sex during pregnancy?	1. Yes 2. No
6. Have you had anal sex (when a man puts his penis in your anus) during pregnancy?	1. Yes 2. No
7. Have you had oral sex during pregnancy? Where you put your mouth on his penis?	1. Yes 2. No
8. Do you suspect your partner has other sex partners?	1. Yes 2. No 3. Don't know/Unsure
9. Is/was your partner's HIV status different from yours?	1. Yes 2. No 3. Don't know/Unsure

B: Knowledge, Attitudes, and Preferences regarding STIs	
***Interviewer read**: "I am now going to ask you some questions about sexually transmitted infections or STIs."*	
During this pregnancy have you had:	1. Yes

10. Abnormal vaginal discharge (green, yellow, foul-smelling)	2. No 3. Don't know/unsure
11. Increased pain during intercourse	1. Yes 2. No 3. Don't know/unsure
12. Pain during urination	1. Yes 2. No 3. Don't know/unsure
13. Vaginal bleeding	1. Yes 2. No 3. Don't know/unsure
14. Genital sores	1. Yes 2. No 3. Don't know/unsure
If no to questions 10-14, skip to Q21	
15. How many days or weeks ago did the symptoms start?	1. <1 week ago 2. 1-2 weeks ago 3. 3-4 weeks ago 4. More than a month ago 5. Don't know/unsure
16. Have you received treatment for the symptoms?	1. Yes 2. No ->**SKIP to Q18**
17. If yes, what kind?	☐ Bactrim ☐ Other: _____
18. Did you notify your partner(s) of your symptoms?	1. Yes 2. No **-> SKIP to Q21**
19. What was your partner(s)' reaction when you notified them?	☐ 1. Willing to get tested or treated ☐ 2. Worried ☐ 3. Angry ☐ 4. Did not believe results ☐ 5. No reaction ☐ 6. Other _____

20. Did your partner(s) receive treatment?	1. Yes No 2. 3. Don't know/Unsure (Probe if treatment is related to treatment received by participant)
21. Before this pregnancy, have you ever been told you have an STI by a healthcare professional?	1. Yes 2. No -> **SKIP to Q27** 3. Don't know/unsure -> **SKIP to Q26**
22. When were you told you had an STI?	1. Less than 12 months ago 2. More than 12 months ago 3. Don't know/unsure
23. Did you receive treatment?	1. Yes **-> SKIP to Q25** 2. No

24. If no, why not?	1. I didn't want to 2. I could not afford it 3. My healthcare provider didn't offer me treatment 4. I was scared to ask my healthcare provider about my symptoms 5. Other _____ ➔ **SKIP to Q26**
25. What were you treated for (check all that apply)?	***(Prompt)*** 1. □ Abnormal vaginal discharge (green, yellow, foul-smelling) 2. □ Increased pain during intercourse 3. □ Pain during urination 4. □ Vaginal bleeding 5. □ Genital sores 6. □ Syphilis 7. □ Other _____ 8. □ Don't recall

26. If you were found to have an STI, what would be your MOST IMPORTANT concern (select one)?	**(Do NOT prompt)** 1. Relieved to get it treated 2. Worried about my partner's reaction 3. Concerned about my partner's fidelity 4. Guilty 5. Worried about my health 6. Worried about my baby's health
27. If you were told you have an STI, who would be the FIRST PERSON who you would tell (select one)?	**(Do NOT prompt)** 1. I would not tell anyone 2. Partner 3. Family member 4. Friend 5. Healthcare worker 6. Teacher 7. Religious leader 8. Traditional healer 9. Spiritual healer
28. If you were told you have an STI, would you believe the result if you didn't feel/see any signs and symptoms?	**(Probe, but do not prompt)** 1. Yes, I understand I could have an STI but not feel the symptoms 2. No, I would not trust the result, I would not take the treatment 3. No, I would not trust the result, but I would still take the treatment
29. Would you notify your partner if you tested positive for an STI in this study?	1. 2. Yes 3. No Not sure yet
30. Do you think your partner would be willing to take medication if you tested positive for an STI in this study?	1. 2. Yes ->**SKIP to Q32** 3. No Don't know/Unsure ->**SKIP to Q32**
31. If no, why do you think your partner would not want to get treated for an STI?	**(Do NOT prompt)** 1. He/she doesn't have time 2. He/she doesn't live close by 3. He/she doesn't like taking medication 4. Other _____
32. How would you prefer a vaginal swab to be taken (select one response)?	1. 2. I would prefer to do it myself I would prefer a nurse to do it for me

