A COMPARISON OF DEPRESSIVE SCORES AMONGST NEWLY DIAGNOSED HIV-INFECTED AND UNINFECTED PREGNANT WOMEN USING THE EDINBURGH DEPRESSION SCALE.

By

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PREFACE

This study represents original work by the author and has not been submitted in any other form to another University. Where use was made of the work of others, it has been duly acknowledged in the text.

The research described in this dissertation was carried out at Prince Mshiyeni Memorial Hospital, King Edward VIII Hospital, and the Women's Health and HIV Research Group, University of KwaZulu-Natal, South Africa under the supervision of XXX.

_____   _____

Puvashnee Nydoo   **XXX**

(211509780)   **(Supervisor)**

DECLARATION

I, Puvashnee Nydoo declare that:

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DEDICATION

For my grandmother, Narasamma Nydoo.

"Just by changing your perspective, you not only alter your own experience, you can change the

world."...Mingyur Rinpoche

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

HIV   Human Immunodeficiency Virus

AIDS   Acquired Immune Deficiency Syndrome

SIV   Simian Immunodeficiency Virus

UNAIDS   The Joint United Nations Programme on HIV/AIDS

WHO   World Health Organisation

DSM-V   Diagnostic and Statistical Manual for Mental Disorder fifth edition

EDS   Edinburgh Depression Scale

KZN   KwaZulu-Natal

ARV   Anti-retroviral

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ABSTRACT

Objective

Prevalence rates of HIV infection in KwaZulu-Natal are high, with a significant amount of those infected being women of reproductive age. A diagnosis of HIV infection has been associated with an increased risk for the development of depression. Antenatal depression is a serious health concern, as it has the potential to cause wide-reaching adverse consequences for both mother and unborn child. Thus the objective of this study is to compare depressive scores between newly diagnosed HIV-infected and uninfected pregnant women in KwaZulu-Natal to elucidate any association between a new diagnosis of HIV infection and the development of antenatal depression.

Methods

102 newly HIV tested Black African pregnant women were recruited from antenatal clinics at two regional hospitals; further stratified into two cohorts based on HIV status (HIV-infected: n=40; HIV-uninfected: n=62). Women's sociodemographic and clinical data were recorded, before being assessed for depression using an IsiZulu version of the Edinburgh Depression Scale.

Results

Of the sample, 9.8% suffered from depression. Prevalence rates of antenatal depression did not differ significantly between the HIV-infected and uninfected cohorts (p=0.79). A diagnosis of HIV infection (p<0.0001) and maternal age (p=0.03) are risk factors for antenatal depression. Unemployment (p=0.09) is a borderline risk factor for the development of antenatal depression.

Conclusion

Prevalence rates of depression are low in our sample. A new diagnosis of HIV infection in pregnancy places women at an increased risk for the development of antenatal depression. Younger age and unemployed status may also influence depression.

CHAPTER ONE

INTRODUCTION

1.1 Background

It is projected that by 2030, depression and Human Immunodeficiency Virus (HIV) infection will be two of the world's foremost contributors of disability (Mathers and Loncar, 2006). A diagnosis of HIV infection is associated with a surge in depressive symptoms (Psaros *et al*, 2009; Manikkam and Burns, 2012). Pregnancy is commonly associated with depression and is a serious health concern, as it impacts on both maternal, and child development and well-being (Bunevicius *et al*., 2009).

A new diagnosis of HIV infection increases this risk of depression in pregnancy (Ramirez-Avila *et al*., 2012). The consequences of antenatal depression in HIV-infected women, especially those who have not initiated anti-retroviral treatment, include poor birth outcomes, such as miscarriage and prematurity, as well as increased development of postnatal depression (Marcus, 2009), and an increase in disease progression, thus affecting both mother and child. Hence studies that determine if HIV-infected pregnant women are more at risk for developing depression than HIV-uninfected pregnant women are urgently warranted. Furthermore, to the best of our knowledge there are very few studies of depression in HIV-infected pregnant women carried out in KwaZulu-Natal. This study will compare the depressive scores between newly diagnosed HIV-infected pregnant women and HIV-uninfected pregnant women using the Edinburgh Depression Scale (EDS).

1.2 HIV

1.2.1 History/origin of HIV Infection

Acquired Immune Deficiency Syndrome (AIDS) is caused by the progression of HIV infection (Sharp and Hahn, 2011). Since its first diagnosis in 1981, over 30 million people have died from AIDS related issues (UNAIDS and WHO, 2005). The two species: HIV-1 and HIV-2, developed on the African continent as zoonotic infections in primate hosts, emanating from a lentivirus known as simian immunodeficiency virus (SIV) (Sharp and Hahn, 2011). SIV infection is transmitted sexually among primates, however, in contrast with HIV, the primates themselves do not become immune deficient (Wessels, 2014). The butchering and the consumption of the infected primates by humans is thought to be the source of first human infections (Peeters *et al*., 2002). The contagion has since

spread worldwide at an unprecedented rate through sexual contact with infected persons, via infected body substances that come into contact with the bloodstream, broken skin or mucous membranes, as well as via mother to child transmission (HSRC, 2005).

1.2.2 Epidemiology

HIV infection has become one of the world's most dire health and developmental challenges. In 2001, globally 29.8 million people were living with HIV infection. By the end of 2012, an estimated 35.3 million people were infected globally, of which 32 million were adults and 3.3 million were children under the age of 15 years (UNAIDS, 2013). According to latest global estimates from UNAIDS (2015), in 2014 there were a total of 36.9 million infected people, with an estimated 2.0 million new infections being reported in that year alone (5600 new infections daily). These statistics highlight the global impact of HIV; however there are specific regions of the world which are disproportionately impacted by this disease. While new cases have been reported in all regions of the world, the HIV/AIDS epidemic has far-reaching effects in low and middle income countries (L'akoa *et al.*, 2013), with more than 90% of HIV-infected individuals living in the developing world (Wessels, 2014).

1.2.3 The South African context

Sub-Saharan Africa remains the most severely affected region by the HIV infection pandemic, accounting for approximately 70% of people living with HIV infections globally (UNAIDS, 2015). With nearly one in every twenty adults living with HIV, Southern African countries have the highest rates of HIV infection worldwide (Wessels, 2014). In this region, South Africa has been significantly impacted by the HIV/AIDS epidemic, with an estimated 11.2% of the population being infected with HIV (Statistics South Africa, 2015). Being home to the highest number of people living with HIV infection in the world, estimated at approximately 6.19 million in 2015 (Statistics South Africa, 2015), this country is considered the epicenter of the global HIV pandemic. Additionally research indicates that the impact of HIV on mortality in South Africa has been significant, with AIDS accounting for 30.5% of all deaths in 2015 (Statistics South Africa, 2015).

