Healing and Functional Outcomes

after

Obstetric Anal Sphincter Injury

in

HIV Positive vs HIV Negative patients

UNIVERSITY OF CAPE TOWN

IYUNIVESITHI YASEKAPA•UNIVERSITEIT VAN KAAPSTAD

Submitted to the University of Cape Town
In partial fulfilment of the requirements
for the MMed (Obstetrics & Gynaecology)

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October 2009

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Declaration

I, Julie van den Berg, hereby declare that this dissertation is my own original work, (with acknowledgements indicated), and that neither the part nor the whole of this dissertation has or will be submitted for any other degree in this or any other university.

I empower the university to reproduce the contents of this dissertation for the purpose of research, either in whole or in part, in any appropriate manner.

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Acknowledgements

Many people contributed in various ways to the successful completion of this dissertation, and I would like to thank some people in particular.

Firstly to my supervisor, Dr Stephen Jeffery, who had the first vision for this project, and was a never-ending source of encouragement, enthusiasm, wisdom, academic support and insight, and who was never too busy to help to guide me through the process.

Secondly, thank you to all my colleagues who helped me in the recruitment process, and specifically those colleagues who are more importantly my friends, whose never-ending support and encouragement directly impacted the success of this project.

I would like to thank Prof. Landon Myer and Mr Henri Carrara for their help with the statistical aspects of this study.
Thank you to my family, friends and loved ones who contributed to this project in a variety of ways, without whose love and support I would never achieve anything.

I am grateful to the women participating in this study for being willing to honestly share with me very personal, and at times embarrassing, information. Without them, this study would not have been possible.

Mostly I would like to give all credit to my Lord God, by whom I am fearfully and wonderfully made, and in whom I live, move, and have my being.

Abstract

Aim: To determine whether HIV-positive patients have a longer time to healing, more complications and poorer functional outcomes after Obstetric Anal Sphincter Injury (OASI) than an HIV-negative control group.

Setting: Mowbray Maternity, New Somerset and Groote Schuur Hospitals of the Western Cape Peninsula Maternal and Neonatal Service.

Methods: Prospective cohort in two parts. Assessment of all patients with OASI between September 2008 and July 2009. Initial documentation, (post sphincter repair) before discharge from hospital; of demographics, details of repair, and pre-pregnancy anal, urinary and sexual function, as well as pre-pregnancy perineal pain. Six week postpartum follow-up of anal and urinary continence, sexual function and perineal pain, as well as a clinical examination.

Results: Sixty-eight women were enrolled including 54 who were HIV-negative and 14 who were HIV-positive. Thirty-six women attended follow-up; 28 HIV-negative and 8 HIV-positive. HIV-positive women were significantly more likely to experience pre-pregnancy urgency (50.0% vs 14.8%, p=0.0094). HIV-positive women were significantly more likely to experience solid stool incontinence (mean Wexner Score 0.9 vs 0.1; p=0.041) and have a negative lifestyle impact (mean Wexner Score 0.9 vs 0.1; p=0.007), as well as experiencing more postpartum stress urinary incontinence

(incidence 37.5% vs 0%; p=0.0078) than their HIV-negative counterparts at six-weeks postpartum. There were no significant differences in healing, infection, anal sphincter integrity or tone, between the two groups.

Conclusion: HIV-positive patients experience significantly more solid stool incontinence and have poorer lifestyle impact scores after OASI at six weeks postpartum. They also experience more pre-pregnancy urgency and postpartum stress urinary incontinence than HIV-negative controls. HIV-positive women also have lower baseline sexual function scores than their HIV-negative counterparts.

List of Abbreviations

AFUD	American Foundation for Urologic Disease
AIDS	Aquired Immuno-deficiency Syndrome
ART	Anti-retroviral Therapy
ASFQ	Abbreviated Sexual Function Questionnaire
ASSA	Actuarial Society of South Africa
CDC	Centers for Disease Control
CSP	Comprehensive Service Plan
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (Edition IV)
EAS	External Anal Sphincter
FSD	Female Sexual Dysfunction
HAART	Highly Active Anti-retroviral Therapy
HIV	Human Immuno-deficiency Virus
HPV	Human Papillomavirus
IAS	Internal Anal Sphincter
MOU	Midwife Obstetric Unit
OASI	Obstetric Anal Sphincter Injury
PMTCT	Perinatal Mother-To-Child Transmission
PNTML	Pudendal Nerve Terminal Motor Latency
PPIP	Perinatal Problem Identification Programme
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised Controlled Trial
SUI	Stress Urinary Incontinence
UTI	Urinary Tract Infection
UUI	Urge Urinary Incontinence

Chapter 1: Introduction

1.1 Background

Obstetric Anal Sphincter Injury (OASI) is potentially one of the most debilitating complications associated with vaginal delivery. For a young woman with a newborn baby, this unfortunate event, with its potential consequence of anal incontinence, can have a devastating impact on her health physically, psychologically and socially.

Obstetric services in Cape Town, as in many parts of South Africa, have become increasingly stretched, and associated with this staff are having to manage a significant number of complications. Adding to this, the Human Immuno-deficiency Virus (HIV) pandemic in South Africa is increasing in our population. The question naturally arises regarding the interplay between OASI and HIV infection. Since we work in a population where there is a high prevalence of HIV, probably amongst the largest in the world, we felt we were in an ideal situation to compare the outcomes of OASI in HIV-positive and HIV-negative patients.

1.2 HIV Infection

1.2.1 Incidence of HIV Infection

The exact prevalence and incidence of HIV in the South African population has been difficult to ascertain due to the fact that HIV is not a notifiable illness. Some of the best data we have are prevalence studies performed by the Department of Health amongst women attending antenatal clinics. The South African Department of Health Study 2006 reported a national HIV prevalence of 29.1% amongst 33 033 women attending antenatal clinics across the country. The highest prevalence was reported in women aged 25-29 years. The prevalence of HIV-positive women in Western Cape antenatal clinics in 2006 was 15.2%. All women in this study were pregnant and thus had engaged in unprotected sexual intercourse, which may have overestimated the prevalence when compared to the general population.

The South African National HIV Survey estimated that 10.8% of all South Africans over the age of two years were living with HIV in 2005. The prevalence amongst South African women was reported to be 13.3%. Interestingly, the survey reported that only 1.9% of women in the Western Cape were HIV-positive. This is significantly lower than the prevalence rates from the antenatal clinic data, and could be due to the small sample size of the study, and the fact that only 55% of eligible people consented to participate. This study also included men, children and non-sexually active women.

The Actuarial Society of South Africa (ASSA 2003) describes a prevalence rate of 5.2 million HIV-positive South Africans in 2003, with a further projection of 5.8 million South Africans being HIV-positive by 2010. They also estimate a rate of 500 000 new HIV infections per year.

1.3 Obstetric Anal Sphincter Injury (OASI)

1.3.1 Incidence of OASI and Risk Factors

The incidence of OASI following vaginal delivery ranges from 0.6-2.4% (Fornell et al 1996; Sultan et al, 1994; Walsh et al, 1996). Established risk factors associated with this injury include birth weight >4kg, primiparity, persistent occipitoposterior position, induction of labour, epidural, prolonged second stage of labour, shoulder dystocia, midline episiotomy and forceps delivery (Rieger et al, 2004; Sultan et al, 1994; Wood et al, 1998; RCOG 2007).

1.3.2 Classification of Perineal Injury

Perineal injuries sustained at vaginal delivery are classified as first, second, third or fourth degree tears. A third degree tear, by consensus, refers to a disruption of the muscles comprising the anal sphincter, while a fourth degree tear refers to disruption of the anal sphincter as well as the rectal mucosa (RCOG, 2007). Both third and fourth degree tears will include varying degrees of damage to the vaginal mucosa and

perineal muscles. The rectal mucosa is seldom disrupted in the absence of anal sphincter injury. Hence for the purpose of this study, OASI will refer to third and/or fourth degree tears.

Anatomically, the anal sphincter comprises the external anal sphincter (EAS) and the internal anal sphincter (IAS). Third degree tears can be complete or partial, and are further subdivided into 3a, 3b and 3c tears. 3a tears involve <50% of the EAS, in 3b tears >50% of the EAS is disrupted and 3c tears involve the IAS as well as the EAS.

1.3.3 Pathophysiology of incontinence after OASI

Anal continence depends on an anatomically intact anal sphincter, as well as normal innervation of the sphincter muscles. The external component of the anal sphincter comprises striated muscle which is under voluntary control, supplied by the pudendal nerve (S2,3,4). The internal anal sphincter is the thickened continuation of the smooth muscle encircling the rectum. This muscle is under autonomic nervous system control. Vaginal delivery will potentially damage this mechanism either by partial or complete anatomical disruption of the sphincter mechanism, or damage to the pudendal nerve. Pudendal nerve terminal motor latency (PNTML) tests measure the time delay between an electrical stimulus applied to the pudendal nerve and resultant muscle contraction. Studies looking at these tests have not shown significant differences between control and OASI groups, implying that varying continence between the two groups is due to anatomical disruption, and not nerve injury (Sultan et al, 1994). This highlights the importance of a good anatomical repair of disrupted sphincters in maintaining continence.

1.3.4 Postpartum Repair Techniques and Outcomes

Repair of OASI, in our clinical setting, involves immediate suturing under regional or general anaesthesia in theatre, using either an end-to-end (approximation) or overlap technique, by a registrar or consultant. Post-operatively, antibiotic prophylaxis and stool softeners are administered to our patients. This practice is in keeping with international standards (Mackenzie et al, 2004; Sultan & Thakar, 2002).

Traditionally, the end-to-end technique was used by obstetricians in the primary repair of OASIs. Unfortunately, rates of incontinence following primary end-to-end repair have been shown to be as high as 40-61% (Pinta et al, 2004; Poen et al, 1998; Sultan et al, 1994), with the lowest documented rates being 7-25% (Mackenzie et al, 2004; Walsh et al, 1996; Wood et al, 1998). These figures, along with evidence of even further deterioration in anal function over time (Fornell et al, 2005), are alarmingly high. The common practice of colorectal surgeons to use an overlap technique for secondary repair of patients with anal incontinence, and the apparent inadequacy of approximation repair in terms of continence outcomes, prompted Sultan et al (1999) to be the first to objectively study the feasibility and outcome of the overlap technique as the primary method of anal sphincter repair (Sultan et al, 1994; Sultan et al 1999). The technique involved separate end-to-end repair of the IAS, (if it was identified as being disrupted), with an overlap repair of the EAS. Results of the study showed that overlap was "not only possible but appears to result in a better outcome than the conventional end-to-end approximation" (Sultan et al, 1999:322). Only two of the 27 women reported symptoms of anal incontinence (8%), and that being for flatus only.

Since that small pilot study there have been several randomized controlled trials (RCTs) comparing overlap to end-to-end repair. Fitzpatrick et al (2000) demonstrated no significant differences between the two groups in terms of faecal incontinence, anal manometry and endoanal ultrasonography at three months postpartum. Garcia et al (2005), in a study that was probably underpowered due to poor follow-up rates, also demonstrated no difference in outcomes between the two techniques at three months post primary repair. The only RCT of overlap and end-to-end repair that followed patients up for 12 months was performed by Fernando et al (2006). This study showed the overlap group to have significantly lower rates of faecal incontinence, faecal urgency and perineal pain at 12 months. There was, however, no significant difference in dyspareunia and quality of life between the two groups. Of note is that in this study, repair was done by clinicians specifically trained in both techniques.

A Cochrane review by Fernando et al (2006) found that the overlap technique was associated with a significantly lower incidence of faecal urgency and lower anal incontinence scores at 12 months post repair, as well as significantly less deterioration of anal continence symptoms at 12 months. There was, however, no difference in

perineal pain, dyspareunia, flatal incontinence and faecal incontinence at 12 months. This review did not, however, recommend the overlap in preference to the end-to-end repair, on the grounds that the experience of the surgeon was not addressed in the studies reviewed.

In 2007, Molander et al published a retrospective study of 42 women sustaining OASI where repair was with the overlap technique. At a mean of 9.4 months of follow-up, 64% of the patients were completely asymptomatic for anal incontinence.
In 2008, Lepistö et al recommended that the overlap technique be employed as the primary repair technique following a prospective case-control study with a retrospective end-to-end control group. Their findings included significantly better Wexner scores at six to nine months postpartum in the overlap group.

Despite best obstetric practice, damage to the anal sphincter will remain a complication of vaginal delivery. The best functional outcome depends on a good anatomical repair, and normal innervation. The obstetrician can only do their best to modify the former, to optimise functional outcomes. In this regard, the evidence would suggest a move toward using the overlap technique of repair. International standards still include using either technique, however.

1.4 Healing

Good functional outcomes for any surgical technique rely on an absence of complications and optimal healing of the wound. Any interference with wound healing will impair outcome despite meticulous surgical technique. A dehisced anal sphincter repair will have significantly poorer function than an intact sphincter.

Factors impacting negatively on the healing of any wound can be classified as local or general. Local factors include infection, a poor blood supply, excessive movement and the presence of foreign bodies. General factors include chronic disease, excess adrenocorticoids and deficiencies of vitamin C, zinc and amino acids (Govan, MacFarlane & Callander, 1995). Human Papillomavirus (HPV) infection and

smoking have been shown to be significant risk factors in the dehiscence of episiotomies (Snyder et al, 1990).

1.4.1 Infections and Wound Healing

Williams and Chames (2006) studied the risk factors for perineal wound breakdown in 59 women. They found that mediolateral episiotomy, operative vaginal delivery, higher order lacerations (ie third and fourth degree) and meconium-stained amniotic fluid led to an increase in wound dehiscence. There was an association with infection in 40.7% of cases. This finding is in keeping with the study by Ramin et al (1992), who also found infection to be associated with 79% of episiotomy dehiscences. Norderval et al (2005) also noted that wound infection complicated 7% of OASIs and that these women had significantly poorer functional outcomes as a result.

Williams and Chames (2006) did not describe any association between pre-existing medical conditions and repair breakdown or infection. There is no mention of the prevalence of HIV in their study population. Breakdown of perineal laceration repair was associated with significant morbidity and the need for additional medical care including longer hospital stays, more out-patient visits, additional theatre time and increased anaesthetic and antibiotic requirements.