	3. Either myself or a nurse can do it 4. I don't want to use a swab at all
33. Will you be able to wait in the clinic today to hear your results? This will take 60 minutes.	1. Yes **->SKIP to NEXT SECTION** 2. No
34. If no, why not?	1. I don't want to stay at the clinic that long 2. I have things I need to do 3. Other _____
35. How would you prefer to receive your results?	1. In person Phone 2. call 3. SMS/WhatsApp 4. Email 5. Other _____
36. Would you only like to receive your results if the results mean you will need to receive medical treatment?	1. 2. Yes 3. No Not sure

We are now going to ask you some questions about your relationship with your partner. Your answers will remain confidential from your partner, but if you feel uncomfortable answering any of these questions notify the study nurse.

C: RELATIONSHIP ASSESSMENT SCALE

On a scale from 1, which is low, to 5, that is high please answer the following questions:	Low				High
37. How well does your partner meet your needs?	1	2	3	4	5
38. In general, how satisfied are you with your relationship?	1	2	3	4	5
39. How good is your relationship compared to most?	1	2	3	4	5
40. How often do you wish you hadn't gotten into this relationship?	1	2	3	4	5
41. To what extent has your relationship met your original expectations?	1	2	3	4	5
42. How much do you love your partner?	1	2	3	4	5

43. How many problems are there in your relationship?	1	2	3	4	5

Hendrick, S. S. (1988). A generic measure of relationship satisfaction. *Journal of Marriage and the Family, 50,* 93–98.

These next set of questions ask about cases of intimate partner violence. If you feel uncomfortable by any of these questions, please notify the study nurse.

D: Intimate Partner Violence Questionnaire

	Q1. During the past 12 months before you became pregnant	Q2. Since you confirmed that you were pregnant	Q3. After you informed your partner of your STI result during the current pregnancy	Q4. During the current pregnancy, would you say this has happened once, twice, three times or more?
*has your **current** husband/partner ever….*				
1. insulted you, humiliated you, or threatened to hurt you?	44. 1. Yes 2. No	45. 1. Yes 2. No	46. 1. Yes 2. No	47. 1. 1 time 2. 2 times 3. 3 times 4. more than 3 times
hurt you physically (i.e. pushing, shoving, hitting, kicking) or used a weapon against you?	48. 1. Yes 2. No	49. 1. Yes 2. No	50. 1. Yes 2. No	51. 1. 1 time 2. 2 times 3. 3 times 4. more than 3 times
physically forced you to have sexual intercourse when you did not want to?	52. 1. Yes 2. No	53. 1. Yes 2. No	54. 1. Yes 2. No	55. 1. 1 time 2. 2 times 3. 3 times 4. more than 3 times

prohibited you from working or took your earnings if you had any income?	56. 1. Yes 2. No	57. 1. Yes 2. No	58. 1. Yes 2. No	59. 1. 1 time 2. 2 times 3. 3 times 4. more than 3 times

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

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

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

(To be completed <u>ONLY</u> at visits B and P <u>for STI-positive women</u>)

Visit Code _____ Patient ID _____

Date (DD/MM/YYYY) _____

We are going to ask you some questions about the notification letter we gave you at the last visit. Your answers will remain confidential and we encourage you to answer all the questions, but if any question makes you uncomfortable please notify the study nurse.