1.2.4 Women and HIV infection

Moreover, women represent approximately half (51%) of adults living with HIV infection and nearly a quarter of new HIV infections worldwide (Centers for Disease Control and Prevention, 2011); with majority occurring in women of reproductive age. With prevalence rates of the virus being three times higher among young women than men of the same age (UNFPA, 2014), it is not surprising that globally, HIV infection is one of the most prominent contributors of maternal death in women of reproductive age (Crompton, 2013). The majority of the estimated 17.4 million women living with HIV globally are from Sub-Saharan Africa, and are of reproductive age (WHO, 2014). According to Chi *et al.* (2013), around 1.5 million HIV-infected women in Sub-Saharan Africa become pregnant each year. In South Africa alone, approximately one-fifth of women in their reproductive ages are HIV-infected (Statistics South Africa, 2015) and recent HIV prevalence rates indicate that up to 22.8% of pregnant women are HIV-infected (Statistics South Africa, 2015). In KwaZulu-Natal province alone, the antenatal rate of HIV infection is approximately 30% (Department of Health, 2012).

1.2.5 HIV diagnosis in pregnancy

Although global HIV testing capacity has increased over time, enabling more individuals to ascertain their HIV status, nearly half of all infected individuals are still unaware of this status. In South Africa it is a standard of care practice for all women attending antenatal facilities to be HIV tested. Hence many women will test for HIV infection for the first time during their pregnancy. A challenge of this diagnosis is that many women will experience serious maternal distress with resultant adverse foetal outcome (Bunevicius *et al.*, 2009).

1.3 Depression

1.3.1 HIV diagnosis and depression

A diagnosis of HIV infection is accompanied by psychological distress (Kotze *et al.*, 2013), with depression being the most common complication (Tate *et al.*, 2003). Spies and Seedat (2014) found that depression is highly prevalent in an HIV-infected population, with HIV-infected individuals being almost twice as likely to be depressed when compared to HIV uninfected individuals (Ciesla

and Roberts, 2001). Depression among these individuals have serious implications for disease progression, as well as quality of life (Bonacquisti *et al.*, 2014).

Suffering from depression should not be confused with everyday bouts of sadness. According to criteria displayed by the Diagnostic and Statistical Manual for Mental Disorder fifth edition (DSM-V) (APA, 2013), major depression is defined as a cluster of symptoms, covering changes in an individual's cognition, affect and behaviour that negatively impacts their daily functioning (educational, social or occupational), which lasts more than two weeks. These symptoms include a pervasive sad or depressed mood, suicidal behaviour, feelings of worthlessness or guilt, difficulty with concentration, loss of energy, a decreased interest in almost all activities, psychomotor retardation or agitation, changes in sleeping patterns (insomnia or hypersomnia), as well as changes in weight (excessive weight gain or loss) or changes in appetite (overeating or undereating). For a diagnosis of major depression to be made, at least five of the above mentioned symptoms must be present daily for more than two weeks (APA, 2013).

1.3.2 Depression in HIV-infected pregnant women

Pregnancy is not always a time of emotional well-being, as more than a third of pregnant women experience substantial depressive symptoms (Manikkam and Burns, 2012), which have been attributed to various psychosocial and biological factors. This highlights the fact that pregnancy on its own carries a risk of depression particularly in the postpartum period without the added burden of a HIV infection diagnosis.

The knowledge and timing of such a diagnosis can have an effect on psychiatric co-morbidities such as depression (Kapetonovic *et al.*, 2014). Studies show that women who are recently diagnosed with HIV infection are at a higher risk of being diagnosed with depression (Ramirez-Avila *et al.*, 2012; Olley *et al.*, 2004). In Zambia, women who knew their status before becoming pregnant were found to be less likely to develop depressive symptoms compared to those diagnosed during pregnancy (Kwalomota *et al.*, 2002). This may be attributed to the relatively short time period for adjustment to

such a diagnosis, the stigma attached to being pregnant whilst HIV-infected (Psaros *et al.*, 2009), as well as the fear of placing the unborn child at risk of HIV infection (Whetten *et al.*, 2008).

Moreover, the impact of a chronic illness, such as that of HIV leads to extensive psychosocial challenges for the individual, which places the mother at a risk of depression during pregnancy (Manikkam and Burns, 2012). In contrast, other studies conclude that there is no significant difference in the rate of depression between a HIV-infected *versus* HIV-uninfected antenatal population (Rochat *et al.*, 2006).

1.3.3 Consequences of antenatal depression in the HIV-infected and uninfected population

Depression in the general population is a considerable health concern. Antenatal depression is even more so, having the potential to compromise the wellbeing of both mother and child (Psaros *et al.*, 2009). These consequential adverse outcomes include obstetric complications such as miscarriage, preterm labour and growth delays (Alder *et al.*, 2007). In addition to the numerous physiological effects that antenatal depression is associated with, depression during pregnancy may also affect a mother's cognitive functioning levels that alter her decision-making capabilities (Manikkam and Burns, 2012). In the case of HIV-infected pregnant women, this impacts the mother's attendance of antenatal facilities as well as a negative adherence of a physician's course of therapy (Natamba *et al.*, 2014), which may aggravate disease progression (Antelman *et al.*, 2007), invariably increasing the risk of adverse maternal and infant outcomes (Field, 2011).

Antenatal depression is an independent risk factor for the development of postnatal depression (Milgrom *et al.*, 2008; Rochat *et al.*, 2013), increasing the risk of development by an estimated 50-60% (Manikkam and Burns, 2012). However, given that traditional forms of antenatal health care with its primary focus placed on physiological health, whilst generally overlooking the psychological health of patients, antenatal depression was regularly underdiagnosed, thus giving considerable attention to depression in the postnatal phase instead (Alder *et al.*, 2011). It is only during the past decade that studies focusing on psychological morbidity among the antenatal population became

more common, with studies indicating that prevalence rates of antenatal depression are higher than that of postnatal depression (Bennett *et al.*, 2004).

In low socio-economic countries such as South Africa (47%), Pakistan (48%) and India (53%), higher rates of antenatal depression are more evident (Rochat *et al.*, 2013; Shah *et al.*, 2011; Gausia *et al.*, 2009), as compared to the prevalence rates recorded in more developed settings, such as 4% in Hong Kong (Lee *et al.*, 2004). However, as 50% of cases of antenatal depression are undetected (Alder *et al.*, 2011) these numbers are probably significantly higher.

1.3.4 Screening for antenatal depression

There is an urgent need to establish whether HIV-infected antenatal women are at a greater risk of depression than HIV-uninfected antenatal women.

Screening is the most widely utilised technique for the early detection of infections and disease. It involves the application of tests, examinations or other procedures that can be promptly applied for the early identification of unrecognised disease or defect (Shah, 1998). However, screening is just a preliminary step in the detection of probable disease and is not a diagnostic instrument (Shah, 1998).