1.4.2 HIV and Wound Infections

HIV causes immunodeficiency by infecting cells with the CD4 surface receptor. The largest population of cells with this receptor are the T-helper lymphocytes. Other cells with the receptor include macrophages, monocytes and central nervous system dendritic cells. Following infection, variable lengths of clinical latency follow, with a steady destruction of CD4 T-lymphocytes. In this way, immunity is impaired, resulting in increased susceptibility to infection (Kumar & Clark, 1998; Gladwin & Trattler, 1999).

A number of authors have reported on the impact of HIV on wound healing. An anecdotal report by Bayley (1990) suggested HIV infection to be more frequently associated with surgical infection than diabetes. A South African study showed

abdominal wound sepsis following gynaecological surgery to be significantly higher in HIV-positive individuals (Jjuuko & Moodley, 2002). Local sepsis after haemorrhoidectomy has been shown to be significantly higher in patients with AIDS compared to controls and HIV-positive patients without clinical AIDS (Morandi et al, 1999). In Malawi, studies showed wound sepsis to be increased in HIV-positive patients with compound tibial fractures. Of interest, however, is that this was not the case in orthopaedic implant surgery where no preoperative contamination was demonstrated (Harrison et al, 2002; Harrison et al, 2004).

1.4.3 HIV and Wound Healing in the Absence of Infection

HIV is a multisystem disease that causes chronic illness and this is not only through its association with infection. Immunological disease such as HIV-associated nephropathy, cardiomyopathy, encephalopathy, peripheral neuropathy, malignancy and pancytopaenia are a few examples of non-infective HIV pathologies causing chronic illness. The question then arises as to whether HIV-positivity per se will impair wound healing. Hewitt et al (1996) showed no significant difference in time taken to full wound healing between HIV-positive and -negative patients undergoing elective haemorrhoidectomy. In addition, they did not demonstrate a difference in healing between HIV-positive patients and those patients with a clinical diagnosis of Acquired Immunodeficiency Syndrome (AIDS), as defined by the 1993 Centers for Disease control (CDC) criteria. These finding are however, not confirmed by other studies.

In a retrospective review of anorectal surgical procedures by Safavi et al (1991), wound healing was significantly poorer in patients with clinical AIDS compared to the earlier stage HIV-positive patients. Lord (1997) showed that only 40% of anorectal wounds in HIV-positive patients were healed by three months.
Other studies looking at healing following anorectal surgical procedures have shown that HIV-negative patients heal quicker than those who are HIV-positive. Patients with AIDS appear to display the longest time to healing (Morandi et al, 1999; Nadal et al, 1998).

There are varying reports on the impact of CD4 count on anorectal wound healing, with some studies showing no association (Eriguchi et al, 1997; Hewitt et al, 1996; Safavi et al, 1991) and others demonstrating a significant link between lower counts and delayed wound healing (Morandi et al, 1999; Nadal et al, 1998).
Literature investigating the relationship between HIV infection, CD4 counts, wound sepsis and healing outcomes in emergency and elective surgery is available, but there are currently no studies describing these relationships to the outcomes of OASI repairs.

1.5 Functional outcomes after OASI

1.5.1 Anal Incontinence

Anal incontinence refers to one or more of faecal (solid or liquid stool), and/or flatal incontinence. As discussed previously, rates of anal incontinence vary after OASI, with overall rates of between 20 and 61% (Pinta et al, 2004; Rieger et al, 2004; Sultan et al, 1994; Walsh et al, 1996). A number of studies have shown anal incontinence rates for solid stool ranging from 7-20%, liquid stool incontinence from 8-18%, flatal incontinence from 7-41% and faecal urgency from 6-26% (Fornell et al, 2005; Gjessing et al, 1998; Pinta et al, 2004; Poen et al, 1998; Rieger et al, 2004; Sultan et al, 1994; Walsh et al, 1996; Wood et al, 1998).

Fornell et al (2005) studied women 10 years after OASI. In their cohort where they had an 80% follow-up rate, five of their original 51 women with OASI had undergone secondary repair. The remainder reported significant incontinence to flatus and liquid stool compared to controls.

Anal continence can be assessed by history, examination and special investigations (Sultan & Thakar, 2002). Symptoms include incontinence to flatus, liquid stool, solid stool and faecal urgency. These are best assessed using continence and quality of life questionnaires.
Clinical vaginal and rectal examination includes assessment of wound healing, presence of complications, scar tenderness and sphincter tone.

Useful special investigations include endoanal ultrasonography to look for a defect in the IAS and/or EAS, and anal manometry. Pudendal nerve terminal motor nerve latency testing has not been shown to be of benefit and is not standard practice (Poen et al, 1998; Sultan et al, 1994).

Endoanal ultrasonography can demonstrate defects in the internal and/or external anal sphincter. Defects have been detected in 15-88% of women after OASI, and 20-33% of controls (Pinta et al, 2004; Poen et al, 1998; Rieger et al, 2004; Sultan et al, 1994; Sultan et al, 1999). Anal incontinence is associated with defects in the IAS, EAS or both (Poen et al, 1998; Sultan et al, 1994).

Mackenzie et al (2003) showed no direct relationship between defects detected on ultrasound and symptoms of anal incontinence. Rieger et al (2004) also failed to show a statistically significant association between symptoms and an ultrasonographically detected sphincter defect. Women with sonographically demonstrated defects can also be completely asymptomatic, whereas 31-80% of symptomatic women have no demonstrable sphincter defect (Gjessing et al, 1998; Poen et al, 1998; Sultan et al, 1994). Sultan et al (1994) looked specifically at endoanal ultrasonography in women who had sustained an OASI, and found that 85% had a demonstrable defect whilst only 47% had symptoms.

Anal manometry measures the maximum resting pressure of the anal sphincter, and the maximum squeeze pressure. Maximum resting pressure has been shown to be significantly lower in women with faecal incontinence and OASI (Fornell et al, 2005; Gjessing et al, 1998; Sultan et al, 1994). Maximum squeeze pressure is lower in women with OASI, and this has been shown to deteriorate with time. Lower maximum squeeze pressures are however not always associated with incontinence symptoms (Fornell et al, 2005; Gjessing et al, 1998; Pinta et al, 2004; Poen et al, 1998).

1.5.2 Urinary Incontinence

Urinary incontinence is associated with normal vaginal delivery both in the absence and presence of OASI. The rates of urinary incontinence following vaginal delivery with OASI range from 13-50%, compared to 9-40% in the absence of sphincter disruption (Altman et al, 2007; Fenner et al, 2003; Tetzschner et al, 1996; Wagenius

& Laurin, 2003). In the retrospective case-control study of 654 women by Wagenius and Laurin (2003), there was no significant difference in the rate of urinary incontinence between women with OASI and controls. Borello-France et al (2006) also did not detect a difference in urinary incontinence between controls and subjects with OASI in their prospective study reviewing women at six weeks and six months postpartum.

1.5.3 Sexual function

Sexual function depends on a complex interplay of many variables. In addition to physical factors in the postpartum period, psychological, emotional and environmental factors also play an important role in sexual function. Deterioration in sexual function during pregnancy and the postpartum period have been linked to depression and fatigue. However, relationship satisfaction is a protective factor for sexual desire and satisfaction (DeJudicibus & McCabe, 2002).

Rates of dyspareunia in the first 2-3 months postpartum in women delivering vaginally range from 41-45% (Goetsch, 2000; Signorello et al, 2001). Although dyspareunia is common in women with an intact perineum or first degree tear, Signorello et al (2001) report that women with a third or fourth degree tear have a two to three-fold increase in dyspareunia at three months. Other studies have confirmed the increased incidence of dyspareunia at three months in women with higher order perineal injuries (Andrews et al, 2007). The study of Norderval et al (2005) reported de novo dyspareunia in 15% of women at a mean of 27 months after OASI.

Ability to achieve orgasm, sexual sensation and satisfaction were poorer at six months postpartum in the study by Signorello et al (2001), compared to these parameters antenatally. On the other hand, Fornell et al (2005) showed no difference in libido, ability to achieve orgasm or enjoyment of sexual intercourse between study and control groups either at six months or ten years after injury. Lubrication at arousal was the only parameter that was impaired in their study group at six months, but this had improved at ten years follow-up. Decreased lubrication has been shown to be

associated with episiotomy, but no relationship has been demonstrated between episiotomy and arousal, orgasm or sexual satisfaction (Ejegård et al, 2008).
One study has reported that 17% of women experienced anal incontinence during sexual intercourse after OASI (Gjessing et al, 1998). No other studies have documented anal incontinence during intercourse.

1.5.4 Perineal pain

Postpartum perineal pain can impair the activities of daily living such as walking, sitting and driving. It is reported that on day one postpartum, 75% of women with an intact perineum, 95% of women with first- or second-degree tears, and 100% of those with an OASI, report significant perineal pain (Macarthur & Macarthur, 2004).
Pain remains on day seven for women with OASI, with 91% still reporting pain compared to only 38% for an intact perineum and 60% for a first or second-degree tear. At six weeks postpartum, there was no significant difference between rates of pain in any of the above groups of women.

There is a paucity of further data on perineal pain after anal sphincter injury with most of the literature reporting on pain after episiotomy or in relation to repair techniques (Fernando et al, 2006).

Chapter 2: Materials and Methods

2.1 Study Aims

The primary aim of this study was to determine whether HIV-positive patients have poorer functional anal continence outcomes after OASI, than an HIV-negative control group, at similar time points postpartum.

Secondary aims of the study were to determine:

- Whether HIV infection confers a longer time to healing, and more complications, after an OASI;
- The incidence of all types of perineal complications in our study population after OASI irrespective of HIV status;
  and
- Factors associated with healing outcomes in HIV-positive and negative patients.

2.2 Study Objectives

The objectives of the study were to determine:

1. The differences in anal incontinence, urinary incontinence, sexual dysfunction and perineal pain after OASI in HIV-positive and HIV-negative patients compared to their pre-delivery status
2. The relationship of surgical technique to functional outcomes in our patients where the surgeons are usually Obstetrics and Gynaecology registrars
3. The incidence and effect of the use of prophylactic antibiotics after anal sphincter repair
4. The relationship of CD4 count to rates of healing, complications and functional outcomes in the HIV-positive patient group
5. The role of antiretroviral therapy, if any, on healing and outcomes after OASI in the HIV-positive women

2.3 Study Setting

The study was performed in the Cape Town metropolitan area, where there is a tiered obstetric healthcare system. This falls within the design of the Comprehensive Service Plan (CSP) for the Implementation of Healthcare 2010, as published by the Western Cape Department of Health in 2007. Levels of care include primary, secondary and tertiary. A well designed referral system exists whereby patients are seen at, or referred to, different levels of care as appropriate. The metropole has two tertiary centres, including Groote Schuur and Tygerberg Hospitals. The University of Cape Town is associated with Groote Schuur Hospital, and it is within this hospital's drainage area that the study was performed.

Primary level care is offered by midwives at Midwife Obstetric Units (MOUs). Secondary level care is by referral to Mowbray Maternity and New Somerset Hospitals. These two hospitals refer to the tertiary Groote Schuur Hospital when necessary. Only the secondary and tertiary hospitals have full-time cover by doctors. Care is rendered by consultants, registrars, medical officers and interns. Any identified OASI occurring at primary care level is referred to one of the above three hospitals as per the referral drainage design.
Perinatal Problem Identification Programme (PPIP) statistics for 2006 reported more than 34 000 deliveries of more than 1kg in the Cape Town metropole falling under the Groote Schuur Hospital drainage and referral system. Of these, approximately 16 000 were at primary care level, 14 000 at secondary care level, and 5 000 at tertiary level.

All patients are routinely offered HIV testing at booking. Dedicated HIV counsellors are responsible for this testing. The result is stamped onto the antenatal card after the patient has been informed of the result and counselled. If she is HIV-positive, a CD4 count is performed.

All antenatal HIV-positive patients with a CD4 count of less than 200 are referred to an HIV clinic in the area where they live, where they are offered Highly Active Antiretroviral Therapy (HAART). This medication is dispensed by doctors at the HIV clinics and not the obstetric doctors. Patients continue their care at these HIV clinics postpartum. Antenatal patients with CD4 counts greater than 200 are offered

antiretrovirals antenatally according to the Provincial Health Department's Prevention of Mother-to-Child Transmission (PMTCT) guidelines. At present this includes zidovudine (AZT) 300mg bd orally from 28 weeks gestation until delivery, and Nevirapine 200mg orally within the 12 hours prior to delivery.

2.4 Study Design

This study was a prospective cohort study. The first part of the study involved recruiting the patients sustaining an OASI from labour ward and/or theatre records, while they were still in hospital. At recruitment, demographic details, relevant details of the injury, the surgical repair and the patient's immediate post-operative course were documented. Information regarding pre-pregnancy anal continence, urinary continence, sexual function and perineal pain was recorded, using questionnaires during an interview with the patients. Patients were then given a referral letter to the Groote Schuur Hospital Perineal Clinic for follow-up six weeks after sphincter repair. It was at this follow-up visit that the second part of the study took place.

At the six week follow-up visit, patients were assessed for symptoms of anal incontinence, urinary incontinence, sexual dysfunction and perineal pain by interview, using the same questionnaires. Any history of interim complications or re-admission was noted. The patients were examined to clinically assess wound healing, anal tone and to assess them for any clinical evidence of a sphincter defect.
Anorectal manometry and endoanal ultrasonography were not performed. The main outcome measures of the current study were clinical assessment of functional symptoms experienced by the patients, and physical signs on examination.

Although enrolment was allowed by any suitably qualified participating medical practitioner, ultimately the patients were only enrolled by the principal investigators. Likewise the patients were followed up by the principal investigators as well.

2.5 Patient Recruitment

Since patients with OASI are treated at either Somerset, Mowbray or Groote Schuur Hospitals, they were enrolled from the wards of these hospitals while still in-patients, in the immediate post-partum period.

Any woman between the ages of 18 and 70, of any parity and race, who had sustained a third or fourth degree perineal laceration was considered suitable for recruitment. Both HIV-positive and HIV-negative women were enrolled. There had to be documented evidence in the patient's folder as to her HIV status, and word of mouth status was not accepted. A negative HIV test in pregnancy was accepted and not re-tested. The HIV-positive women acted as cases, and the HIV-negative women as the controls. Patients had to be able to communicate English or Afrikaans for the purpose of accurate informed consent and data collection, and completion of questionnaires. Exclusion criteria were an unknown or unproven HIV status, or a previous obstetric anal sphincter injury.