1. How many sex partners did you report during the last STIP study visit?	1. One 2. More than one: *complete additional questionnaire for each partner* 3. None: *end interview*
2. Did you give your partner(s) the notification letter within 7 days of your clinic visit?	1. Yes → *skip to #4* 2. No
3. If no, why not?	1. Partner was not home 2. Partner does not live clo se by 3. Partner does not have time 4. I did not think it was important 5. I misplaced the paper 6. I was afraid he will blame me 7. I was afraid of anger or abuse 8. I do not have a relationship with him 9. Other _____ → *skip to #11*
4. What was your most important motivation for notifying your partner?	1. 2. Health of the baby Health of my partner

	3. My own health 4. Because the clinic staff recommended it 5. Other _____
5. What was your partner's reaction when you gave him the notification letter?	1. 2. Willing to get tested or treated Worried 3. Angry 4. Did not believe results 5. No reaction 6. Other _____
6. How did your partner treat you after you notified him?	1. Accused me of promiscuity or infidelity 2. Argued or fought with me 3. Refusal of sexual intercourse 4. Violence 5. Other _____
7. Did your partner come to the clinic for treatment to your knowledge?	1. 2. Yes No → *skip to #10* 3. Not sure
8. Did he take the medication to your knowledge?	1. Yes 2. No 3. Don't know/ unsure
9. What do you think was his primary motivation to coming to the clinic for treatment?	1. Health of the baby 2. His health 3. My own health 4. Our health 5. The clinic letter 6. Other _____ 7. Don't know/ unsure
10. What was the most important barrier to your partner's coming in for treatment?	1. Work 2. Transportation 3. Time 4. Embarrassment/shame Hesitant to come to a maternal obstetric ward 5. Other _____ 6. . Don't know/ unsure
11. How would you have preferred to notify your partner if given different options?	***Do not prompt*** 1. Phone call from a health care provider 2. Text message from the clinic 3. Email message from the clinic 4. Give me treatment to give my partner 5. Would not notify

	6. Other _____
12. Would you prefer the notification be anonymous?	1. I would prefer anonymous notification 2. I do not prefer anonymous notification 3. I do not have a preference
13. Who have you told about your STI result (check all that apply)	1. 2. ☐ No one ☐ Partner 3. ☐ Family member 4. ☐ Friend 5. ☐ Healthcare worker 6. ☐ Teacher 7. ☐ Religious leader 8. ☐ Traditional healer 9. ☐ Spiritual healer 10. ☐ Other _____

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

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

Signed Study Coordinator: _____ Date: _____/_____/_____

Appendix B:

Consent Forms

STIP Informed Consent for pregnant women

Version 1.0, 14th July 2017

TITLE OF RESEARCH: Sexually transmitted infections during pregnancy (STIP) in Cape Town: a prospective study

INTRODUCTION:

Good Morning/Afternoon. My name is _____. I work for the University of Cape Town, in Cape Town. We would like to ask you to participate in a study looking at how many pregnant women have sexually transmitted infection (STI) testing in pregnant women. This study is being run by researchers from CIDER, in collaboration with the University of Cape Town, South Africa. We have selected this clinic in Cape Town to recruit study participants, the Gugulethu Midwife Obstetric Unit in Cape Town. Before you decide whether or not you want to take part, I would like to tell you more about this study, what the risks and benefits are to you and your unborn baby, and what would be expected of you. If you agree to participate, I will ask you to sign a form or make your thumb print mark confirming your willingness to participate. I will give you a copy of the signed consent form to keep. Please read it carefully, or if you would rather me read it to you, I can do that as well. Please do not hesitate to ask me any questions.