Screening tools for depression were developed as rating scales, allocating numerical values to a range of questions or statements based on the individuals complex feelings, behaviour and affect. However, screening for antenatal depression is not a straightforward task, given that some symptomology of depression may overlap with that of the somatic complaints of pregnancy itself (Psaros *et al.*, 2009). The need for determining if there is a significant difference in the rate of depression between HIV-infected and uninfected pregnant women is highlighted by the fact that depression has been listed as one of the two leading causes of death in antenatal and postnatal women in the United Kingdom (Lewis, 2004). Although a 'gold standard' screening tool for depression in the antenatal population has not yet to be identified, studies have begun to evaluate the use of several depression screening tools that have been developed or modified including that of the Edinburgh Depression Scale (Murray and Cox, 1990).

1.3.4.1 The Edinburgh Depression Scale

This scale was originally established in 1987 and named the Edinburgh Postnatal Depression Scale (Cox *et al.*, 1987), as it was developed as a screening tool for postpartum depression. It is one of most extensively used and researched screening tool amongst pregnant women (Boyd *et al.*, 2005). It has also been validated as a depression screening tool for non-pregnant individuals (Becht *et al.*, 2001), giving rise to a new nomenclature: the Edinburgh Depression Scale (EDS) (Murray and Cox, 1990). This is a 10-item self-rating depression scale that relates to the individuals depressive symptoms during the week prior to administration. The EDS has been validated in both postnatal and antenatal Black South African women (Lawrie *et al.*, 1998; De Bruin *et al.*, 2004; Manikkam and Burns, 2012), and specifically amongst newly diagnosed HIV-infected antenatal women in South Africa (Rochat *et al.*, 2006).

1.4 Study aim and objectives

Numerous studies have concluded that major depression is highly prevalent among the HIV-infected population (Ciesla and Roberts, 2001; Manikkam and Burns, 2012; Spies and Seedat, 2014). Unfortunately there still remains conflicting reports on the impact of a diagnosis of HIV infection on the development of antenatal depression. Whilst some studies have found evidence of an HIV diagnosis increasing the risk of antenatal depression, others report that it had no significant impact on the prevalence of antenatal depression. However, given the serious consequences of antenatal depression in HIV-infected women, the study aim and objectives are as follows:

1.4.1 Aim of the study: To compare depressive scores between newly diagnosed HIV-infected and uninfected pregnant women using the Edinburgh Depression Scale (EDS) in KwaZulu-Natal, South Africa.

1.4.2 Specific objectives:

1. To administer and assess the Edinburgh Depression Scale in newly diagnosed HIV-infected and uninfected pregnant women.
2. To compare depressive scores between the infected and uninfected cohort.
3. To assess intra-group depressive scores with patient demographics.

With the information obtained from the study, we will be able to aid proper diagnosis, management and treatment, thus contributing to an improvement in the quality of life of the depressed mother and

infant. Conducting this study will essentially be a first step in creating a benchmark for screening for depression in the pregnant population, as well in HIV associated pregnancies; thereby facilitating early diagnosis and appropriate treatment.

CHAPTER TWO

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DEPRESSIVE SCORES IN NEWLY DIAGNOSED HIV-INFECTED AND UNINFECTED PREGNANT WOMEN

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Abstract

Background: Prevalence rates of HIV infection in KwaZulu-Natal are high, with a significant amount of those infected being women of reproductive age. A diagnosis of HIV infection has been associated with an increased risk for the development of depression. Antenatal depression is a serious health concern, having the potential to cause wide-reaching adverse consequences for both mother and unborn child.

Aim: To compare depressive scores between newly diagnosed HIV-infected and uninfected pregnant women.

Setting: Antenatal clinics at two regional hospitals in KwaZulu-Natal, South Africa

Methods: A cross-sectional questionnaire based analysis of 102 newly HIV tested Black African pregnant women (HIV-infected: *n*=40; HIV-uninfected: *n*=62) was conducted. Women's sociodemographic and clinical data were recorded, before being assessed for depression using an IsiZulu version of the Edinburgh Depression Scale.

Results: Of the total study population, 9.8% suffered from depression, irrespective of HIV status. Prevalence rates of antenatal depression did not differ significantly between the HIV-infected and uninfected cohorts (p=0.79). A new diagnosis of HIV infection (p<0.0001) and maternal age (p=0.03) were risk factors for antenatal depression. Unemployment was a borderline risk factor (p=0.09) for the development of antenatal depression.

Conclusion: Prevalence rates of depression were low. Knowledge of a new diagnosis of HIV infection at the first antenatal visit places women at an increased risk for the development of depression during pregnancy. Younger age and unemployment influences depression. This study provides an important step in documenting the need

for screening for antenatal depression in HIV associated pregnancies in a South African population group.

Introduction

Women represent approximately half (51%) of adults living with HIV infection worldwide [1]; with the majority of infections occurring in women of reproductive age. Furthermore, the majority of women living with HIV globally are from Sub-Saharan Africa, and an estimated 1.5 million of these women become pregnant each year [2]. In South Africa, one-fifth of women in their reproductive ages are HIV infected and recent HIV prevalence rates indicate that up to 22.8% of pregnant women are HIV infected [3]. In the province of KwaZulu-Natal (KZN) alone, the antenatal rate of HIV infection is approximately 30% [4].

Antenatal depression is a considerable health concern; having the potential to compromise the wellbeing of both mother and infant [5]. Adverse outcomes include obstetric complications such as miscarriage, preterm labour, low birth weight babies and fetal growth restriction; as well a negative effect on the cognitive functioning of the mother [6].

A diagnosis of HIV infection is accompanied by psychiatric distress, with depression being a common complication [7]. A new HIV diagnosis increases this risk of depression in pregnancy [8]. Depression in HIV infected pregnant women can negatively impact the adherence of antenatal regimes, which may aggravate disease progression [9], invariably increasing the risk of adverse maternal and infant outcomes.

The knowledge and timing of this diagnosis can also affect the development of depression. Studies found that women who are recently diagnosed with HIV infection are at a higher risk of depression; whilst women who know their HIV status before becoming pregnant were less likely to develop depressive symptoms [8]. These symptoms were attributed to the relatively short time period for adjustment to the diagnosis, the stigma attached to being pregnant whilst HIV infected [5], as well as the fear of placing the unborn child at risk of HIV infection [6].

However, it is controversial whether HIV infection impacts the frequency of depressive rates in pregnant women. Since KZN is considered to be the global epicentre of the HIV pandemic [4], its high prevalence rates of HIV in pregnancy and the likelihood of the burden of antenatal depression, we are well positioned to study the trio of HIV infection, depression and pregnancy. Thus the aim of this study is to compare depressive scores between newly diagnosed HIV infected and HIV uninfected pregnant women using the Edinburgh Depression Scale (EDS) in KZN to elucidate any association between a new diagnosis of HIV infection and the development of antenatal depression.