The study was publicised in the three hospitals, and data collected by the principal investigators. The patients were given a study referral letter at enrolment, so that at the 6 week follow-up visit they could be clearly identified as study participants.

During the second part of the study, follow-up questionnaires and the clinical examination were completed by the principal investigators at the Groote Schuur Hospital Perineal Clinic.

The women were each advised that should she have complications between discharge from hospital and the six week follow-up visit, she should contact the Groote Schuur Perineal Clinic or her local Day Hospital for assessment.

Enrolment began in September 2008 after approval for the study was obtained from the University of Cape Town's Faculty of Health Sciences Ethics Committee (REC REF 276/2008).

2.6 Data Collection

All data for the study was collected by the principal investigators, who alone had access to the completed data sheets, consent forms, and enrolment logs. After indentifying eligible study participants, the investigators explained the study to the patients and provided them with a patient information sheet designed for the study, and if the patient agreed to participate, an informed consent form was signed by the patient (See Appendices 1 and 2).

Data collection sheets were designed by the principal investigators, and included use of recognised scoring and assessment systems, specifically the Wexner Score for anal incontinence (Vaizey et al, 1999), a 10 point Visual Analogue Scale (VAS) for perineal pain, and the Abbreviated Sexual Function Questionnaire (ASFQ) for sexual function (Guay A et al, 2004). The same data questionnaires were used for both parts of the study. The only differences in the data collection sheets for the two parts of the study were the inclusion of a demographics proforma for the first part of the study, and a clinical examination proforma for the second part (follow-up visit). (See Appendix 3).

The data was immediately entered onto an Excel Spreadsheet on a password controlled computer, accessed only by the principal investigators. Original paper data was kept in a secure locked location accessed only by principal investigators.

An Enrolment Log kept a record all eligible participants, and whether or not they were enrolled in the study. Reasons for non-enrollment, non-eligibility or loss were documented.

2.7 Sample Size and Statistical Analysis

The sample size calculations for this study were based on a significance level of 0.05 and an intention for the study to have at least 80% power.
We estimated an event rate of 20% for symptoms of anal incontinence amongst HIV-negative women, as per the most common baseline rates in the literature.

The literature suggests that 50% of HIV-positive women will not heal completely (Lord, 1997; Morandi et al, 1999; Safavi et al, 1991). It was thus deemed likely that these women would have symptoms of anal incontinence. We therefore estimated an event rate of 50% amongst the HIV-positive women.

Using the lowest incidence quoted of 0.6% of deliveries being complicated by OASI, we anticipated at least 200 OASIs in our service annually. Using the Stata Statisitics programme, a sample size of 100 HIV-negative and 50 HIV-positive patients was determined to give the study a power of 94%. This confirmed that the study would have adequate statistical power to detect a clinically meaningful difference in the occurrence of incontinence following OASI between HIV-positive and HIV-negative women.

Data entered into the Excel Spreadsheet was transferred to the SPSS 17.0 Statistical Analysis Program. Frequencies and descriptive figures were determined for the data, and tests for significance were calculated using the Mann-Whitney Test, after application of the Shapiro-Wilk test indicated that the data was not normally distributed.
In addition, online interactive statistical programs were used to determine Fisher's Exact significance tests and Relative Risk Calculations for the results obtained (www.graphpad.com/quickcalcs/index.cfm;www.phsim.man.ac.uklrisk/Default.aspx).

2.8 Ethical Considerations

Ethical approval for the study was granted by the University of Cape Town Faculty of Health Science's Ethics Committee (REC REF 276/2008; see Appendix 4).

The patient information sheet, as well an explanation by the recruiting doctor, served to enable the patients to make an informed decision on whether or not to consent to being enrolled in the study. An informed consent form was signed by participants, a principal investigator and one witness. Enrolment was on a purely voluntary basis, and it was made clear to patients that their HIV status would be documented, as well as other information from their folder. They were also advised that participation

would involve a clinical examination at the six week follow-up visit. Patients unable to legally give their own consent would be invited to join in the study if they and that person with their power-of-attorney consented to their participation. However, all patients enrolled were able to consent for themselves. Of note, the Ethics Committee Approval designated that only women older than 18 year of age be enrolled.

Due to the extreme sensitivity of studying outcomes of HIV status, priority was placed on ensuring complete confidentiality once a patient was enrolled. Only the patient's folder number and study number was recorded on the data collection sheets, with no names documented. However, a separate patient tracking sheet was used to keep a record of the patient's name, folder number, study number and her contact details. This was used to contact the patient only if she did not attend her follow-up appointment, in order to give her the opportunity of rescheduling if she so chose. The patient tracking sheet was kept securely by the principal investigators, in a file separate to the data collection sheets.
Folder numbers and names were not entered into the password-controlled computer database. A separate and confidential master participation sheet kept a record of patient folder numbers linked to study numbers. Only the principal investigators had access to the original data collection sheets, patient tracking sheets, consent forms, master participation sheet and the enrollment log. Patients were recruited in private.

Any patient choosing not to be enrolled in the study still had access to follow-up at the Groote Schuur Perineal Clinic, through routine inter-hospital referral by their discharging doctor. Thus there was no discrimination of care to those choosing not to be enrolled in the study. Patients were advised of this.

Patients enrolling in the study were reimbursed for the transport costs to their follow-up appointments. This was to try and ensure that the cost of transport did not keep asymptomatic patients away from their follow-up appointment, and to ensure no financial burden was placed on the patient by being enrolled in the study. Reimbursement took place at the Perineal Clinic and not in advance. Reimbursement was at a fixed rate of R20,00 per patient.

There was no new procedure, drug or technique being studied on the patients enrolling in this study. There was no extra care being provided to the patients in this study, and there were no health risks to being enrolled in the study. The only potentially negative effects of this study on the participants were if they felt embarrassed about the nature of the information obtained, questions asked or examination performed, and the possible inconvenience of attending the follow-up visit.

It was anticipated that this study would actually be of benefit to all patients invited to participate, even if they declined enrolment. The main advantages included that the study highlighted to the patients exactly what type of injury they sustained, how and why it was repaired and the potential adverse consequences. They were also made aware that help was available should she experience any complications, and exactly how and where to access this specialised help and follow-up. There were no direct health benefits resulting from enrolment that would not be otherwise available.

The fact that only patients who could communicate in English or Afrikaans were enrolled in the study was in order to protect the patients. The study focussed on two very sensitive issues, namely HIV status and anal continence, and we did not wish to enrol patients who may be at a disadvantage if they did not fully understand the nature of the study. We did not want language difficulties to compromise the patient's right to autonomy and privacy, nor to result in inaccurate data collection.

The Declaration of Helsinki (2000) and the Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa [2008], were both consulted in the Ethical and Study Design principles set out in the study protocol.

2.9 Budget

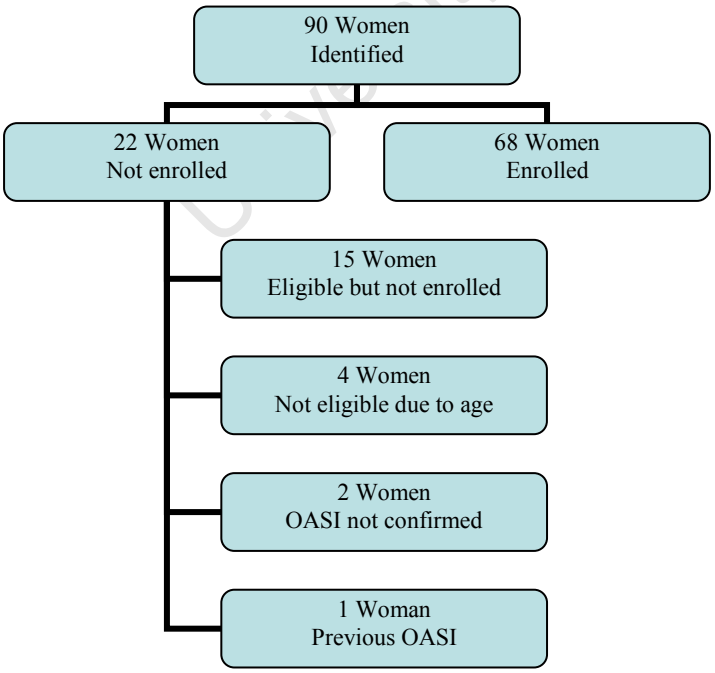
The costs of the study were carried by the principal investigators. There was no external sponsorship for the study.

Chapter 3: Results

3.1 Demographics

From 1 September 2008 to 31 July 2009, 90 patients with OASI were identified. Sixty-eight of these women were enrolled in the study (Figure 1). Fifteen patients were not enrolled due to discharge prior to enrolment and these women were also not referred to the Groote Schuur Hospital Perineal Clinic, nor were they contactable from details in hospital records. Four patients were too young for enrolment (<18 years); two women were recorded as having OASI but on examination of patient and theatre notes this could not be confirmed; and one patient was excluded due to having had a previous OASI. Only 36 patients attended the Perineal Clinic for follow-up at the time of analysis, resulting in a loss to follow up of 47.1%. Of the 32 patients lost to follow up, the majority were untraceable using the contact details given at enrolment, whilst a minority were no longer in the area, and others did not give a reason for not following up.

Figure 1 Eligible patients identified during study period



At baseline, three demographic parameters were assessed (Table 1).
The age and parity of the women were not normally distributed. The median age of all the women was 24 and the median parity was 1. Forty-seven women were Black (69.1%), twenty (29.4%) were Coloured, and one (1.5%) was White. Of the 68 women, 14 (20.6%) were HIV-positive and 54 (79.4%) were HIV-negative.

There was a statistically significant difference in age and ethnic group between the HIV-positive and HIV-negative women with an OASI (Table 1), with HIV-positive women being older and of the Black ethnic group.

Table 1 Demographic characteristics of women enrolled in study

	Total Sample (n=68)	HIV pos (n=14)	HIV neg (n=54)	p-value
Median Age	24 (21-26)*	27 (23-32)*	24 (20-26)*	0.03[#]
Median Parity	1 (1-2)*	1 (1-1)*	1 (1-2)*	0.24[#]
Ethnic Group				
Black	47 (69.1%)	14 (100%)	33 (61.1%)	0.0001[†]
Coloured	20 (29.4%)	0	20 (37.0%)	1.00[†]
White	1 (1.5%)	0	1 (1.9%)	1.00[†]

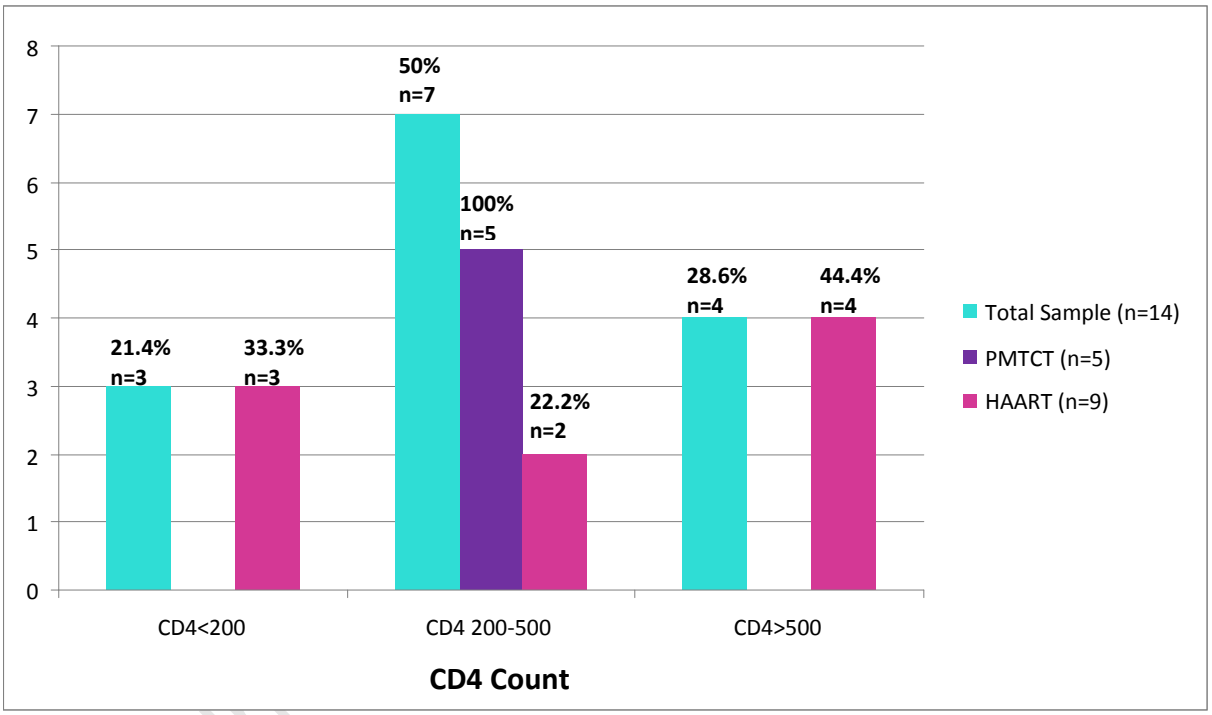
*Inter-quartile range
[#]Mann-Whitney Test
[†] Fisher's Exact Test

3.2 CD4 counts and Treatment of HIV-positive patients

Of the 14 HIV-positive women, the mean CD4 count was 351 (SD +/- 152.9), with a range of 105 to 560. Three women had a CD4 count less than 200, seven women had a CD4 count between 200 and 500, and four women had a CD4 count more than 500 (Figure 2).

All of the women were on anti-retroviral therapy (ART). Five women were on the Perinatal Mother-to-Child Transmission (PMTCT) prevention program, all of whom had CD4 counts between 200 and 500; and nine women were on Highly Active Anti-retroviral Therapy (HAART) (Figure 2).