PURPOSE OF THE STUDY

This study is being conducted to determine how best to provide testing for sexually transmitted infections, specifically Chlamydia trachomatis (Chlamydia), Neisseria gonorrhoeae (gonorrhoeae) and Trichomonas vaginalis, to pregnant women during antenatal care visits in South Africa. The purpose of the study is to look at how best to provide such a testing program, and what the impact might be on mother to child transmission of HIV. The testing of Chlamydia, gonorrhoeae, and Trichomonas Vaginalis infections during pregnancy are not routinely done in South Africa. Typically, only women who have symptoms are tested. As such, unless a pregnant woman has symptoms, they would not be offered treatment. Many women do not have symptoms, so they do not get treated. If you or other pregnant women are infected with Chlamydia, gonorrhoeae or Trichomonas Vaginalis, and are not tested and treated during pregnancy, you might be at risk of having a miscarriage, your unborn baby may not grow and develop properly, you may give birth too early, or your baby might be born underweight.

By taking part in this study you will help us collect data that will inform how to best provide STI testing and treatment programs for pregnant women, and reduce the number of pregnant women infected with STIs.

For you to participate in this study you must be:

1) 18 years old or older,

2) attending your first antenatal care visit for this pregnancy,

3) living in Gugulethu and surrounding areas,

4) planning to give birth in Cape Town,

5) willing to participate in the study.

We will recruit 400 pregnant women that will be tested for Chlamydia, gonorrhoeae, and Trichomonas Vaginalis. If you or any other woman is found to be infected, you will be given treatment for any of the tested for conditions immediately.

DO I HAVE TO PARTICIPATE?

Taking part in this study is voluntary. If you choose not to participate, your care at this clinic will NOT be affected today or in the future. If after you join the study, you decide that you no longer want to be involved, you can speak with one of the nurses or study staff, and we will remove you from our list and not be contacted again. You will be given a copy of this form with a special study number on it that is your study identification number. Please keep this in case you want to withdraw from the study at any time. Again, if you decide you do not want to be involved anymore, the care that the clinic will provide you and your baby will NOT be affected.

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

- The study includes three visits. One today, one in the third trimester (if you are not already in your third trimester today), and a final visit one week after you give birth.

- At each visit, we will ask you to provide three self-collected swabs of your vagina that we can then test for Chlamydia, gonorrhoeae, and Trichomonas Vaginalis infections. If you test positive you will receive treatment on the same day.

o the study nurse will explain to you exactly how to collect a vaginal swab so that we can get the best sample for testing. Also, we will collect some information from your medical file, and our study nurse will ask you some questions.

- We would also like your permission to remove your name and any personal identifying information from your specimen and store any remaining sample for future testing. This future testing may include, but not limited to, looking for other diseases.

- In order to follow you up through a week post-birth, we need to collect several forms of contact information from you. This will include phone number(s), email addresses, and home addresses, for you, family members (including your partners or father of your child), friends, or others that may help us find you if we lose touch. Your participation in each visit may take about 1-2 hours. This will include collecting samples

from you, asking you a few questions, and running the test. If you test positive for Chlamydia, gonorrhoeae, and/or Trichomonas Vaginalis we will immediately give you medication to get rid of your infection.

- If you test positive for an STI, we highly recommend that you return with your partner to the clinic for treatment.

WHAT ARE THE POTENTIAL RISKS?

Taking a swab of your vagina will not harm you in any way. You may experience minor discomfort and possibly mild pain which will last only a few seconds. You are free to stop collecting a specimen for us at any stage. If you are diagnosed with Chlamydia, gonorrhoeae, and/or Trichomonas Vaginalis it may cause some stress for you and your partner(s), because having to tell your partner(s) that you have a sexually transmitted infection can be uncomfortable. If you think your partner(s) will inflict emotional or physical abuse on you as a result of finding out that you have Chlamydia, gonorrhoeae, and/or Trichomonas Vaginalis, please discuss your participation in our study with a member of the study team. We will provide supportive counselling to you and your partner(s) to ensure that you both get the treatment you need to be healthy. We can also refer you for supportive counselling to address any potential problems in your relationship. If problems do arise, we will ask you to contact us at the number below so that we can assist in referring you for additional social services in your area.