Research methods and design

Study design: A cross-sectional questionnaire based analysis of depressive scores in newly HIV tested pregnant women was conducted

<u>Study site and study population:</u> From August to October 2016 a sample of 102 pregnant women (62 HIV uninfected and 40 HIV infected) were recruited from antenatal clinics at two regional hospitals in KwaZulu-Natal, South Africa. Patients were recruited based on the study's inclusion and exclusion criteria. Given the study design, only newly HIV tested women were included. Only Black South African women were included as there is a higher percentage of this population group attending these hospitals than other demographic groups. Additional inclusion criteria included being isiZulu speaking, and period of gestation (either second or third trimester). Pregnant women previously tested for HIV, non-Black South African patients and those that declined entry into the study were excluded. Furthermore, patients in the first trimester of pregnancy, those with medical and surgical complications, as well as individuals with a previous history of psychiatric illness were excluded.

<u>Data collection:</u> While women waited for their routine antenatal appointment, the purpose and nature of the study was explained to the whole group by the research nurse. Research participants were then given individual patient information sheets in isiZulu and invited to participate. Socio-demographic and clinical data including maternal age, gestational age, parity, whether the pregnancy was planned or unplanned, area of residence, level of education, employment status, substance use, relationship status, HIV status, and CD4 cell counts were recorded on a structured data sheet and participants were then assessed for depressive symptomology using the Edinburgh Depression Scale (EDS). This 10-item self-report scale relates to an individual's depressive symptoms during the past 7 days. Each item is scored on a 4-point scale with a total score range of 0 – 30, where a higher score indicates greater distress. It focuses on the individuals cognitive and affective depressive symptoms, whilst omitting somatic symptoms which could be confounded by normal pregnancy-

related changes. It was originally established in 1987 and named the Edinburgh Postnatal Depression Scale, as it was developed as a screening tool for postpartum depression [10]. However, this scale is now also validated as a screening tool for depression during pregnancy [11], giving rise to a new nomenclature: the Edinburgh Depression Scale. It is an easily administered questionnaire, and has been previously validated in antenatal Black South African women [6], and specifically amongst newly diagnosed HIV-infected antenatal women in South Africa [12]. The EDS was translated into an isiZulu version for the purpose of this study and then completed in the form of interviews by each participant with the assistance of a Zulu speaking research nurse. Given the cut-off score for likely depression, women who scored ≥13 were offered referrals to the psychiatric clinic at either hospital.

Data analysis: Data was analysed using GraphPad Prism 5.00 for Windows (GraphPad Software, San Diego California USA) and STATA version 12 (StataCorp LP, College Station, Texas USA). Parametric tests were performed. Continuous variables were described in terms of means ± standard deviations, and categorical variables using their frequencies and percentages. T-tests were generated to examine the associations between categorical variables and depressive scores. Spearman's Correlation Coefficients were generated to determine the association between continuous variables and depressive scores. Frequency distributions were also calculated. Statistical significance was determined by a p-value of < 0.05.

Ethical consideration: Prior to the commencement of study activities, ethical approval (BE271/16) and permission to conduct the study at a large district and a tertiary referral hospital was obtained. All participants signed a written informed

consent form and were ensured confidentiality and anonymity through the use of research codes.

Results

<u>Patient socio-demographic data:</u> Background characteristics of study population are depicted in Table 1. Maternal age of the sample ranged from 17 to 40 years, with a mean ± standard deviation of 25 ±5.30 years. More than two thirds of the participants had completed secondary school education (62.5% HIV-infected versus 69.4% HIV-uninfected); unemployment rate was high across the sample, with 70% for HIV-infected versus 80.6% for HIV-uninfected women. The majority of women were single (90% - HIV-infected versus 93.6% - HIV-uninfected); whilst 80% of HIV-infected and 87.1% of HIV-uninfected women had not planned to fall pregnant. Of the 102 women, 14.7% reported having miscarriages in previous pregnancies, with more cases reported in the HIV-uninfected cohort (16.1%).

Table 1. Background characteristics of study population

Characteristics	HIV-infected (n=40)	HIV-uninfected (n=62)
	n (%) or mean ± SD	
Age (years)	28(4.86)	22(2.83)
Gestational age (weeks)	18(5.31)	20(5.75)
Planned pregnancy (%)		
Yes	8(20)	8(12.90)
No	32(80)	54(87.10)
Area of residence (%)		
Urban	40(100)	57(91.94)
Rural		5(8.06)
Highest level of education (%)		
No formal education	1(2.5)	0(0)
Primary school	1(2.5)	0(0)
Secondary school	25(62.5)	43(69.4)
University	13(32.5)	19(30.6)
Employment status (%)		
Employed	12(30)	12(19.4)
Unemployed	28(70)	50(80.6)
Relationship status (%)		
Single	36(90)	58(93.6)
Married	4(10)	4(6.4)
CD4 cells count (cells/mm3)	425(165.25)	0(0)

Age, gestational age and CD4 cell counts are presented as mean ± SD (Standard deviations). Planned pregnancy, area of residence, level of education, employment status and relationship status are presented as frequencies (n) and percentages (%).

<u>Prevalence and correlates of depression:</u> Evaluation of the EDS demonstrated a Cronbach's alpha of 0.76. As shown in Figure 1, of the sample of 102 women, 10 (9.80%) had an EDS score of ≥13, indicating probable depression; majority falling within the HIV-infected cohort (7.8%) and 18.6% of HIV-infected women displayed symptoms of significant distress. No depression was reported by 50% of HIV-uninfected women. Analysis among women's total depressive scores from the EDS, irrespective of depressive severity, showed a significant association between depression and HIV