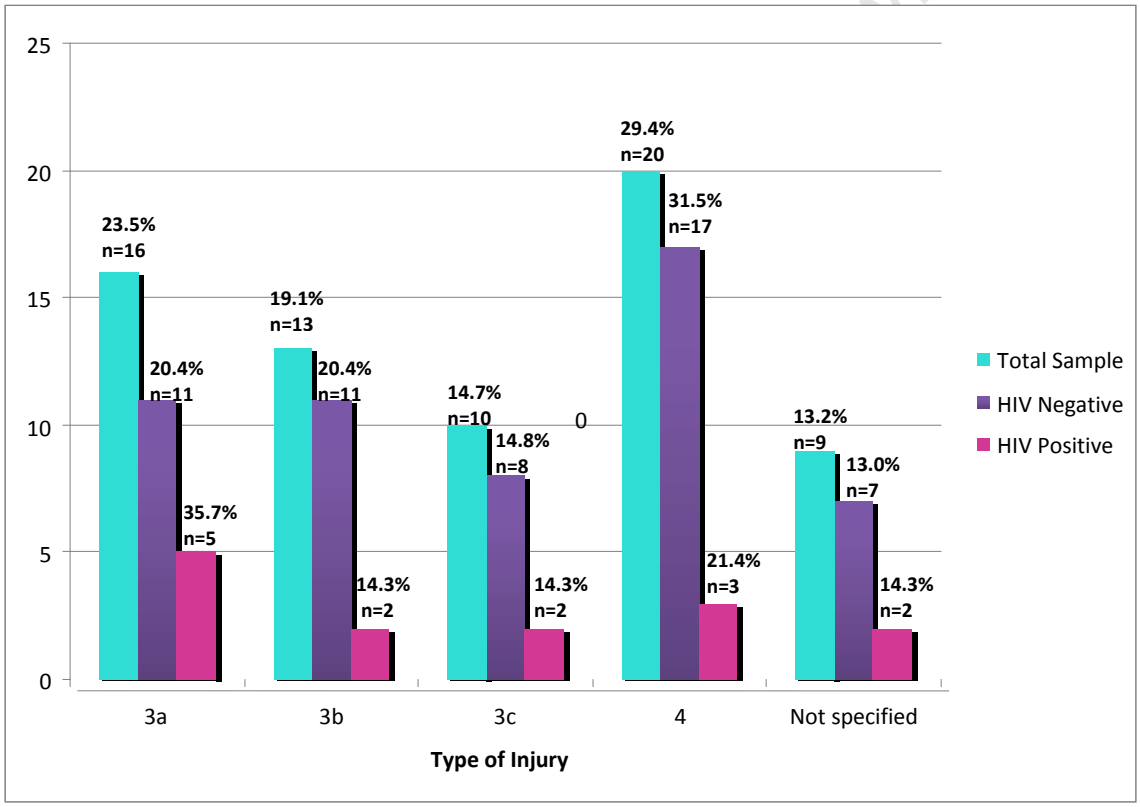
Figure 2 Relationship of CD4 count to Anti-retroviral Therapy



3.3 Distribution of OASI

Of the 68 women, 16 (23.5%) sustained a 3a tear, 13 (19.1%) a 3b tear, 10 (14.7%) a 3c tear, and 20 (29.4%) sustained a fourth degree tear. Nine (13.2%) tears were not classified in the patient's delivery or operation notes (Figure 3). There was no statistically significant difference in the type of injury sustained between the HIV-positive and HIV-negative women (Figure 3).

Figure 3 Distribution of OASI



3.4 Management of OASI

Twenty-six (38.2%) tears were repaired by the end-to-end method, 27 (39.7%) by the overlap technique, and in 15 (22.1%) patients the technique used was not described in the patient's notes (Figure 4). There was no significant difference between the technique of repair employed if the patient was HIV-positive or –negative.

Antibiotics were prescribed for 66 (97.1%) of the women enrolled. The two women not receiving antibiotics were both were HIV-negative.

Figure 4 Technique of anal sphincter repair

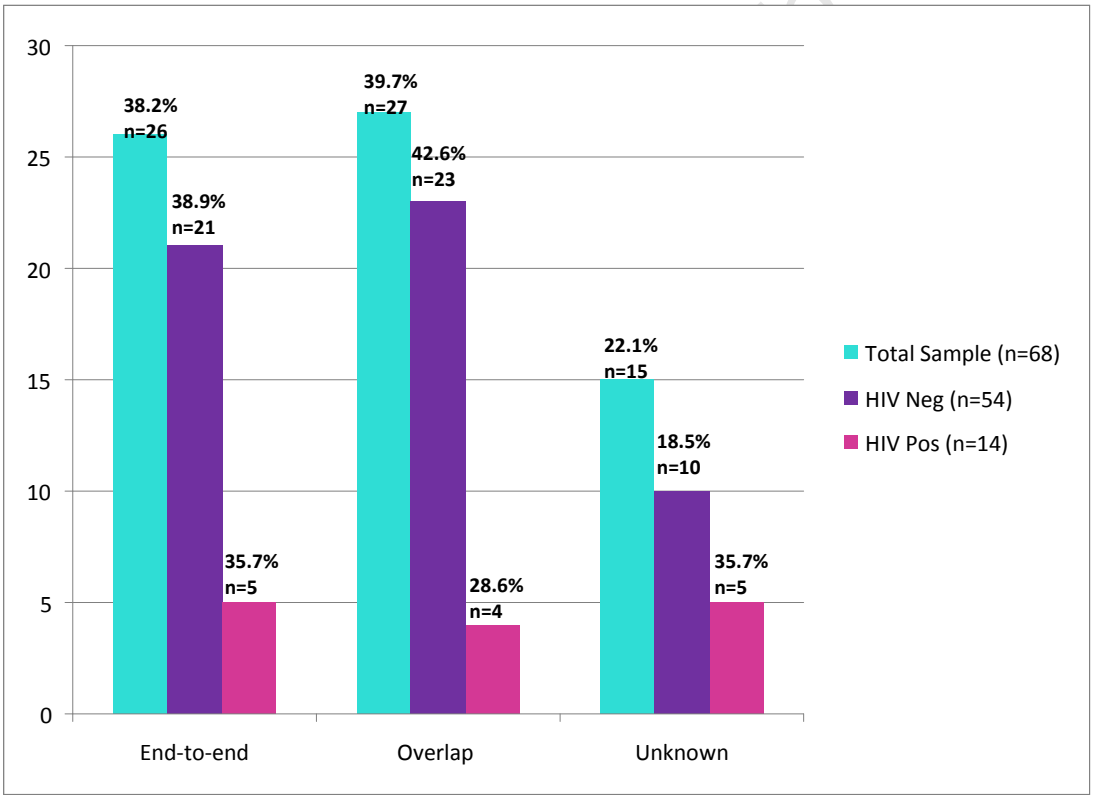
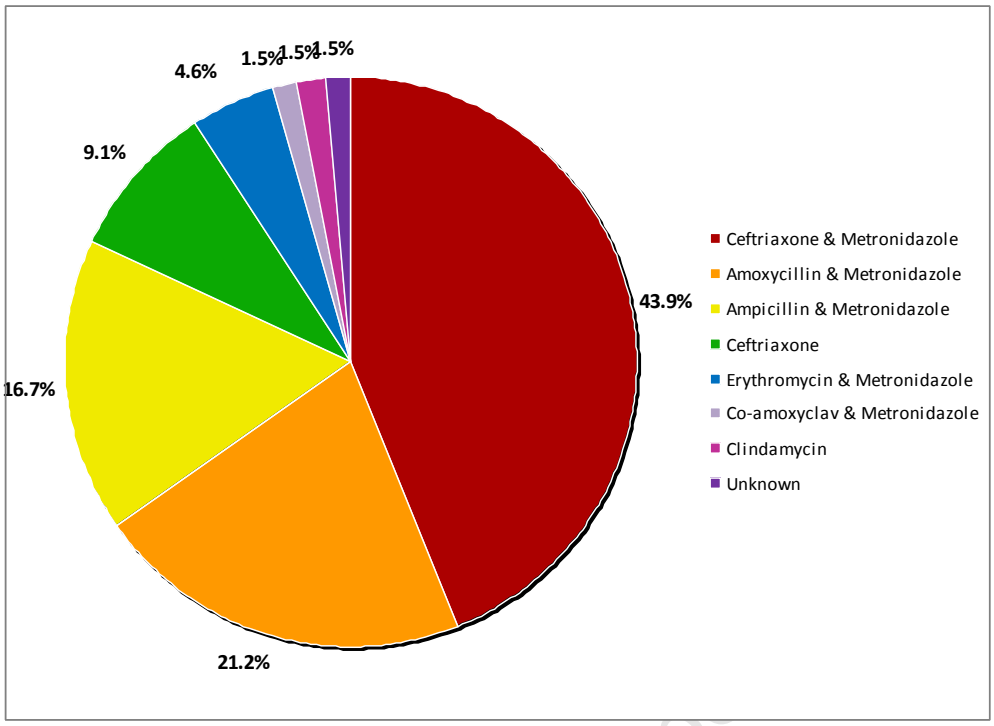


Figure 5 Types of Antibiotics prescribed post-repair



3.5 Pre-pregnancy Functional Assessment

3.5.1 Anal Continence

Table 2 depicts the Wexner scoring system. Each category is assigned a score of 0-4 and the overall Wexner score for the five categories gives a score out of 20. The mean Wexner Score prior to the index pregnancy in our study was 0.4 (Table 3). Mean scores for solid stool incontinence, liquid stool incontinence, flatal incontinence, pad usage and lifestyle impact were low throughout the sample, with no significant differences between the HIV-positive and HIV-negative groups (Table 3). None of the women reported any solid stool incontinence prior to their pregnancy.

Table 2 The Wexner Score

Type of Incontinence	*Never*	*Rarely* *<1/month*	*Sometimes* *<1/week >=1/month*	*Usually* *<1/day >=1/week*	*Always* *>=1/day*
Solid Stool Incontinence	0	1	2	3	4
Liquid Stool Incontinence	0	1	2	3	4
Flatal Incontinence	0	1	2	3	4
Pad Usage for Faecal Incontinence	0	1	2	3	4
Lifestyle Impact	0	1	2	3	4

0 = perfect continence
20 = complete incontinence

Table 3 Pre-pregnancy Wexner Scores for anal continence

Mean Wexner Score[§]	Total Sample (n=68)	HIV Pos (n=14)	HIV Neg (n=54)	p-value*
Overall Wexner Score (0-20)	0.4	0.6	0.4	0.70
Solid Stool Incontinence (0-4)	0.0	0.0	0.0	-
Liquid Stool Incontinence (0-4)	0.1	0.1	0.1	0.94
Flatal Incontinence (0-4)	0.1	0.3	0.1	0.62
Pad usage for Faecal Incontinence (0-4)	0.1	0.1	0.1	0.95
Lifestyle Impact (0-4)	0.1	0.1	0.1	0.93

*Mann-Whitney
[§]Score range given in brackets

3.5.2 Perineal Pain

Using a visual analogue pain scale, graded 0-10 (with 0 being no pain at all), all 68 women reported almost no pain of the perineum on walking, sitting and resting (Table 4). All mean scores were less than 1, with no differences between the two groups (Table 4).

Table 4 Mean pre-pregnancy pain score by visual analogue scale

	Total Sample (n=68)	HIV Pos (n=14)	HIV Neg (n=54)	p-value*
Walking	0.2	0.1	0.2	0.79
Sitting	0.3	0.1	0.4	0.97
Resting	0.1	0.0	0.1	0.92

*Mann-Whitney

3.5.3 Urinary Function and Symptoms

A statistically significant difference was found between the HIV-positive and -negative women in the experience of urgency prior to the index pregnancy (p=0.01; Table 5). A total of 15 (22.1%) women experienced urgency in the entire cohort, with only eight out of 54 HIV-negative women (14.8%) experiencing urgency, while seven of the 14 HIV-positive women (50%) reported experiencing urgency (p=0.01; Table 5). Eight (14.8%) of the HIV-negative women also experienced urge incontinence, and three (21.4%) of the HIV-positive women suffered from urge incontinence (p=0.68; Table 5).

There was no difference in urge or stress incontinence between the two groups (Table 5). The incidence of both stress and urge incontinence was 16.2% across the entire cohort (Table 5). The most prominent urinary symptoms for the entire sample were double-voiding (13.2%) and post-micturition dribbling (11.8%). Less commonly, straining (5.9%), hesitancy (7.4%), poor stream (5.9%) and incomplete emptying (5.9%) were reported by the cohort. There was however no significant difference in these symptoms between the two groups (Table 5).

Table 5 Pre-pregnancy urinary function and symptoms

	Total Sample (n=68)	HIV Pos (n=14)	HIV Neg (n=54)	p-value
Mean Frequency daily (#)	3.9	3.9	3.9	0.45*
Mean Nocturia (#)	1.1	1.4	1.0	0.16*
Urgency	15 (22.1%)	7 (50.0%)	8 (14.8%)	0.01†
Urge Incontinence	11 (16.2%)	3 (21.4%)	8 (14.8%)	0.68†
Stress Incontinence	11 (16.2%)	2 (14.3%)	9 (16.7%)	1.00†
Straining	4 (5.9%)	1 (7.1%)	3 (5.6%)	1.00†
Hesitancy	5 (7.4%)	0	5 (9.3%)	0.58†
Poor Stream	4 (5.9%)	1 (7.1%)	3 (5.6%)	1.00†
Double Voiding	9 (13.2%)	2 (14.3%)	7 (13.0%)	1.00†
Incomplete Emptying	4 (5.9%)	1 (7.1%)	3 (5.6%)	1.00†
Post-micturition Dribbling	8 (11.8%)	3 (21.4%)	5 (9.3%)	0.35†

*Mann-Whitney Test
†Fisher's Exact Test

The mean number of voids per day was 3.9, which was comparable between the two groups (p=0.45; Table 5). The mean number of voids during the night was 1.1, again comparable between the HIV-positive and HIV-negative groups (p=0.16; Table 5).

3.5.4 Sexual Function

The mean scores on the Abbreviated Sexual Function Questionnaire (ASFQ) were higher in the HIV-negative group for 13 out of the 15 domains (Table 6). However, only two of these domains reached statistical significance: those for the *frequency* of experiencing vaginal lubrication during intercourse (Domain 11; p=0.02), and the *quantity* of "pulsating/tingling" in

the vaginal/genital area during intercourse (Domain 10; p=0.04) (see Table 6). The *frequency* of vaginal/genital "pulsating/tingling" was higher in the HIV-negative group, but did not reach statistical significance (Domain 9; p=0.06).