You may also receive a false positive in which your result shows that you have a sexually transmitted infection, but in reality you do not. You may also receive a false negative DO NOT have a sexually transmitted infection, but in reality you DO. These cases are very rare and our tests are very reliable. The risk of a false positive is that you take medication that you may not need, or that your partner may inflict emotional or physical abuse on you as a result of finding out your result. If you have a false negative result, you will not get treatment for an infection that you may have which you could transmit to your baby during birth.

WHAT ARE THE BENEFITS?

If you are found to be infected, you and your partner(s) will benefit from receiving treatment. However, if you are NOT infected, there may not be any direct benefit for you, but your participation may help us answer our research questions and help us inform health programs for pregnant women in the future.

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

CONFIDENTIALITY.

Information that will be collected from your medical files and during your interviews with our study nurse will be kept confidential. Only the researchers will be able to see it. We will not tell anyone about your participation, and we will make every effort to protect your privacy and confidentiality. Your name will not be linked to your information. Only the special number we give you will be able to identify you, and only the researchers will know what your number is. We will lock this information up with a lock and key.

CAN I LEAVE THE STUDY?

It is your choice if you want to be in this research study. You can leave the study at any time. Please inform the study staff, or by calling the number below, if you would like to leave the study.

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.

FOR ADDITIONAL INFORMATION:

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

Professor Landon Myer

School of Public Health and Family Medicine

Faculty of Health Sciences, University of Cape Town

Tel: 021 406 6661

Email: Landon.Myer@uct.ac.za

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

Professor Marc Blockman

Chair, Human Research Ethics Committee

Faculty of Health Sciences, UCT

Tel: 021 406 6338

Email: marc.blockman@uct.ac.za

CONSENT FOR STUDY PARTICIPATION (MOTHER)

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 additional component. I know that after choosing to be in this component, I may withdraw at any time. My participation is voluntary. I understand that whether or not I take part 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 (DD/MM/YYYY)

Staff member's name_____

_____

Signature of study staff Date (DD/MM/YYYY)

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 (DD/MM/YYYY): _____

Thank you.

MOTHER'S CONSENT FORM- Participant Copy

1. I have read the patient information sheet, or it has been read to me.
2. I understand the contents of the patient information sheet.
3. I agree to participate in the STI testing and treatment study
4. I agree to provide specimen as explained in the patient information sheet.
5. I understand that I will receive the usual standard of care offered by this clinic.

Patient name: _____

Signature: _____

Date (DD/MM/YYYY): _____

Name of the person obtaining consent: _____

Designation: _____

Signature: _____

Date (DD/MM/YYYY): _____

CONSENT FOR STUDY PARTICIPATION (INFANT)

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 permit my child to be in this additional component. I know

that after choosing to be in this component, I may withdraw my child at any time. I am voluntarily allowing my child to participate in this study. I understand that whether or not my child takes part will not affect their health care services received today, or at any time in the future.

Please indicate your consent with your signature.

Child's name _____

Mother's name _____

_____

Signature of Mother Date (DD/MM/YYYY)

Staff member's name_____

_____

Signature of study staff Date (DD/MM/YYYY)

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 (DD/MM/YYYY): _____

Thank you.

PATIENT CONSENT FORM (INFANT)- Participant Copy

1. I have read the patient information sheet, or it has been read to me.
2. I understand the contents of the patient information sheet.
3. I agree to permit my child's participation in the STI testing and treatment study
4. I understand that my child will receive the usual standard of care offered by this clinic.