status and maternal age, which are further highlighted in figures 3 and 4 respectively. The total depressive scores differed significantly between HIV-infected (M=10.43, SD=3.46, n=40, 95% CI: 9.317393-11.53261) and the HIV-uninfected (M=6.77, SD=3.13, n=62, 95% CI: 5.979836-7.568551) women (p<0.0001). HIV-infected women were more prone to higher scores on the EDS than HIV-uninfected women (t= -5.52, df=100). Total depressive scores differed significantly with maternal age of women at the 0.05 level of significance, indicating that younger women were more inclined to higher scores of depression (r=0.21; p=0.03). There were no significant correlations between level of education (p=0.55); whether pregnancy was planned or not (p=0.87); relationship status (p=0.65); CD4 cell count (p=0.69) and severity of depressive scores. There was a trend association between employment status and total depressive scores (p=0.09). Unemployed women (M=8.55; SD=3.34; n=78; 95% CI: 7.80-9.30) were more depressed than employed women (M=7.08; SD=4.61; n=24; 95% CI: 5.13-9.03).
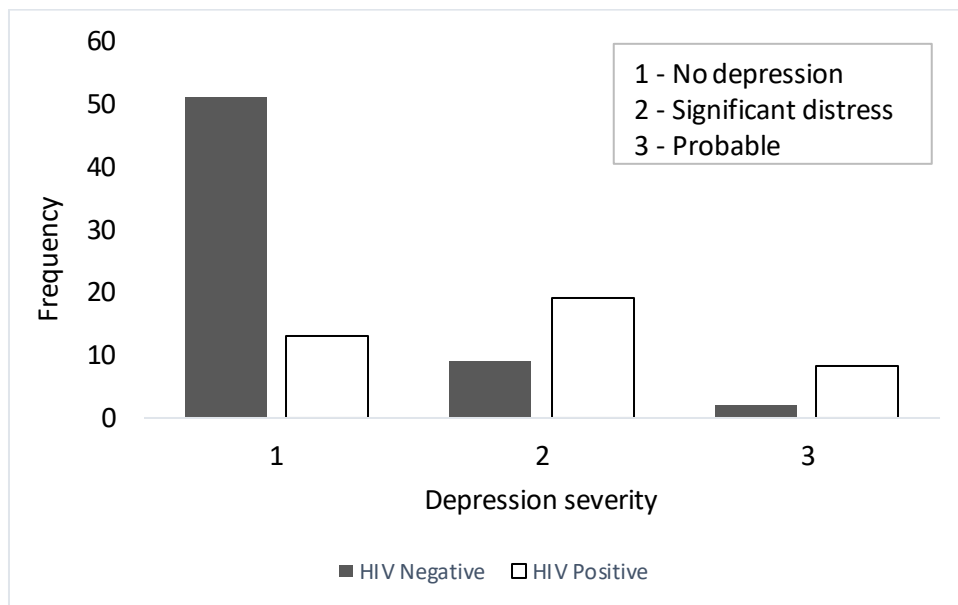
Figure 1. Prevalence of depressive symptoms among 102 newly diagnosed HIV-infected and HIV-uninfected pregnant women in KwaZulu-Natal, South Africa. No depression: EDS scores of 0 to 9; significant distress: EDS scores of 10 to 12; probable depression: EDS scores of 13 to 30.
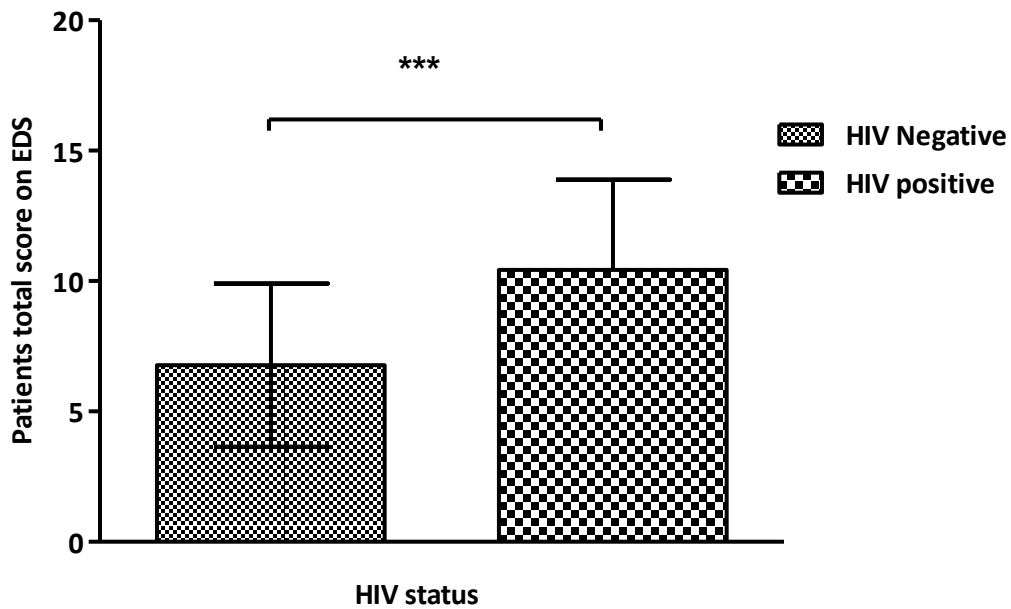
Figure 2. Depressive scores of HIV-infected vs HIV-uninfected pregnant women. Results are presented as mean ± standard deviations. * Total depressive scores differed significantly between the HIV-infected and HIV-uninfected cohorts, p<0.0001.**
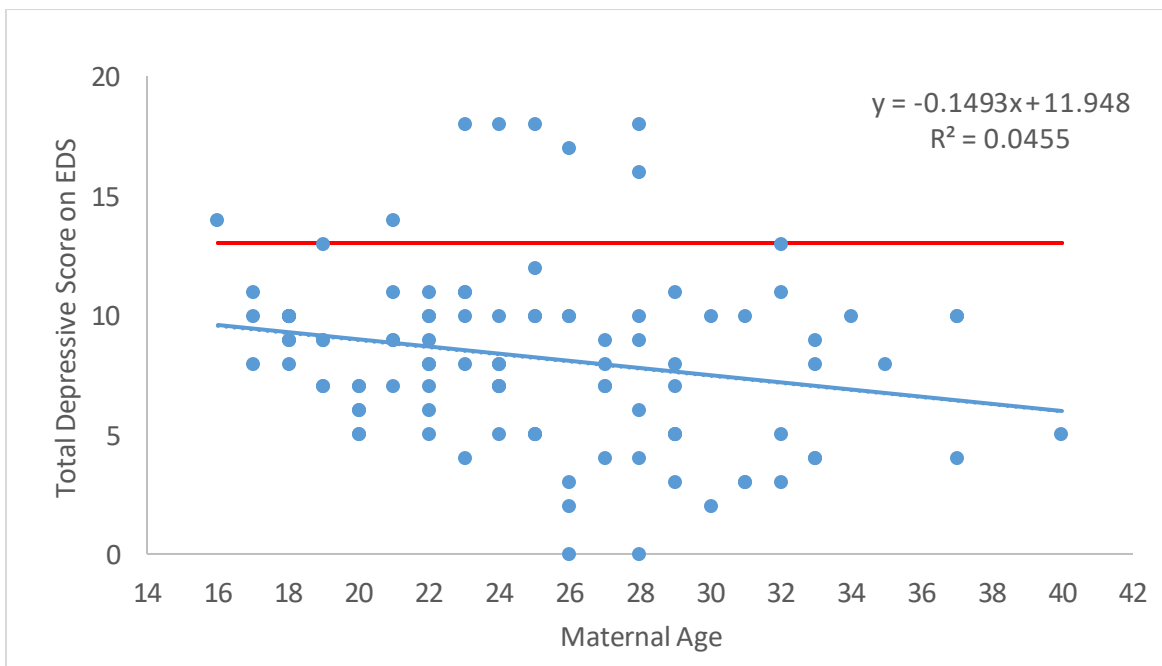
Figure 3. Correlation between maternal age and total depressive scores on the EDS. The red line represents the cut-off score for probable depression (13) on the EDS.* Total depressive scores differed significantly with maternal age of women, p=0.03.

Discussion

<u>Key findings:</u> A new diagnosis of HIV infection during pregnancy can affect the severity of depressive scores. In this study we used the EDS to evaluate the prevalence and severity of depressive scores in newly diagnosed HIV-infected and HIV-uninfected pregnant women in order to elucidate the role of a new diagnosis of HIV infection in the development of depression.