Table 6 Abbreviated Sexual Function Questionnaire Mean Scores

Mean Score over a 4 week period[§]	Total Sample (n=68)	HIV Pos (n=14)	HIV Neg (n=54)	p-value*
1. Frequency of pleasurable thoughts about sexual activity (1-5)	3.0	3.0	3.1	0.82
2. Desire to be sensually touched or caressed (1-5)	3.2	3.1	3.3	0.48
3. Desire to participate in sexual activity (1-5)	3.1	3.1	3.0	0.90
4. Frequency of initiation of sexual activity (1-5)	2.4	1.9	2.6	0.09
5. Frequency of intercourse with vaginal penetration (0-6)	1.9	2.0	1.9	0.72
6. Glad anticipation of sexual activity (1-5)	3.2	2.7	3.3	0.07
7. Frequency of vaginal warmth during sexual activity (0-5)	3.0	2.4	3.1	0.09
8. Quantity of vaginal warmth during sexual activity (0-5)	2.5	2.4	2.5	0.68
9. Frequency of vaginal/perineal "pulsating/tingling" sensation during sexual activity (0-5)	2.0	1.5	2.2	0.06
10. Quantity of vaginal/perineal "pulsating/tingling" sensation during sexual activity (0-5)	2.0	1.5	2.2	0.04
11. Frequency of vaginal wetness/lubrication during sexual activity (0-5)	3.4	2.8	3.6	0.02
12. Quantity of vaginal wetness/lubrication during sexual activity (0-5)	2.8	2.5	2.9	0.14
13. Frequency of experiencing orgasm (0-5)	2.8	2.3	3.0	0.09
14. Quality of orgasms experienced (0-5)	3.3	2.8	3.4	0.44
15. Ease of reaching orgasm (0-5)	2.7	2.1	2.8	0.14

*Mann-Whitney
[§]Score range given in brackets

The only two domains in which the HIV-positive women scored higher AFSQ mean scores, were in the desire to have intercourse (Domain 3), and the frequency of intercourse (Domain 5) (Table 6). These higher scores also did not reach statistical significance.

3.6 Postpartum Healing and Functional Assessment

3.6.1 Postpartum Clinical Examination

Of the 38 women who were followed up at an average of six weeks postpartum, 28 (77.8%) were completely healed clinically (Table 7). Only two (5.6%) women had evidence of infection, and both of these women were HIV-negative. These were not the two women who were not prescribed antibiotics. Three (8.3%) women had a partial dehiscence of the anal sphincter, and seven (19.4%) had a granuloma (Table 7). Twenty-five of the 36 (69.4%) women followed up had normal sphincter tone, the remaining 11 (30.6%) had decreased sphincter tone (Table 7). Clinically, 27 (75%) women had sphincters that were completely intact, and nine (25%) had a partial defect palpable (Table 7). None of the women had a complete sphincter defect clinically.

At follow-up, 16 (44.4%) women experienced perineal pain to touch (Table 7). The most common area for pain to be felt was at the 10 o'clock through 2 o'clock positions (See Appendix 3). The mean Oxford score for the cohort of women at follow-up was 2.3 (Table 7), with a score range of 0 to 5.

The HIV-positive women had a higher percentage of poorer wound healing than the HIV-negative women (87.5% vs 75.0%; p=0.65) and less evidence of current infection (0% vs 7.1%; p=1.00) (Table 7). They were also more likely to have a partial wound dehiscence (12.5% vs 7.1%; p=0.54), decreased sphincter tone (50% vs 25%; p=0.21), a partial sphincter defect (37,5% vs 21.4%; p=0.38) and more perineal pain (62,5% vs 39,3%; p=0.42) than their HIV-negative counterparts (Table 7). None of these differences were statistically significant (Table 7).

Table 7 Clinical examination findings at 6 weeks postpartum

	Total Sample (n=36)	HIV Pos (n=8)	HIV Neg (n=28)	p-value
Complete healing	28 (77.8%)	7 (87.5%)	21 (75.0%)	0.65†
Current Infection	2 (5.6%)	0	2 (7.1%)	1.00†
Partial Wound Dehiscence	3 (8.3%)	1 (12.5%)	2 (7.1%)	0.54†
Granuloma	7 (19.4%)	1 (12.5%)	6 (21.4%)	1.00†
Normal tone	25 (69.4%)	4 (50.0%)	21 (75.0%)	0.21†
Decreased tone	11 (30.6%)	4 (50.0%)	7 (25.0%)	0.21†
Sphincter completely intact	27 (75.0%)	5 (62.5%)	22 (78.6%)	0.38†
Partial Sphincter defect	9 (25.0%)	3 (37.5%)	6 (21.4%)	0.38†
Complete Sphincter defect	0	0	0	-
Oxford Score	2.3	2.3	2.4	0.72*
Perineal Pain present	16 (44.4%)	5 (62.5%)	11 (39.3%)	0.42†

*Mann-Whitney
† Fisher's exact test

3.6.2 Postpartum Anal Continence Assessment

The mean overall Wexner Score (out of 20) at six weeks postpartum was 1.3 (Table 8). The HIV-positive women had a higher overall Wexner Score at this time, but the difference was not statistically significant (p=0.21) (Table 8).

The mean Wexner Score for solid stool incontinence was 0.3, and this score was higher amongst the HIV-positive women, but not statistically significant (p=0.36) (Table 8). The HIV-positive women also had a higher mean Wexner Score for liquid stool incontinence (0.3 vs 0.2), flatal incontinence (0.4 vs 0.1) and pad usage for purpose of faecal incontinence (0.9 vs 0.3), but these differences also did not reach significance (Table 8). The mean Wexner Score

for lifestyle impact was 0.3, again higher in the HIV-positive women but not statistically significant (p=0.18) (Table 8). Only two women had a Wexner score greater than 10, and both of these patients had sustained a 3b tear.

Table 8 Wexner Scores of anal continence at 6 weeks postpartum

Mean Wexner Score[§]	Total Sample (n=36)	HIV Pos (n=8)	HIV Neg (n=28)	p-value*
Overall Wexner Score (0-20)	1.3	3.3	0.8	0.21
Solid Stool Incontinence (0-4)	0.3	0.9	0.1	0.36
Liquid Stool Incontinence (0-4)	0.2	0.3	0.2	0.51
Flatal Incontinence (0-4)	0.2	0.4	0.1	0.72
Pad usage for purpose of Faecal Incontinence (0-4)	0.4	0.9	0.3	0.24
Lifestyle Impact (0-4)	0.3	0.9	0.1	0.18

*Mann-Whitney
[§]Score range given in brackets

Table 9 Relative Risk of Anal Continence Events

Women with events (#)	HIV Pos (n=8)	HIV Neg (n=28)	Relative Risk (95% Confidence Interval)
Solid Stool Incontinence	2	1	7.0 (0.98-48.86)
Liquid Stool Incontinence	2	2	3.5 (0.66-17.14)
Flatal Incontinence	1	1	3.5 (0.38-30.63)
Pad Usage for Anal Incontinence	3	2	5.3 (1.16-22.72)
Lifestyle Impact	3	2	5.3 (1.16-22.72)
Wexner Score >10 at 6weeks post-partum	1	1	3.5 (0.38-30.63)

The Relative Risk for solid stool incontinence in HIV-positive compared to HIV-negative women was 7.0, approaching but not reaching statistical significance. The Relative Risk of Lifestyle Impact was significant at 5.3 (95% CI 1.16-22.72), as was the Relative Risk of requiring pad usage for anal incontinence, also being 5.3 (95% CI 1.16-22.72) (Table 9).

3.6.3 Postpartum Pain Assessment

The mean visual analogue pain score on walking was 0.4, on sitting 0.5 and at rest 0.1 (Table 10). The pain scores were lower in the HIV-positive group for sitting (0.3 vs 0.6) and resting (0.0 vs 0.1), but higher for pain on walking (0.5 vs 0.4). These differences did not reach statistical significance (Table 10).

Table 10 Pain scores 6 weeks postpartum by visual analogue scale

	Total Sample (n=36)	HIV Pos (n=8)	HIV Neg (n=28)	p-value*
Walking	0.4	0.5	0.4	0.96
Sitting	0.5	0.3	0.6	0.72
Resting	0.1	0.0	0.1	0.90

*Mann-Whitney

3.6.4 Postpartum Urinary Symptoms and Function

The mean number of daily voids at six weeks postpartum was 3.6 for the 36 women who attended follow-up. The mean number of night-time voids was 1.3 (Table 11).
Ten (27.8%) women said they experienced urgency, but the difference in urgency between the HIV-positive and -negative women was not statistically significant (p=0.11) (Table 11). Six (16.7%) of all the women followed up reported urge incontinence (Table 11).
Three (8.3%) of the women reported stress incontinence, all of whom were HIV-positive, and when compared to HIV-negative women this difference was significant (p=0.01) (Table 11).

The mean frequency of stress incontinence in these women was 4.7, correlating to approximately 2 to 3 episodes of stress incontinence weekly.

Only one (3.6%) woman reported straining, one (3.6%) reported hesitancy, one (3.6%) experienced poor stream and two (7.1%) reported double voiding (Table 11). All these women were HIV-negative, with no significant difference between the groups (Table 11). None of these women reported incomplete emptying or post-micturition dribbling (Table 11).

Table 11 Urinary function and symptoms 6 weeks post-partum

	Total Sample (n=36)	HIV Pos (n=8)	HIV Neg (n=28)	p-value
Mean Frequency daily (#)	3.6	3.0	3.8	0.12*
Mean Nocturia (#)	1.3	1.8	1.1	0.21*
Urgency	10 (27.8%)	3 (37.5%)	7 (25.0%)	0.11†
Urge Incontinence	6 (16.7%)	3 (37.5%)	3 (10.7%)	0.11†
Stress Incontinence	3 (8.3%)	3 (37.5%)	0	0.01†
Mean Frequency of Stress Incontinence (#)	4.0	4.7	0	-
Straining	1 (2.8%)	0	1 (3.6%)	1.00†
Hesitancy	1 (2.8%)	0	1 (3.6%)	1.00†
Poor Stream	1 (2.8%)	0	1 (3.6%)	1.00†
Double Voiding	2 (5.6%)	0	2 (7.1%)	1.00†
Incomplete Emptying	0	0	0	1.00†
Post-micturition Dribbling	0	0	0	1.00†

*Mann-Whitney
†Fisher's Exact Test

3.6.5 Sexual Function postpartum

Only five women had resumed sexual activity at the follow-up visit, three of whom were HIV-positive and two who were HIV-negative (Table 12). The mean ASFQ Scores were higher (indicating better function) in the HIV-negative women than in the HIV-positive women for all

Table 12 Sexual Function 6-week post-partum

Mean Score over a 4 week period[§]	Total Sample (n=5)	HIV Pos (n=3)	HIV Neg (n=2)	p-value*
1. Frequncy of pleasurable thoughts about sexual activity (1-5)	1.4	1.3	1.5	0.80
2. Desire to be sensually touched or caressed (1-5)	2.0	1.3	3.0	0.20
3. Desire to participate in sexual activity (1-5)	1.2	1.0	1.5	0.40
4. Frequency of initiation of sexual activity (1-5)	1.2	1.0	1.5	0.40
5. Frequency of intercourse with vaginal penetration (0-6)	1.0	1.0	1.0	1.00
6. Glad anticipationn of sexual activity (1-5)	1.6	1.0	2.5	0.20
7. Frequency of vaginal warmth during sexual activity (0-5)	1.6	1.7	1.5	0.80
8. Quantity of vaginal warmth during sexual activity (0-5)	1.4	1.3	1.5	1.00
9. Frequency of vaginal/perineal “pulsating/tingling” sensation during sexual activity (0-5)	1.4	1.3	1.5	1.00
10. Quantity of vaginal/perineal “pulsating/tingling” sensation during sexual activity (0-5)	1.4	1.3	1.5	1.00
11. Frequency of vaginal wetness/lubrication during sexual activity (0-5)	2.8	3.0	2.5	0.80
12.Quantity of vaginal wetness/lubrication during sexual activity (0-5)	2.2	1.7	3.0	0.40
13. Frequency of experiencing orgasm (0-5)	1.6	1.0	2.5	0.20
14. Quality of orgasms experienced (0-5)	1.8	1.0	3.0	0.40
15. Ease of reaching orgasm (0-5)	2.0	1.0	3.5	0.20

[§]Score range given in brackets
*Mann-Whitney

domains except Domain 7 of vaginal warmth and Domain 11 of vaginal lubrication (Table 12), where the HIV-positive women scored higher. The highest mean AFSQ scores were 2.8 for the frequency of vaginal lubrication (Domain 11) and 2.2 for the quantity of vaginal lubrication (Domain 11). The lowest overall scores were for the frequency of intercourse (Domain 5; score = 1.0), desire to participate in sexual activity (Domain 3; score = 1.2) and initiation of sexual activity (Domain 4; score = 1.2) (Table 12).

3.7 Relationship of Antibiotic Usage to Clinical Examination Findings

Both of the women who were not prescribed antibiotics attended follow-up. Neither of these women had evidence of infection, wound dehiscence, granuloma, partial sphincter defect or decreased sphincter tone, but one of them experienced pain to touch (Table 13).

Table 13 Relationship of antibiotic usage to clinical findings

	Total (n=36)	Antibiotics (n=34)	No Antibiotics (n=2)	p-value†
Infection present	2 (5.6%)	2 (5.9%)	0	1.00†
Partial Dehiscence	3 (8.3%)	3 (8.8%)	0	1.00†
Granuloma	7 (19.4%)	7 (20.6%)	0	1.00†
Partial Sphincter defect	9 (25.0%)	9 (26.5%)	0	1.00†
Decreased Sphincter Tone	11 (30.6%)	11 (32.4%)	0	1.00†
Pain	16 (44.4%)	15 (44.1%)	1 (50.0%)	1.00†

†Fisher's Exact Test

3.8 Relationship of Overall Wexner Score to Technique of Repair

Seventeen (47.2%) of the women attending follow-up had an end-to-end repair, 11 (30.6%) had an overlap repair and for eight (22.2%) the repair technique was unknown (Table 14). Only two women had an overall Wexner Score >10, one of which was associated with an end-to-end repair, and the other with an unknown repair technique. There was no association between an overall Wexner Score greater than or less than 10, and technique of repair (Table 14).