Child's name _____

Patient name: _____

Signature: _____

Date (DD/MM/YYYY): _____

Name of the person obtaining consent: _____

Designation: _____

Signature: _____

Date (DD/MM/YYYY): _____

Appendix C:

Human Research Ethics Committee Approval for the Sexual Transmitted Infection in Pregnancy

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

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

11 October 2017

HREC REF: 454/2017

Prof Landon Myer
Epidemiology and Biostatistics
Public Health & Family Medicine
Falmouth Building

Dear Prof Myer

PROJECT TITLE: EPIDEMIOLOGY OF SEXUALLY TRANSMITTED INFECTIONS (STI) DURING PREGNANCY IN CAPE TOWN: A PROSPECTIVE STUDY

Thank you for submitting your response to the Faculty of Health Sciences Human Research Ethics Committee dated 12 September 2017.

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

- The Informed Consent Form contains the following line: *'We would like to ask you to participate in a study looking at how many pregnant women have sexually transmitted infection (STI) testing in pregnant women.'* We assume this is an error and that it should read: 'We would like to ask you to participate in a study looking at how many pregnant women have sexually transmitted infection (STI) testing in pregnant women.'

- The Informed Consent Form now contains an infant consent form (which wasn't there previously). We assume that this is also an error as the protocol doesn't mention any procedures for infants. Please clarify.

Approval is granted for one year until the 30 October 2018.

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

Please quote the HREC REF in all your correspondence.

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

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

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Appendix D:

Human Research Ethics Committee Approval renewal for the Sexual Transmitted Infection in Pregnancy

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	30.9.21
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	15/9/2020

Note: Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.
Please clarify your plan for research-related activities during COVID-19 lockdown

Comments to PI from the HREC
Thank you for the deviation document Thank you for the deviation document

Principal investigator to complete the following:

1. Protocol information

Date (when submitting this form)	8/9/2020		
HREC REF Number	454/2017	Current Ethics Approval was granted until	28.02.2020
Protocol title	Epidemiology of sexually transmitted infections (STIs) during pregnancy in Cape Town: A prospective study		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes X 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	Landon Myer		
Department / Office Internal Mail Address	Faculty of Health Sciences, Public Health and Family Medicine Observatory 7925		

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

1.1 Does this protocol receive US Federal funding?	☐ Yes	✓☐ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval? **Note:** Any annual approvals for **Full Committee** review MUST be submitted on the monthly HREC submission dates. (Please send electronic copy for full committee review to hrec-enquiries@uct.ac.za)	☐ Yes	✓☐ No
If yes in 1.2 please complete section 1.3 below for invoicing purposes		
1.3 Annual Approval for **full committee** review	- R 3450 (inclusive of vat)	
For invoicing purposes, please provide:		
Sponsor's name		
Contact person		
Address		
Telephone number		
Email Address		

2. List of documentation for approval

N/A

3. Protocol status (tick ✓)

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

4. Enrolment

Number of participants enrolled to date	242
Number of participants enrolled, since last HREC Progress report (continuing review)	0

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

Additional number of participants still required	0

5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	0

6. Cumulative summary of participants

Total number of participants who provided consent	242
Number of participants determined to be ineligible (i.e. after screening)	
Number of participants currently active on the study	0
Number of participants completed study (without events leading to withdrawal)	242
Number of participants withdrawn at participants' request (i.e. changed their mind)	0
Number of participants withdrawn by PI due to toxicity or adverse events	0
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	0
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up.	0
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	0

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:
Study ended in January 2019, we are continuing with data analyses and publication of study data in 2020.

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

✓☐	No prior violations or exceptions have occurred since the original approval
☐	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved

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

☐	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

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

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS006).
Specific changes in the amended protocol and consent/assent forms must be **bolded**, *italicised* or tracked and all changes must include a rationale.

10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.
No unanticipated adverse events since the last progress report

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

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

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

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

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

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

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

12. Level of risk (tick ✓)

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

12.2 Please provide a narrative summary of recent relevant literature that may have a bearing on the level of risk.

13. Statement of conflict of interest

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

14. Signature

My signature certifies that the above is complete and correct.			
Signature of PI		Date	8/9/2020

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