We report a low prevalence rate of depression regardless of HIV status across the study population. Notably, the majority of women displaying scores consistent with depression were from the HIV-infected cohort. However, when only considering women with probable depression (equivalent to a score of ≥13), no significant difference in the prevalence of depression between the HIV-infected compared to the HIV-uninfected cohorts were found (p=0.79).

Moreover, our study reports that women's total depressive scores, irrespective of depressive severity was significantly different between HIV-infected and uninfected pregnant women. Higher depressive scores were demonstrated in the HIV-infected cohort, highlighting that a new diagnosis of HIV infection predisposes a pregnant women to a greater risk of developing depression. Interestingly, among the HIV-infected cohort of our study, the majority of women displayed significant distress rather than probable or severe depression. This was also highlighted in other studies which found a diagnosis of HIV infection to increase the risk and severity of emotional distress in pregnant women [13].

A significant difference in maternal age was noted between the study cohorts. HIV-infected pregnant women were much older than HIV-uninfected pregnant women. Additionally we found that as maternal age increased, the level of depression

decreased, demonstrating that younger women were more inclined to develop depression.

Also as expected, unemployed pregnant women were more depressed than employed women. Although only borderline significant (p=0.09), an unemployed status was noted to have a minor effect on severity of depressive scores.

Discussion of key findings: Our study demonstrates that 9.8% of pregnant women displayed symptoms of depression, irrespective of HIV status. This rate of depression contradicts previous literature in which higher prevalence rates of depression were found in similar settings: 38.5% in urban KZN and 47% in rural KZN [6, 12]. Our low rate of depression may be attributed to South Africa's shift to a low-middle income country, in which prevalence of antenatal depression (15.6%) are similar to our study [14]. This was corroborated by the fact that 95% of women in our sample resided in urban areas and that the majority of women had a moderate-high level of education. Furthermore, the gestational periods at which women were recruited differed with previous studies, which could further explain our low prevalence of depression [8, 15].

We report that total depressive scores on the EDS, irrespective of depressive severity, differed significantly between the HIV-infected and uninfected cohort. This finding is not novel and evidence of elevated depressive scores among HIV-infected pregnant women have been previously reported [6]. It is possible that in our group, because we interviewed only newly diagnosed pregnant women, these results may be attributed to an adjustment reaction to the recent report of a positive HIV diagnosis. Analogous evidence supporting this hypothesis have been noted previously [5]. Nevertheless, our

finding suggests that a new diagnosis of HIV-infection in pregnancy increases the development of depression.

However, we did not find a difference in prevalence rates of depression between the HIV-infected and HIV-uninfected cohorts. Similar findings were reported in HIV-infected and uninfected pregnant women in South Africa and USA [12, 16]. Yet, our finding contradicts other reports, in which prevalence of depression was significantly greater among HIV-infected pregnant women [6, 8]. Our finding might be explained by the province's high HIV prevalence rate, which has destigmatised the disease, thus making a diagnosis of HIV infection more acceptable. Additionally accessibility to antiretroviral therapy and medical regimes has improved in South Africa, and has led to decreased mortality by slowing the progression of HIV to full-blown AIDS; thus shifting the status of a HIV infection from a death sentence to a chronic illness, may also be a factor explaining these findings. Similar correlations are also evident in other studies, in which the idea of HIV infection as a chronic disease has made a diagnosis increasingly normalised [17].

Maternal age is a predictor of depression, indicating that younger women are at a greater risk of developing depression than older women [15]. Our results corroborate these findings, in that younger maternal age was associated with a higher level of depression. The analogous rates of depression between both cohorts may be further explained by the increased maternal age of the HIV-infected cohort.

Unemployed women were at a greater risk of developing depression than employed women in this study. This may be elucidated by the increased financial and social support one receives when having a permanent job. This finding has been

demonstrated previously [14], and is evidence that socio-economic circumstances contribute to the development and severity of depression.

In contrast to previous reports we were unable to demonstrate correlations between level of education; planned pregnancy; relationship status and CD4 cell counts [6, 18]. With regard to education and relationship status, failure to attain any significant difference in our study may be due to the unequal sample size between the study cohorts and the majority of women falling within the secondary school and single categories respectively. Although other studies have found lower CD4 cell counts to be associated with higher rates of depression [18], our study did not find any difference in depressive rates according to CD4 cell count.

Strengths and limitations: This study reports and compares depressive scores of newly diagnosed HIV-infected and HIV-uninfected pregnant women in KZN, South Africa. It provides valuable information on the prevalence; as well as the role played by HIV-infection and other sociodemographic and clinical data as risk factors for depression in pregnant women, in a province that is the foremost contributor to the global HIV pandemic. The EDS also demonstrated good internal reliability, with a Cronbach's alpha of 0.76, indicating that women in this study were consistent in their response.

Our study has limitations. One is the relatively small sample size, accompanied by the unequal sample size between cohorts. The study population was limited to Black African women, therefore it is not known whether the results can be generalizable to other populations. Furthermore, certain variables noted in previous studies that were found to be associated with depression were not assessed in the current study. Finally,

the cross-sectional design of the study limits us to mere associations and prevents actual causal inferences.

Recommendations: Given the likelihood of the burden of antenatal depression on the quality of life of both mother and infant, future studies conducting research on a larger sample involving all three trimesters of pregnancy and following delivery are recommended.

Conclusion: We report a low prevalence of depression in pregnancy, irrespective of HIV status, which may be attributed to the improved perception of HIV infection in South Africa. Additionally we report that a new diagnosis of HIV infection in pregnancy exacerbates the risk for the development of depression. Moreover, we demonstrate that younger maternal age and unemployment increases the development of depression. Furthermore, we report similar rates of depression between HIV-infected and uninfected cohorts. This study provides an important step in documenting the need for screening for antenatal depression across all three trimesters and following delivery in HIV associated pregnancies.

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Contribution to authorship: All authors have contributed significantly to this paper. JM, PN and TN were all involved in the conception and design of the study. PN

was involved in carrying out data collection, analysis and writing up of work. JM and TN were involved in the critical review and editing of the manuscript.

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CHAPTER THREE

SYNTHESIS

The prevalence rate of Human Immunodeficiency Virus (HIV) infection in KwaZulu-Natal Province is high (Department of Health, 2012), with a significant amount of those infected being women of reproductive age (Kalumba *et al.*, 2013). A diagnosis of HIV infection can result in negative psychological outcomes and has been associated with an augmented risk for the development of depression (Kotze *et al.*, 2013; Tate *et al.*, 2003; Psaros *et al.*, 2009; Manikkam and Burns, 2012). A diagnosis of depression is a serious health concern; antenatal depression even more so, as it has the potential to cause wide-reaching adverse consequences for both the mother and the unborn child (Psaros *et al.*, 2009). These include obstetric complications and poor birth outcomes, such as miscarriage, preterm labour and fetal growth restriction, as well as an increased risk for the development of postnatal depression (Alder *et al.*, 2007; Marcus, 2009). In addition to the physiological effects associated with antenatal depression, it may also affect the cognitive functioning of a woman, thus altering decision-making capabilities (Manikkam and Burns, 2012).