Table 14 Relationship of Wexner Score to Technique of Repair

	Total (n=36)	Wexner >=10 (n=2)	Wexner <10 (n=34)	p-value[†]
End-to-end	17 (47.2%)	1 (50.0%)	16 (47.1%)	1.00
Overlap	11 (30.6%)	0	11 (32.4%)	1.00
Other	8 (22.2%)	1 (50.0%)	7 (20.6%)	0.40

[†] Fisher's exact test

3.9 Relationship of CD4 count to clinical healing

Table 15 Relationship of CD4 count to clinical healing findings

	CD4<200 (n=3)	CD4 200-500 (n=7)	CD4 >500 (n=4)
Wound not healed	1	0	0
Infection	0	0	0
Dehiscence	1	0	0
Granuloma	1	0	0
Wexner >=10	0	0	1
Urgency pre-pregnancy	0	6	1

One HIV-positive woman was not completely healed, and this patient had a CD4 count less than 200 (Table 15). Another HIV-positive woman had partial wound dehiscence and a

granuloma and she also had a CD4 count less than 200 (Table 15). One patient with a CD4 count greater than 500 was the only HIV-positive patient with an overall Wexner Score more than 10 out of 20 (Table 15). Six HIV-positive women experiencing urgency prior to pregnancy had a CD4 count of 200-500, and one had a CD4 count greater than 500.

3.10 Relationship of Anti-retrovirals to clinical healing

The one HIV-positive woman with a wound not completely healed was on the PMTCT program, and the one patient with wound dehiscence was on HAART. The woman with a Wexner Score >10 and a CD4 count >500 (Table 15), was on the PMTCT program (Table 16).

Table 16 Relationship of Anti-retrovirals to Clinical Healing Findings

	PMTCT (n=5)	HAART (n=3)	Nil (n=0)
Wound not healed	1	0	0
Dehiscence	0	1	0
Granuloma	0	1	0
Wexner >=10	1	0	0
Urgency pre-pregnancy	7	1	0

Chapter 4: Discussion

The incidence of OASI in the literature is reported as 0.6-2.4% (Fornell et al 1996; Sultan et al, 1994; Walsh et al, 1996). This approximates to a minimum of 187 OASIs that can be expected in our service annually. Our study indentified 90 women, giving an incidence of 0.26% annually and 0.24% in the 11 month enrolment period. This incidence is lower than rates reported in the literature, and it is suspected that OASIs are being underreported. A large proportion of our patients delivered with only a midwife in attendance. It is well established in the literature that detection of OASI is higher if doctors are in attendance at delivery (Andrews et al, 2006). We suspect that patients with OASI are being missed in our service.

The incidence of HIV-positive women in our service was 20.6%, compared to the 2006 estimate of 29.1% nationally and 15.2% in the Western Cape (South African Department of Health Study 2006). It is anticipated that the incidence of HIV-positivity is increasing at a rate of 500 000 cases annually (ASSA 2003). This increase in prevalence in the Western Cape is in keeping with the anticipated rate of increasing HIV infection, and the national prevalence.

This study showed that HIV-positive women with an OASI were significantly older in comparison to the HIV-negative women with an OASI (median age 27 years vs 24 years). HIV-positive women with an OASI were also more likely to be of Black ethnicity. This is hard to account for, but the age difference is possibly due to the fact that older women are likely to have been sexually active for longer, and hence have more years of exposure to HIV infection.

The mean CD4 count of the HIV-positive women in this study was 351. By current Western Cape protocols, only women with CD4 counts less than 200, (and most recently 250), qualify for Highly Active Antiretroviral Therapy (HAART). All women in this study were receiving some sort of Antiretroviral Therapy (ART), and the majority were receiving HAART (Figure 2). It is reassuring that HIV-positive pregnant women are having their disease identified and managed, and that HAART is becoming more accessible to our population.

It is of interest that 29.4% of OASIs in this study were 4th degree tears, followed by 3a (23.5%), 3b (19.1%) and 3c tears (14.7%). Scheer at al (2008) report rates of 48%, 42%, 5% and 5% for 4th, 3a, 3b, and 3c tears respectively. It is also unsurprising that the nature of injury was independent of HIV status.

Only 36 of the 68 women enrolled in our study attended follow-up at six weeks. This is a loss to follow-up of 47.0%. The problem of loss to follow up after perineal injury is also reported by other authors (Garcia et al, 2005; Williams et al, 2005). The stress and time constraints of caring for a new baby, a possible reluctance to attend follow-up in the absence of subjective problems, geographic migration and the cost limitations of attending hospital, may be the reasons for this high loss-to-follow-up rate. Unfortunately this large loss to follow-up severely compromises the power of the study and the consequent conclusions we are able to draw from the data.

Pre-pregnancy anal continence assessment using the Wexner score showed no significant anal incontinence, as may be expected in a young, predominantly nulliparous population. Likewise, baseline pain scores were almost negligible.
The postpartum anal incontinence experienced by our cohort as determined by Wexner scores was low in our cohort. The mean overall Wexner score was 1.3. All scores for solid stool, liquid stool and flatal incontinence, as well as pad usage and lifestyle impact were higher in the HIV-positive women. None of these differences were significant however. This is likely related to small numbers of women who attended follow-up. Of note, all mean scores on the Wexner analysis were 0.9 or less, which equates to rare episodes of incontinence, pad use or lifestyle impact ie less than once per month.

We determined the relative risk of HIV-positive women developing solid stool incontinence to be 7.0 (95% CI 0.98-48.86), approaching but not reaching statistical significance. The HIV-positive women did however have a significantly higher relative risk of requiring the use of a pad for anal incontinence events post-injury (RR 5.3; 95% CI 1.16-22.72) and for negative lifestyle impact (RR 5.3; 95% CI 1.16-22.72). Of note is that these calculations of relative risk show slightly different statistical significance levels compared to the p-values reported previously. The reason for this is the statistical error due to the small sample size, where on rare

occasions p-values do not correlate with 95% confidence intervals. The p-value is taken to be more accurate than a confidence interval in this circumstance. Thus we would have to conclude that the differences elicited may in fact not be significant, based on the p-values on Wexner score assessments.

The one HIV-positive woman with a Wexner score greater than 10 had a CD4 count greater than 500, and had received ART as part of PMTCT program only. Again, it is not possible to draw conclusions about the impact of CD4 count and ART on OASI due to the small numbers followed up in this study.

The technique of repair of OASI has been the subject of extensive investigation in the literature. Sultan et al (1999) first proposed the overlap technique as a viable repair option for OASI, and suggested it to be superior to the approximation technique. Subsequently there have been four RCTs investigate this issue, one which also compares different suture materials (Williams et al, 2005). Three of these trials showed no difference between the two techniques at three months follow-up (Fitzpatrick et al, 2000; Garcia et al, 2005; Williams et al, 2005), but the fourth trial showed better outcomes in the overlap group at 12 months post-repair, but not at three months postpartum (Fernando et al, 2006).
Of note, the trial by Fitzpatrick et al (2000) did not repair the IAS separately to the EAS, nor were tears classified into 3a, 3b, 3c or 4th degree tears. Norderval et al (2005) specifically designed their trial to repair the IAS separately to the EAS. They showed better continence outcomes than previously documented figures, with a mean Wexner score of 1.13 in 62 patients followed up at an average of 27 months post repair.

In the Cochrane review, Fernando et al (2006) suggested that the overlap repair may have better functional outcomes, but they did not go as far as recommending it beyond reasonable doubt. Lepistö et al (2008), however, recommended the institution of the overlap technique as the primary method of repair, due to significantly fewer incontinence symptoms experienced in their patients repaired by the overlap technique, as well as a significantly lower incidence of persistent EAS rupture in the overlap group, when compared to patients repaired with an end-to-end technique.

In our study, 26 (38.2%) cases were repaired by the end-to-end technique and 27 (39.7%) using the overlap technique. The method of repair in the rest of the cohort was not documented in the theatre notes. This is in keeping with trends of surgical technique employed that is documented in the literature. The literature further reports that 50% of obstetric consultants and 55% of obstetric and gynaecology trainees use the overlap technique for repair of OASI (Fernando et al, 2002).

It would appear that the overlap technique was more commonly used in the HIV-negative patients than the HIV-positive patients (42.6% vs 28.6%), but this difference was not statistically significant. Since the numbers of this study are small, and the differences in technique employed in the two groups not statistically significant, we will not draw conclusion about the tendency seen in the HIV-negative group. This study was also not designed for this purpose.

Only two women in this cohort were not prescribed antibiotics. This is not in keeping with international standards (Mackenzie et al, 2004; Sultan & Thakar, 2002) or local hospital policies. It is not clear whether these were accidental or purposeful omissions. Commonly used antibiotics were combinations of Ceftriaxone & Metronidazole (43.9%), Amoxycillin & Metronidazole (21.2%), and Ampicillin & Metronidazole (16.7%) (Figure 5). Norderval et al (2005) did not employ routine prescription of antibiotics, and noted wound infection in five of the 74 women in their study. Three of these women had been prescribed prophylactic antibiotics. Four of the five women with wound infections experienced incontinence, and this incontinence was considered severe, with Wexner scores >10 in two of them. The authors felt that the current evidence does not support routine antibiotic prophylaxis, but that in light of the poor outcomes after infection, antibiotic prophylaxis remains a viable proposal. The incidence of wound infection at six weeks in our study was 5.6%, and these women were both HIV-negative and had received prophylactic antibiotics (Table 7).

The most interesting and unexpected finding in the pre-pregnancy urinary functional assessment was that of significantly higher rates of urgency in the HIV-positive women (p=0.01). This was not associated with urge incontinence.
The reason for this difference is not entirely understood, and has not previously been documented in HIV-positive women. All the women experiencing urgency had CD4

counts above 200 (Table 15), and only one of them was on HAART (Table 16). This finding may be a confounding error due to the HIV-positive women being significantly older than the HIV-negative women at baseline (27 cf 24). It is unclear whether this 3 year age disparity alone could account for this difference.

Hermieu et al (1996) investigated a range of micturition disturbances in 39 HIV-positive patients (predominantly male). Twenty-seven patients had urological abnormalities including what they termed hyperactive bladder (63.0%), detrusor sphincter dyssynergia and a noncontractile hypoactive bladder, amongst others. A neurological diagnosis was identified in 61.5% of the 27 patients (specifically cerebral toxoplasmosis and HIV encephalitis). Voiding disturbances varied in the study, but 41% of the patients experienced frequency with urgency and incontinence. They conclude that "urgency probably is related to detrusor hyperactivity and can be treated adequately by anticholinergic medications" (Hermieu et al, 1996:158).
It cannot be established whether abnormal neurology is an aetiological factor in our patients, as urgency was an isolated symptom in the absence of straining, hesitancy, incomplete emptying etc. It would also be expected that if neurology were implicated in these patients, the effect would have persisted postpartum. However the lack of this finding postpartum may be due to the low follow-up numbers. Acute urinary retention has been associated with HIV-seroconversion (Lebovitch and Mydlo 2008).

The antiretroviral drug Indinavir has been associated with urgency and urolithiasis, but the majority of our patients experiencing urgency were not on HAART, and none on Indinavir (Jaradat et al, 2000; Lebovitch and Mydlo 2008).

It is possible that undiagnosed urinary tract infection (UTI) may have been responsible for the urgency in our cohort. Fabian et al (2009) determined that 30% of HIV-positive, ART-naïve patients had leukocyturia on urinary dipstix screening. Of these patients, 29.1% cultured an infective organism. A potential relationship between tuberculosis and sexually transmitted infection with sterile leukocyturia was postulated, and the study recommended that urine dispstix screening be employed in the care of HIV-positive women. Lebovitch and Mydlo (2008) report UTIs to be most common when CD4 count is less than 500, with an incidence of UTI of 17%. They also comment that most voiding symptoms are related to UTI, or neurological

involvement. It is remarkable that there is very little other data on the incidence of UTI in HIV-infected women.

A Zambian study in 1991 reported a uniformly congested cystoscopic appearance of the bladder mucosa in HIV-positive patients with painful urinary frequency, suprapubic pain and haematuria. This had not previously been documented. There were no associated bladder ulcers and patients had a normal bladder capacity. A non-specific histological appearance similar to that of interstitial cystitis was seen, except that mast cells were absent in all samples (Elem et al, 1991).
There was no other information in the literature on painful bladder syndrome, interstitial cystitis and the overactive bladder syndrome in association with HIV-infection. Bladder pain was not assessed by our study, and this may be a useful and interesting symptom to investigate in a future study. Clearly there remains much work to be done in the area of HIV, and its association with UTIs and urinary symptoms.

Urinary incontinence appears to be associated with OASI. In 2008, Scheer et al, showed OASI to be an independent risk factor for stress urinary incontinence (SUI) and poorer lifestyle impact scores at 10 weeks postpartum in a group of 100 women with OASI when compared to a 104 controls. Tetzschner et al (1996) demonstrated SUI in 18%, urge urinary incontinence (UUI) in 1%, and mixed incontinence in 13% of their subjects between two and four years postpartum. They also demonstrated an association between incontinence and a higher degree of perineal injury.
Wagenius and Laurin (2003) on the other hand, showed no difference in urinary continence between women with OASI and controls at four years postpartum. Borello-France et al (2006) also did not detect a difference at six weeks and six months postpartum in their study of women with OASI and controls. The rate of postpartum SUI in our cohort was 8.3%, with significantly more HIV-positive women experiencing SUI (p=0.01). Again, this could be accounted for by the HIV-positive women being an average of 3 years older, however this difference was not evident at baseline, when in fact the number of women assessed (68) was greater. Only 28 women attended follow-up, and yet this difference was still found to be significant. The rate of urgency at follow-up was higher than at baseline (27.8% vs 22.1%), but at the postpartum assessment the significant difference between HIV-positive and negative women no longer reached significance. The rate of postpartum urge

incontinence across the cohort was 16.7%. Baydock et al (2009) showed a rate of 12% for UUI and 23% for SUI in follow-up of 632 women without OASI 4 months postpartum. The higher rate of pre-pregnancy urgency and post-partum stress incontinence amongst HIV-positive women could also be an error as a result of the HIV-positive women in this population being older
and mostly confined to one population group, which could have accounted for differences between groups.

We were unable to find any studies on sexual function in low socio-economic, urban South African women. Sexual function is a difficult area to study, as it is a field where anatomy, physiology, psychology, psychiatry, sociology, culture, pathology, religion and inter-personal relationships become intricately and inseparably linked. It is widely acknowledged, however, that there is a paucity of useful data in this field, particularly using standardised definitions.

The American Foundation for Urologic Disease (AFUD) compiled a multidisciplinary consensus guideline in 1999 for diagnosing and classifying sexual dysfunction (Basson et al, 2000). The 4 broad categories of classification include hypoactive sexual desire disorders, sexual arousal disorders, orgasmic disorders and sexual pain disorders. This classification uses similar categories to those of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) of the American Psychiatric Association, but differs in that the latter concentrated on psychiatric disorders and subjective distress, and does not reflect organic pathologies as in the AFUD classification.

Female sexual dysfunction (FSD) has a reported incidence of 25-63% (Heiman 2002; Sidi et al, 2007). In defining dysfunction, it is crucial that the problem causes personal distress to the patient. This makes assessing the literature and recognising true problems difficult. FSD is more common in women who are younger and less frequently sexually active (Laumann et al, 1999; Sidi et al, 2007). However, Sidi et al (2007), report higher educational status, a longer marital relationship, 4+ children, and an older partner as risk factors for FSD. Laumann et al (1999), on the other hand, showed higher education and marriage to be associated with less FSD. Derogatis and Burnett (2008) showed sexual dysfunction to increase with age, but that the associated

personal distress of these symptoms decreased. West et al (2004) reported variable effects of marriage on FSD. They also comment on the techniques of collecting data about sexual dysfunction. FSD was less likely to be reported if the patient was interviewed in person, whereas the incidence was higher if a self-administered questionnaire was used.

In our study of 68 women, the mean scores on the Abbreviated Sexual Function Questionnaire (ASFQ) in the desire domain indicated that the women felt desirous of sexual activity, a desire to be touched, having pleasurable sexual thoughts, and looking forward to intercourse with scores ranging between 3.0 and 3.2 (equating to "sometimes" for all the above domains) in a four week period (Table 6). There was no difference between HIV-positive and negative patients. The prevalence of sexual desire disorders in the literature, ranges from 20 to 69.6% (Derogatis and Burnett, 2008; Hayes et al, 2006; Sidi et al, 2007). Laumann et al (1999), reporting on data from the USA 1992 National Health and Social Life Survey, report low levels of sexual desire in less educated women, Black women, women of lower socioeconomic status (also shown by West et al in 2004) and younger, unmarried women.

Sexual arousal can be present in the absence of sexual desire, and conversely sexual desire can be present in the absence of sexual arousal (Basson et al, 2004). Sexual arousal can be subjective sexual excitement, or physiological effects such as genital lubrication, congestion, and other somatic responses (Basson et al, 2000). The prevalence of decreased sexual arousal ranges from 20 to 60.9% (Hayes et al, 2006; Sidi et al, 2007; West et al, 2004). Arousal is affected by lower levels of sexual activity, and sexual victimisation (Laumann et al, 1999). Of note, the HIV-negative women were significantly more likely to experience lubrication - and a greater intensity of vaginal pulsating/tingling - during intercourse, than the HIV-positive women. The HIV-negative women scored higher in all arousal domains. In the study by Sidi et al, amongst Malaysian women in a primary care setting, and the incidence of decreased vaginal lubrication was 50.4% (2007). They determined that normally lubricated women are 70 times less likely to experience sexual dysfunction than those with decreased lubrication.

Orgasmic dysfunction has a prevalence of 20-59.1% (Hayes et al, 2006; Sidi et al, 2007; West et al, 2004), but is only classified as a disorder if it is persistent or recurrent, is absent despite high levels of arousal, and causes personal distress (Basson et al, 2000). Risk factors for difficulty achieving orgasm include not being married, having a lower level of education and a lower socio-economic status (Laumann et al, 1999).

The mean frequency of achieving orgasm in our study was 2.8, which equates to "often" (Table 6). Twenty-five percent of women reported achieving orgasm with every sexual encounter, and 16% reported never achieving orgasm (Table 6). According to the mean AFSQ scores, orgasms were described as being "moderately pleasurable" when achieved, and that achieving orgasm was "neither easy nor difficult" (Table 6). Again, the HIV-negative women had consistently higher scores in the orgasm domain, but this difference did not reach statistical significance.

There is a paucity of literature on sexual function in HIV positive women. Luzi et al (2009) report a high prevalence of FSD in HIV-positive women, due to self-perceived body image changes, specifically abdominal fat accumulation. There was no association between FSD and clinical staging, CD4 count, viral load or cumulative exposure to ART drug classes.
Bell et al (2006) carried out a retrospective survey of FSD amongst HIV-positive women attending HIV clinics in the United Kingdom. Half the women reported sexual problems or dissatisfaction, and contextual issues appeared to be the predominant factor. Of note, 60% of HIV physicians appeared to neglect enquiring about sexual function.

Given the interplay of psychosocial, circumstantial and likely complicating medical factors in a population of HIV-positive women of lower socio-economic status, it is likely that FSD may be highly prevalent in our population. Though this was not established by the small sample size in this study, it is an area worth investigating further.

In our study, only 5 (13.9%) women had resumed sexual activity at six weeks follow-up, three of whom were HIV-positive and two HIV-negative. This compares to a rate

of 40% sexual activity at seven weeks postpartum by Andrews et al (2008), where degree of perineal injury did not affect resumption of sexual activity; and a rate of 20% reported by Signorello et al (2001) at six weeks postpartum.

In a study by Macarthur and Macarthur (2004), 20% of women with OASI reported perineal pain at six weeks, compared to 13% of women with episiotomies, and 4% of those who had had a first or second degree tear. The relative risk of pain at six weeks after OASI was 5.2 (95% CI 0.6-32.1).
The mean postpartum pain scores in our study population, per 10-point visual analogue scale were 0.4, 0.5 and 0.1 for walking, sitting and at rest, respectively (Table 10). There were no significant differences between the HIV-positive and negative women. Andrews et al (2008) reported mean scores of 1.04, 0.63 and 0.58 on an 11-point visual analogue scale for pain on movement, sitting and at rest for women with a 3a OASI, and scores of 1.23, 1.53 and 1.12 respectively for the women with 3b, 3c or 4th degree OASIs, at seven weeks postpartum.
Perineal pain was elicited to touch on clinical examination in 16 (44.4%) of our 36 women, five (62.5%) of whom were HIV-positive and 11 (39.3%) HIV-negative (Table 7). This difference was not statistically significant.

A clinically detectable partial anal sphincter defect was found in nine (25%) and a complete sphincter defect in none of the women in our cohort. There was no significant difference between the HIV-positive and negative groups.

4.1 Limitations

The study was a predominantly clinical study, since resource constraints prevented objective measurements such as endoanal ultrasonography and manometry. Thus the study relied heavily on questionnaires as measurement tools. This could have introduced measurement bias, though the design of the study attempted to be minimise this. Patients completing the questionnaire could have made errors in recall of their pre-pregnancy functional status. The tools used could have been inadequately sensitive measures, though to prevent this we used validated tools elsewhere described and used. Patients were spoken to in private and every attempt was made to minimise any embarrassment they might feel in reporting their functional status, as the investigators were very aware of the sensitive nature of functions under investigation. The

principal investigators who conducted the questionnaires and follow-up clinical examinations could have been subject to expectation bias, as the study was not blinded. Another limitation was the omission of gathering data on any previous pelvic floor muscle training, or perineal injury other than OASI.

The study was designed to enrol all eligible women with an OASI. Analysis revealed that the 2 groups, HIV-positive and HIV-negative, had significant differences in age and race. This could have contributed to differences elicited in outcomes, as the study was not designed to match or pair study participants. This could have resulted in selection bias which also limits interpretation of results.

The use of questionnaires and predefined tools makes the study easily reproducible. Generalisability of results remains to be confirmed however, as this study lacked sufficient power and is the first and only study to look at the issue of OASI in relation to HIV-infection.

The study is underpowered due to inability to enrol sufficient patients in the enrolment period. Added to this is the massive loss to follow-up of 47%. Although loss to follow-up is elsewhere documented in the literature, this sadly added to the limitation in the interpretation of our results in a study of already small numbers. Due to the lack of power, the results of the study remain speculative, and should be interpreted with caution.

Chapter 5: Conclusion

This study provides useful data on a population on which there is almost no information in the literature. We report on baseline (pre-pregnancy) assessment of female sexual function, urinary function, perineal pain and anal continence in urban, younger, predominantly non-White South African women. Prior to this study, there was no data on the impact of HIV-infection on OASI and perineal pain, and very little on the relationship of HIV to urinary symptoms and sexual dysfunction.

Despite the small sample size, large loss to follow-up and resultant lack of power of the study, we made some interesting findings. With further recruitment more significant findings may yet be elicited, hopefully with sufficient power to be clinically relevant.

From our study, it is suggested that anal continence is impaired after OASI in HIV-positive women. HIV-positive women had higher mean Wexner scores in each domain, and higher relative risks for all domains. Unfortunately the differences failed to reach statistical significance. These findings were despite the absence of infection at six weeks and may be related to HIV being a chronic disease affecting tissues and healing. No relationship with CD4 count or Anti-retroviral Therapy was elicited in this study.

Interesting and not completely understood findings were found in the assessment of pre and post-partum urinary function. HIV-positive women had significantly more pre-pregnancy urgency, a finding not previously documented. Though this did not persist postpartum, it may with further recruitment and a larger sample size at follow-up. Also of interest was the significantly higher incidence of stress incontinence in the HIV-positive women postpartum. This could be an error due to baseline age and race differences in the groups, but it could also be a real difference – possibly related to urinary tract infection, poorer healing in general, or possibly an effect of HIV on the perineal muscles and tissue – and certainly warrants further investigation.

Sexual function data for our population is valuable in that it draws attention to a grossly neglected area of study for our patients. Though more attention is given to female sexual function in the international data, there remains little for women in developing countries, and none for HIV-positive women in developing countries. This study showed interesting trends for sexual function. The HIV-negative women scored higher for all domains except desire and frequency of intercourse. The increased frequency of intercourse could have been instrumental in the cause of the HIV-infection. Two arousal domains did reach significance between the groups, namely frequency of vaginal lubrication during intercourse and quantity of vaginal pulsating/tingling. Both of these domains were higher in the HIV-negative women. These findings all point to a need for further investigation into the sexual functioning of HIV-positive women, with more in-depth quantitative analyses to elicit the exact extent and origins of any dysfunctions.

Perineal pain is a common and often ignored area that affects not only women with OASI, but to a degree, all women who deliver vaginally. Pain scores between our two groups were similar - and reassuringly - low, at six weeks postpartum.

This study is the first in its field, and despite small numbers has already yielded significant, interesting, and concerning findings. We recommend further and ongoing investigation into the impact of HIV on OASI, as well as urinary and sexual functioning in relation to HIV infection.

Appendices

Appendix 1

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Consent Form

Healing and Functional Outcomes after Obstetric Anal Sphincter Injury in HIV-positive vs HIV-negative patients

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- I, _____(name of participant/legal guardian), hereby agree to participate in the above study conducted between Groote Schuur, Mowbray Maternity, and New Somerset Hospitals.
- I have read the attached Patient Information Sheet and this Consent Form, and have had the opportunity to ask questions about the study.
- I consent to disclose my HIV status to the study investigators, as well as any other relevant medical information from my medical records that is of relevance to the study.
- I understand that the study entails personal and private questions, as well as a physical vaginal and rectal examination.
- I agree to my responses being used for medical education and research on the condition that my privacy is respected and anonymity ensured so that I will not be personally identified in/by the study.
- I understand that I am under no obligation to participate in the study.
- I understand that the study will be in two phases approximately 6 weeks apart, and that I have the right to withdraw from the study at any time.
- I understand that I will be reimbursed a fixed, prearranged amount for transport costs incurred by the study only, and receive no other renumeration for participation in the study.

Signature of Participant: _____

Name of person obtaining consent: _____
Signature of person obtaining consent: _____

Name of Witness: _____
Signature of Witness: _____

Date: _____

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA•UNIVERSITEIT VAN KAAPSTAD

Toestemmings Vorm
Studie op
Gesondheid en Werking van die Anus na ‘n Skeur tydens Geboorte in MIV-positiewe en MIV-negatiewe pasiënte

Ondersoekers: **Dr Julie van den Berg**
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- Ek,_____(naam van pasiënt/wettige voog), stem hiertoe in tot deelname aan bogenoemde studie wat gedoen sal word by Groote Schuur, Mowbray Maternity en Somerset Hospitale.
- Ek het die aangehegde Ingligting Stuk gelees en hierdie Toestemmings Vorm, en het die geleentheid gehad om vrae te vra oor die studie.
- Ek gee toestemming dat my MIV status bekend gemaak mag word aan die ondersoekers, sowel as ander relevante mediese en privaat vrae, sowel as vaginale en anale ondersoeke.
- Ek stem toe dat die inligting wat ek gee gebruik gaan word vir mediese onderrig en navorsing op voorwaarde dat my reg op privaatheid gerespekteer word en date k anoniem sal bly tydens die studie.
- Ek verstaan dat ek onder geen verpligting is om deel to neem aan die studie nie
- Ek verstaan dat die studie in twee fases geskied, ongeveer 6 weke uit mekaar en date k die reg het om te enige tyd te onttrek.
- Ek verstaan date k vergoeding sal kry teen ‘n vasgestelde vooraf bepaalde koste vir vervoer slegs vir die doeleindes van die studie en date k geen ander vergoeding sal ontvang vir deelname aan die studie nie.

Handtekening van deelnemer:_____

Naam van persoon wat toestemming kry:_____
Handtekening:_____

Naam van Getuie:_____
Handtekening:_____

Datum:_____

Appendix 2 Patient Information Sheet

1. **Why have I been invited to participate in this study?**
   You have been asked to participate in this study because you have had an anal sphincter injury during your vaginal delivery.