With a diagnosis of HIV infection in pregnancy, the negative effects of antenatal depression on a women's cognitive functioning and decision-making capabilities can deter proper attendance and the following of antenatal anti-retroviral regimes; leading to an increase in disease progression, further affecting both mother and child (Manikkam and Burns, 2012; Antelman *et al.*, 2007). Despite this fact, limited data on the prevalence of antenatal depression among the HIV-infected population are available, and it is still controversial whether a diagnosis of HIV infection has an impact on the frequency of depressive rates in pregnant women. Thus this study compares depressive scores between newly diagnosed HIV-infected and uninfected pregnant women in KwaZulu-Natal using the Edinburgh Depression Scale (EDS) to determine if there is an association between a new diagnosis of HIV infection and the development of antenatal depression.

In our study, we found that irrespective of HIV status, only 9.8% of pregnant women displayed symptoms of depression. These results are in contrast to previous reports which found a greater prevalence of antenatal depression in similar settings: 38.5% in urban KwaZulu-Natal; 39% in Cape Town; 41%-47% in rural KwaZulu-Natal; and 48.7% in Mpumalanga (Manikkam and Burns, 2012; Hartley *et al.*, 2011; Rochat *et al.*, 2006; Rochat *et al.*, 2013; Peltzer *et al.*, 2016). The low rate of

depression observed in our study is similar to those found in other low-middle income countries (Fisher *et al*., 2012), which may be attributed to the fact that South Africa is no longer considered a developing country. Moreover, 95% of women in our study population resided in urban areas and the level of education completed by the majority of women was moderate to high, further highlighting this fact. Additionally, the gestational periods at which women were recruited for our study differed from other studies, and could also account for the dramatic differences in prevalence rates of depression (Manikkam and Burns, 2012; Ayele *et al*., 2016). Consequently, more research involving all trimesters of pregnancy are warranted. Nevertheless, the EDS screening tool in our study demonstrated good internal reliability, with a Cronbach's alpha of 0.76, indicating that women in this study were consistent in their response. Notably, the strength of our findings is the fact that we focused on a new diagnosis of HIV infection, before the initiation of anti-retroviral (ARV) treatment.

Our study did not demonstrate a difference in the prevalence of depression between the HIV-infected and HIV-uninfected cohorts. Similar findings were reported in HIV-infected and uninfected pregnant women in South Africa (low-middle income) and the USA (middle-high income), wherein a diagnosis of HIV infection did not predispose the development of depression (Rochat *et al*., 2006; Rubin *et al*., 2011; Bonacquisti *et al*., 2014). Yet, this finding is contradictory to other reports of elevated rates of depression in HIV-infected pregnant women (Kwalomota *et al*., 2002; Olley *et al*., 2004; Whetten *et al*., 2008; Ramirez-Avila *et al*., 2012; Manikkam and Burns, 2012; Natamba *et al*., 2014).

Given that the province of KwaZulu-Natal is considered to be the epicentre of the global HIV pandemic (Department of Health, 2012), a diagnosis of HIV infection is a common occurrence. Support structures are high and the disease has been significantly destigmatised, making a diagnosis of HIV-infection less traumatic. These factors may account for the low prevalence in our study. Furthermore, the accessibility to ARV therapy and medical regimes in South Africa particularly for pregnant women has improved tremendously over the years, leading to decreased mortality rates by slowing down the progression of HIV to full-blown AIDS. This has resulted in the shift of the status of a diagnosis HIV infection from a death sentence to a chronic illness, which might also be a factor contributing to our findings. The normalisation of a diagnosis of HIV infection due to its chronicity was also evident in other studies (Letteney and Heft LaPorte, 2004; Deeks *et al*., 2013).

Maternal age is a predictor of depression, indicating that younger women are at a greater risk of developing depression than older women. (Ayele *et al.*, 2016; Koleva *et al.*, 2011). Our results corroborate these findings, in that younger maternal age was associated with a higher level of depression. The analogous rates of depression between both cohorts may be further explained by the increased maternal age of the HIV-infected cohort.

However, when evaluating overall depressive scores on the EDS, irrespective of depressive severity, we found that scores differed significantly between the HIV-infected and uninfected cohorts. Higher depressive scores were noted among the HIV-infected cohort. This result is not novel and evidence of elevated depressive scores among HIV-infected pregnant women have been previously reported (Rochat *et al.*, 2006 and Manikkam and Burns, 2012). Since we interviewed only newly diagnosed HIV-infected women in this study, it is possible that these results may be attributed to only an adjustment reaction to the recent report of a positive diagnosis. Similar data substantiating this hypothesis have been noted previously (Lyketsos *et al.*, 1994; Psaros *et al.*, 2009). Nevertheless, our finding suggests that a new diagnosis of HIV-infection in pregnancy increases the development of depression.

We also demonstrated that unemployed women in both cohorts displayed elevated scores consistent with significant distress and probable depression on the EDS. These finding are corroborated (Fisher *et al.*, 2012; Peltzer *et al.*, 2016; Olley *et al.*, 2004; Manikkam and Burns, 2012), and is evidence that an individual's socio-economic circumstances may play a role in the development and severity of depression.

In contrast to our findings, the level of education; planned pregnancy; relationship status and CD4 cell counts are found to be risk factors for the development of depression (Manikkam and Burns, 2012; Kapetanovic *et al.*, 2009). With regard to education and relationship status, failure to attain any significant difference may be due to the fact that the majority of women in our study fell within the secondary school and single categories respectively. Nevertheless, this study highlights the high rate of unplanned pregnancies found in this country. However, this was not found to be a risk factor for the development of depression. Additionally, although other studies have found lower CD4 cell

counts to be associated with elevated rates of depression (Kapetanovic *et al*., 2009), we did not find any difference in depressive rates in our population stratified by CD4 cell count.

As far as we are aware this study is only one of the few studies to report and compare the depressive scores of newly diagnosed HIV-infected and HIV-uninfected pregnant women in KwaZulu-Natal, South Africa. This study provides valuable information on the prevalence; as well as the role played by HIV-infection and other sociodemographic and clinical data as risk factors for the development of depression in pregnant women, in a province that is the foremost contributor to the global HIV pandemic. Additionally our methodological tool used for the assessment of depressive symptomology- the EDS, displayed good internal reliability in this study.

Limitations of this study include, the relatively small sample size, accompanied by the unequal sample size between cohorts. Additionally the study population was limited to Black African women, therefore it may not be generalizable to other populations. Finally, the cross-sectional design of the study limits causal inferences.

In conclusion, this study reports a low prevalence of depression across the study population. Similar rates of depression were found between the HIV-infected and HIV-uninfected cohorts. Nevertheless, our findings indicate that a new diagnosis of HIV infection in pregnancy places a woman at risk for the development of depression, exacerbating antenatal depression. This study also demonstrates that younger maternal age and unemployment elevates antenatal depression. Given the likelihood of the burden of antenatal depression on the quality of life of mother and infant, future studies conducting research on a larger sample involving all three trimesters of pregnancy and following delivery are recommended. This study provides a vital step in documenting the need for screening for antenatal depression in HIV associated pregnancies.