2. **What is an obstetric anal sphincter injury?**
   An obstetric anal sphincter injury is often called a third or fourth degree tear. This means that during vaginal delivery a tear occurs that reaches from the vagina to the anus. The muscle around the anus, that usually keeps the anus closed, is torn.

3. **What are the consequences of an anal sphincter injury?**
   If the muscles of the anal sphincter are not repaired by stitching them back together, there is a high risk that the anal sphincter will not work properly, and this can result in leakage of flatus(wind) and stool(faeces). This is why an anal sphincter injury is always repaired surgically. Even after a surgical repair, there is a risk that some women will experience the problems of leakage of flatus and stool. Other problems can include leakage or urine, pain, and pain on sexual intercourse.

4. **Why does my HIV status need to be known?**
   This study is investigating whether or not being HIV positive causes delayed healing and more problems, after repairing the muscles around the anus.

5. **Who will have access to the information I give?**
   Only the doctors involved in the study will have access to the information provided on the questionnaire. Patient participation is completely anonymous. Once the study is finished, the results will be written up in a thesis, presented to other doctors, and possibly be published in a medical journal.

6. **What will happen if I don't enter the study?**
   Nothing. Patients not joining in the study will still be followed up at Groote Schuur Hospital to make sure that they do not have any complications.

7. **What will happen if I have problems after I leave the hospital?**
   Patients can either attend the follow-up clinic at Groote Schuur Hospital on the day they are given an appointment, or attend any Emergency Casualty Department or Day Hospital if they need care before that time.

8. **What will I gain from being in the study?**
   Joining in the study will not give you any extra medical care or information that is not available to all patients. However, patients in the study will be reimbursed for transport costs to attend the follow-up appointment.

9. **What are the risks to being in the study?**
   There are no real risks to being enrolled in the study.

10. **What is expected from me in the study?**
    All that is expected from you in the study is your consent for us to access confidential information from your medical records, to answer a questionnaire at enrolment, and to complete another questionnaire as well as undergo a vaginal and rectal examination at the 6-week follow-up visit.

11. **How long is my involvement in the study?**
    Involvement in the study only involves the data collected in hospital, and at the 6 week follow-up visit. Any extra hospital visits or follow-up will be as a normal patient and not as part of the study.

12. **Can I change my mind about the study?**
    If you want to stop involvement in the study, you are free to do so at any time.

Pasiënt Inligting Bladsy

1. **Hoekom is ek uitgenooi om deel to neem aan hierdie studie?**
   Jy is uitgenooi on deel to neem aan die studie ondat jy ‘n anale skeuring gehad het tydens normale geboorte.

2. **Wat is ‘n anale skeuring tydens geboorte?**
   ‘n Anale skeuring word dikwels ‘n derde of vierde graadse skeur genome. Dit beteken dat tydens geboorte ‘n skeur ontwikkel vanaf die vagina tot by die anus. Skeuring van die spier wat gewoonlik die anus toe hou vind plaas.

3. **Wat is die gevolge van ‘n anale skeuring?**
   Indien die anal espier nie met steke geheg word nie, is die risiko groot dat die anale spier nie korek sal funksioneer nie. Dit kan veroorsaak dat winde en stoelgang kan voorkom. Om die rede word ‘n anale skeuring altyd chirurgiese herstel. Selfs na chirurgie kan sommige vrouens nog steeds lekking ondervind. Ander probleme sluit in urinale druip, pyn en pyn tydens omgang.

4. **Hoekom moet ek my MIV status bekend maak?**
   Die studie prober bepaal of daar ‘n noemenswaardige verskil is by die hersteltye en komplikasies tydens en na anale skeuring tussen MIV-positiewe en negatiewe persone.

5. **Wie sal toegang hê tot die inligting wat ek verskaf?**
   Slegs die dokters wat betrokke is by die studies sal toegang tot u inligting verkry. Die pasiënt se deelname is anoniem. Die resultat sal in ‘n tesis gebruik word, voorgelê word aan ander dokters, en moontlik in ‘n mediese joernal gepubliseer word.

6. **Wat sal gebeur as ek nie deelneem aan die studie nie?**
   Niks. Pasiënte wat nie deelneem nie sal voortgaan op die normale behandeling van die skeur.

7. **Wat gebeur indien komplikasies ontstaan nadat ek die hospitaal verlaat het?**
   Pasiënte kan die Opvolgkliniek besoek soos vir hulle gereël is, of hulle kan by die Ongevalle aanmeld, of die Daghospitaal besoek as hulle hulp nodig het voor hul afspraak.

8. **Watter voordele is daar vir my tydens die studie?**
   Deelname aan die studie gee u nie bykomende toegang tot mediese sorg of inligting wat nie aan ander pasiënte beskikbaar is nie. Pasiënte sal wel verged word vir vervoer kostes om aan opvolgbesoeke deel te neem.

9. **Is daar enige risiko’s vir my verbonde aan die studie?**
   Daar is geen bykomende risiko’s betrokke by die studie nie.

10. **Hoe lank sale k betrokke wees by die studie?**
    Deelname aan die studie sluit slegs in die inligting wat by die hospitaal geneem word en tydens die 6 weke opvolg besoek. Enige ander besoeke of opvolg ondersoeke is vir die pasiënt en vorm nie deel van studie nie.

11. **Kan ek te enige tyd onttrek aan die studie?**
    As u op enige tyd wil onttrek aan die studie is u vry om dit te doen.

Healing and Functional Outcomes after Obstetric Anal Sphincter Injury in HIV Positive vs HIV Negative patients

A prospective case-controlled study.

Part 1 Questionnaire

UNIVERSITY OF CAPE TOWN
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Investigators: Dr Julie van den Berg
Dr Stephen Jeffery
September 2008

Patient Folder Number ☐ Study Number ☐

Date ☐ Pt Phone No: _____

Part 1: Data obtained from folder and/or patient

HIV Status ☐ 1=Positive 2=Negative

If HIV positive, CD4 count ☐ 1= <200 2= 200-500 3= >500

Absolute Value ☐

Antiretrovirals ☐ 1= PMTCT 2= HAART 3= Nil

If HAART, please specify _____

Injury sustained ☐
1= 3rd Degree Tear (3a)
2= 3rd Degree Tear (3b)
3= 3rd Degree Tear (3c)
4= 4th Degree Tear
5=Detail not specified

Technique of Repair ☐ 1= End-to-end 2= Overlap 3=Unknown

Suture Type for anal mucosa _____
Suture Type for IAS _____
Suture Type for EAS _____
Suture for deep subcutaneous tissue _____
Suture type for vagina _____
Suture type for perineum _____

Post-operative antibiotics ☐ 1= Yes 2=No

Specify antibiotics _____

Age ☐

Ethnic Group ☐ 1= Black 2= Coloured
3= White 4= Other _____

Parity ☐

Study Number

Part 2: Data to be obtained from patient

Complete the following questionnaire with regards to status prior to the index pregnancy:

Anal continence (please circle)

The Wexner Score

Type of Incontinence	*Never*	*Rarely* *<1/month*	*Sometimes* *<1/week >=1/month*	*Usually* *<1/day >=1/week*	*Always* *>=1/day*
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

0 = perfect continence
20 = complete incontinence

Perineal Pain (please circle; 0=never; 10=worst imaginable)

Have you ever experienced pain of the perineum on walking?
0 1 2 3 4 5 6 7 8 9 10

Have you ever experienced pain of the perineum on sitting?
0 1 2 3 4 5 6 7 8 9 10

Have you ever experienced pain of the perineum on driving?
0 1 2 3 4 5 6 7 8 9 10

Have you ever experienced pain of the perineum at rest?
0 1 2 3 4 5 6 7 8 9 10

Study Number

Urinary Continence

1. Daily Frequency (number of voids) ☐

2. Nocturia (number of voids) ☐

3. Urgency ☐ 1=Yes 2=No

4. Urge Incontinence ☐ 1=Yes 2=No

Frequency of urge incontinence (please circle)

< 1x per week 2-3 x a week Daily All Day

0 1 2 3 4 5 6 7 8 9 10

5. Stress Incontinence ☐ 1=Yes 2=No

Frequency of stress incontinence (please circle)

< 1x per week 2-3 x a week Daily All Day

0 1 2 3 4 5 6 7 8 9 10

6. Voiding Symptoms

Straining ☐ 1=Yes 2=No

Double Voiding ☐ 1=Yes 2=No

Poor Stream ☐ 1=Yes 2=No

Post Micturition Dribbling ☐ 1=Yes 2=No

Hesitancy ☐ 1=Yes 2=No

Incomplete Emptying ☐ 1=Yes 2=No

Study Number

Sexual Function

1. **Over the last 4 weeks, how often have you had pleasurable thoughts and feelings about sexual activity?**
   Not at all (1) Rarely (2) Sometimes (3) Often (4) Very often (5)

2. **Over the last 4 weeks, how often have you wanted to be sensually touched or caressed by your partner?**
   Not at all (1) Rarely (2) Sometimes (3) Often (4) Very often (5)

3. **Over the last 4 weeks, how often have you wanted to take part in sexual activity?**
   Not at all (1) Rarely (2) Sometimes (3) Often (4) Very often (5)

4. **Over the last 4 weeks, how often have you initiated sexual activity with your partner?**
   Not at all (1) Rarely (2) Sometimes (3) Often (4) Very often (5)

5. **Over the last 4 weeks, how often did you take part in sexual activity with penetration (eg vaginal penetration and intercourse)?**
   Nil (0) 1-2 times (1) 3-4 times (2) 5-8 times (3) 9-12 times (4)
   13-16 times (5) >16 times (6)

6. **Thinking of your sexual life over the last 4 weeks, how often did you look forward to sexual activity?**
   Not at all (1) Rarely (2) Sometimes (3) Often (4) Very often (5)

7. **Over the last 4 weeks, how often did you have a feeling of "warmth" in your vagina/genital area when you took part in sexual activity?**
   I did not take part in sexual activity (-) Not at all (1) Sometimes (2)
   Often (3) Very often (4) Every time (5)

8. **Over the last 4 weeks, in general, how much "warmth" did you feel in your vagina/genital area when you took part in sexual activity?**
   I did not take part in sexual activity (-) None (1) Slightly warm (2)
   Moderately warm (3) Very warm (4) Extremely warm (5)

9. **Over the last 4 weeks, how often did you have a sensation of "pulsating" ("tingling") in your vagina/genital area when you took part in sexual activity?**
   I did not take part in sexual activity (-) Not at all (1) Sometimes (2)
   Often (3) Very often (4) Every time (5)

Study Number

10. Over the last 4 weeks, in general, how much "pulsating" ("tingling") did you notice in your vagina/genital area when you took part in sexual activity?
I did not take part in sexual activity (-) No sensation (1) A mild sensation (2)
A moderate sensation (3) A strong sensation (4) A very strong sensation (5)

11. Over the last 4 weeks, in general, how often did you notice vaginal wetness/lubrication when you took part in sexual activity?
I did not take part in sexual activity (-) Not at all (1) Sometimes (2)
Often (3) Very often (4) Every time (5)

12. Over the last 4 weeks, in general, how much vaginal wetness/lubrication did you notice when you took part in sexual activity?
I did not take part in sexual activity (-) No wetness/lubrication (1)
Slightly wet/lubricated (2) Moderately wet/lubricated (3)
Very wet/lubricated (4) Extremely wet/lubricated (5)

13. Over the last 4 weeks, how often did you have an orgasm when you took part in sexual activity (may be with or without a partner)?
I did not take part in sexual activity (-) Not at all (1) Sometimes (2)
Often (3) Very often (4) Every time (5)

14. Over the last 4 weeks, in general, how pleasurable were the orgasms that you had?
I did not take part in sexual activity(-) Not pleasurable(1) Slightly pleasurable(2)
Moderately pleasurable (3) Very pleasurable (4) Extremely pleasurable (5)

15. Over the last 4 weeks, in general, how easy was it for you to reach orgasm?
I did not have orgasms (0) Very difficult (1) Quite difficult (2)
Neither easy or difficult (3) Quite easy (4) Very easy (5)

Appendix 3 (Part 2 Data Collection Sheet as for Part 1 Data Collection Sheet less demographic data plus postpartum examination data)

Study Number ☐

Part 2: Examination

1. Wound completely healed? ☐ 1= Yes 2= No

2. Evidence of current infection? ☐ 1= Yes 2= No

3. Dehiscence? ☐ 1= Nil 2=Partial 3= Complete

4. Granuloma? ☐ 1= Yes 2= No

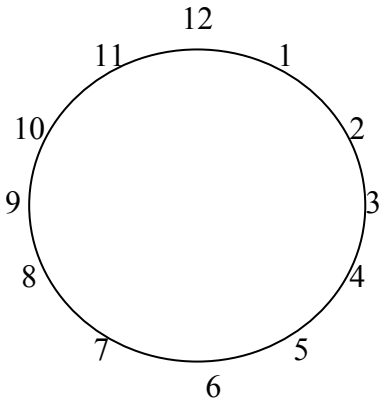
5. Anal Sphincter Tone on pr examination ☐ 1= Normal 2=Decreased

6. Anal sphincter integrity on pr examination ☐ 1= Completely intact 2= Partial defect 3= Complete defect

7. Oxford score for vaginal contraction *(please circle score)*

Score	Findings
0	Nil
1	Flicker of muscle contraction
2	Weak contraction
3	Medium: slight lift of examiner's finger, no resistance
4	Strong: elevation of examiner's finger against light resistance
5	Very strong: elevation of examiner's finger against strong resistance

8. Perineal pain ☐ 1= Yes 2= No
(please circle area of pain)



Appendix 4

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
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12 August 2008

REC REF: 276/2008

Dr J Van Den Berg
Obstetrics & Gynaecology
H Floor
OMB

Dear Dr Van Den Berg

PROJECT TITLE: HEALING AND FUNCTIONAL OUTCOMES AFTER OBSTETRIC ANAL SPHINCTER INJURY IN HIV-POSITIVE VS HIV-NEGATIVE PATIENTS

Thank you for submitting your study to the Research Ethics Committee for review.

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

Approval is granted for one year till the 15th August 2009.

Please submit an annual progress report if the research continues beyond the expiry date. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file.

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

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

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