CHAPTER FOUR

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APPENDICES

25 July 2016

Ms P Nydoo (211509780)
Discipline of Obstetrics and Gynaecology
School of Clinical Medicine
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Protocol: Comparison of the Edinburg depression scale (EDS) and the Beck depression inventory secondary edition (BDI-II) as screening tools for depression in newly diagnosed HIV positive pregnant women.
Degree: MMedSc
BREC reference **number: BE271/16**

EXPEDITED APPLICATION

The Biomedical **Research** Ethics Committee has considered and noted your application received on 08 April 2016.

The study was provisionally approved pending appropriate responses to queries raised. Your response received 25 July 2016 to queries raised on 20 July 2016 have been noted and approved by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given **full ethics approval.**

This approval is valid for one year from **25 July 2016.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its meeting taking place on **16 August 2016.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor J Tsoka-Gwegweni
Chair: Biomedical Research Ethics Committee

cc supervisor: jmog@ukzn.ac.za
cc postgraduate administrator: molemong@ukzn.ac.za

Biomedical Research Ethics Committee
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EDINBURGH DEPRESSION SCALE*

Also known as the Edinburgh Postnatal Depression Scale (EPDS)*

BLACK DOG INSTITUTE

Today's Date: ____/____/____ **Weeks pregnant:** ____**or weeks postnatal** _____

Surname: _____**Given Name(s):** _____

TOTAL SCORE ☐

INSTRUCTIONS:

Please colour in one circle for each question that is the closest to how you have felt in the <u>PAST SEVEN DAYS.</u>

1. I have been able to laugh and see the funny side of things:
○ As much as I always could
○ Not quite as much now
○ Definitely not so much now
○ Not at all

2. I have looked forward with enjoyment to things:
○ As much as I ever did
○ Rather less than I used to
○ Definitely less than I used to
○ Hardly at all

3. I have blamed myself unnecessarily when things went wrong:
○ Yes, most of the time
○ Yes, some of the time
○ Not very often
○ No, never

4. I have been anxious or worried for no good reason:
○ No, not at all
○ Hardly ever
○ Yes, sometimes
○ Yes, very often

5. I have felt scared or panicky for no very good reason:
○ Yes, quite a lot
○ Yes, sometimes
○ No, not much
○ No, not at all

6. Things have been getting on top of me:
○ Yes, most of the time I haven't been able to cope at all
○ Yes, sometimes I haven't been coping as well as usual
○ No, most of the time I have coped quite well
○ No, I have been coping as well as ever

7. I have been so unhappy that I have had difficulty sleeping:
○ Yes, most of the time
○ Yes, sometimes
○ Not very often
○ No, not at all

8. I have felt sad or miserable:
○ Yes, most of the time
○ Yes, quite often
○ Not very often
○ No, not at all

9. I have been so unhappy that I have been crying:
○ Yes, most of the time
○ Yes, quite often
○ Only occasionally
○ No, never

10. The thought of harming myself has occurred to me:
○ Yes, quite often
○ Sometimes
○ Hardly ever
○ Never

> NB: If you have had ANY thoughts of harming yourself, please tell your GP or your midwife <u>today</u>

Comments: _____
_____

* Murray and Cox 1990   ***** Cox, Holden & Sagovsky 1987

INGXENYE YESIBILI- (uhla)

EDINBURG DEPRESSION SCALE

Lubizwa futhi nge- Edinburgh Postnatal Depression Scale (EPDS).

Usuku: _____/_____/_____   Amasonto ukhulelwe: _____   Noma amasonto ubelethile: _____

SEKUHLANGENE

Sicela uhlikihle kwisikokela esisodwa embuzweni ngamunye osondelene kakhulu nokuthi ubuzizwa unjani ezinsukwini **EZIYISIKHOMBISA EZEDLULE.**

1. Bengikwazi ukuhleka futhi ngibone nokuhlekisa kwaleyonto:

○ Njengoba bekuhlale kwenzeka

○ Akusenzeki njengoba bekwenzeka

○ Akusenzeki kakhulu

○ Akusenzeki kwakhona

6. Izinto ziqale ukubanzima kimi:

○ Yebo, isikhathi esiningi bengingakwazi nokumela isimo

○ Yebo, kwesinye isikhathi bengingakwazi nokumela isimo njengoku-jwayelekile

○ Cha, isikhathi esiningi bengikwazi ukumela isimo ngendlela eyiyo

○ Cha, bengikwazi ukumela isimo kahle njengasekuqaleni

2. Ngikwazile ukuqhubeka nezinto ezingijabulisayo:

○ Njengoba bekuvele kwenzeka

○ Kwehlile kancane kunokujwayelekile/ obekwenzeka

○ Kwehlile kakhulu kunokujwayelekile

○ Sekunzina kakhulu

7. Bengingajabule kangangoba bengisasakwazi nokulala kahle:

○ Yebo, isikhathi esiningi

○ Yebo, kwesinye isikhathi

○ Cha, bekungenzeki njalo

○ Cha, akukaze kwenzeke

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3. Benginokuzisola okungenasidingo uma izinto zingahambanga kahle:

○ Yebo, isikhathi esiningi

○ Yebo, isikhathi esiningana

○ Cha, bekungenzeki njalo

○ Cha, bekungeneki

4. Benginokudinwa noma ngiphatheke kabi kungenasizathu:

○ Cha, akukaze kwenzeka

○ Bekuthuka kwenzeka nje

○ Yebo, kwesinye isikhathi

○ Yebo, isikhathi esiningi

5. Bengizizwa ngisaba noma ngitatazela kungenasizathu:

○ Yebo, isikhathi esiningi impela

○ Yebo, kwesinye isikhathi

○ Cha, bekungenzeki kakhulu

○ Cha, bekungenzeki kwakhona

8. Bengizizwa ngiphatheke kabi noma kungathi ngilahliwe:

○ Yebo, isikhathi esiningi

○ Yebo, isikhathi esiningana

○ Cha, bekungenzeki njalo

○ Cha, akukaze kwenzeke

9. Bengingajabule ngendlela yokuthi bengikhala:

○ Yebo, isikhathi esiningi

○ Yebo, isikhathi esiningana

○ Bekuba yilesosikhathi nje

○ Cha, akukaze kwenzeke

10. Imicabanago yokuzilimaza ike yafika kimi:

○ Yebo, isikhathi esiningana

○ Kwesinye isikhathi

○ Ibifika nje ngalesosikhathi

○ Ayikaze ifike.

Kubalulekile: Uma uke waba **nanoma** yimiphi imicabango yokuzilimaza, sicela ubikele udokotela noma umbelethisi

Comments: _____

_____

* Murray and Cox 1990   * Cox, Holden & Sagovsky 1987