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DEPRESSION AND ANXIETY IN HIV INFECTED INDIVIDUALS ATTENDING HIV TREATMENT FACILITIES AT VARIOUS SITES IN SOUTH AFRICA: OCCURRENCE AND RELATED FACTORS. A DESCRIPTIVE-ANALYTIC STUDY

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A thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfilment of the requirements for the degree of
Doctor of Philosophy

Johannesburg, 2008

Declaration

I, Rita Gillian Marie Thom, declare that this thesis is my own work. It is being submitted for the degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University

Signature

Place:

On the day of 2008

Dedication

This thesis is dedicated to all South Africans affected by the HIV epidemic

Publications and presentations emanating from this thesis

Poster presentation at 7th International AIDS Impact Conference, Cape Town. April 2005: Mental Disorders in HIV-infected individuals ï notes from a focus group discussion with staff at an HIV-treatment centre.

Oral presentation at University of Toronto Department of Psychiatry Grand Ward Round on 19 May 2006: Facing Mental Health Challenges in South Africa.

Poster presentation at American Psychiatric Association Congress, Toronto. 20th to 25th May 2006: Mental Disorders in HIV-infected individuals attending selected HIV-treatment sites in South Africa.

Oral presentation at the University of the Witwatersrand Faculty of Health Sciences Research Day, 23rd August 2006: Mental disorders in HIV-infected individuals in HIV-treatment facilities

Abstract

International literature, most of which originates from First-world countries where HIV predominantly affects socially marginalised minority populations, has well-described the burden of mental disorder, particularly depressive and anxiety disorders in HIV-infected individuals. The few studies conducted in developing countries show contradictory results. This study aimed to describe the occurrence of mental disorders; particularly depressive and anxiety disorders, in a population of HIV-infected individuals attending HIV-treatment sites in Gauteng and Mpumalanga in South Africa from November 2004 to November 2005.

A cross-sectional descriptive-analytic study, it included a clinical diagnostic interview and a semi-structured interview to explore postulated risk and protective factors, including demographic, clinical and psychosocial variables, for depressive and anxiety disorders in HIV-infected individuals. Three hundred and two (302) individuals were interviewed at the Perinatal HIV Research Unitôs associated Wellness clinics and at the Chris Hani Baragwanath Hospitalôs Nthabiseng HIV clinic.

Just over thirty percent of participants had a current mental disorder and the lifetime prevalence of mental disorder was 40%. Almost 17% of participants had a current depressive disorder and almost 16% had a lifetime depressive disorder. The occurrence of major depressive disorder, current and lifetime, was 3.64% and 10.26% respectively. Sixty percent of participants with lifetime major depressive disorder had their first onset after diagnosis of HIV status. The occurrence of current and lifetime anxiety disorder was almost 4%.

Substance use disorders were common, affecting 7.6% of the participants at time of interview. Lifetime prevalence of substance use disorders was 18.9%, suggesting that knowledge of HIV status or other interventions may have resulted in this significant decrease.

Identified significant risk factors for depressive disorder included a history of a lifetime depressive disorder, moderate or severe psychosocial stress and feelings of isolation. Being in a support group was found to be a protective factor against depressive disorder.

While the results in this study are conservative compared to those of other similar South African studies in HIV-infected individuals, there was a statistically significantly increased occurrence of depressive and anxiety disorders (combined) compared to general population prevalence studies of these disorders in South Africa. Ways of improving access to mental healthcare for HIV-infected individuals and the general population, are discussed

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List of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral treatment
ARV	Antiretroviral
CBT	Cognitive Behavioural Therapy
CD4 cells	Helper lymphocytes
CD8 cells	Killer lymphocytes
CES-D	Centre for Epidemiologic Studies ï Depression Scale
CHB	Chris Hani Baragwanath Hospital
CHC	Community Health Centre
CIDI	Composite International Diagnostic Interview
CIS	Clinical Interview Schedule
CNS	Central nervous system
CRF	Case Report Form
DIS	Diagnostic Interview Schedule
DSM	Diagnostic and Statistical Manual
DSM-IV TR	Diagnostic and Statistical Manual for the Diagnosis of Psychiatric Disorders, Fourth Edition, Revised
ECA	Epidemiologic Catchment Area
EDL	Essential Drug List
GAD	Generalised Anxiety Disorder
GCP	Good Clinical Practice
GHQ	General Health Questionnaire
GMC	General Medical Condition
HAART	Highly Active Antiretroviral Treatment
HAD	HIV-Associated Dementia
HAM-A	Hamilton Anxiety Rating Scale
HAM-D	Hamilton Depression Rating scale
HIV	Human Immunodeficiency virus
HSRC	Human Sciences Research Council
ICD	International Classification of Diseases
IDU	Injection Drug User
IHDS	International HIV Dementia Scale
MADRS	Montgomery-Asberg Depression Rating Scale
MCMD	Minor Cognitive Motor Disorder
MDD	Major Depressive Disorder
MDE	Major Depressive Episode
MINI	Mini International Neuropsychiatric Interview
MRC	South African Medical Research Council
MSM	Men who have sex with men
NGO	Non-governmental organisation
NK cells	Natural Killer cells
NOS	Not Otherwise Specified
NRF	National Research Foundation
PCP	Pneumocystis carinii pneumonia
PHRU	Perinatal HIV Research Unit
PLWA	People living with AIDS
PSE	Present State Examination

PTSD	Post-traumatic stress disorder
RDC	Research Diagnostic Criteria
SASH	South African Stress and Health Survey
SCAN	Schedules of Clinical Assessment in Neuropsychiatry
SCID	Structured Clinical Interview for DMS
SRQ	Self-reporting Questionnaire
SSRI	Serotonin Specific Reuptake Inhibitor
SUD	Substance Use Disorder
TAC	Treatment Action Campaign
TB	Tuberculosis
UNAIDS	Joint United Nations Programme on AIDS
WHO	World Health Organisation
WMH	World Mental Health (survey)

CHAPTER 1

INTRODUCTION

1.1 Background

South Africa is an emerging economy in a state of significant transition; from a country isolated by apartheid, to one taking its place on the global playing field. The HIV epidemic in South Africa is one of the biggest challenges facing post-Apartheid South Africa. It impacts at social, political and personal levels. The lack of sufficient trained healthcare professionals and the financial burden of managing over 5 million people infected with Human Immunodeficiency Virus (HIV), now and into the future (UNAIDS/WHO, 2006b:Annexure 2), have created an enormous challenge for the country, and health services in particular, to address. However, this challenge offers opportunities, as it has created an imperative need to develop our health system to provide the best care possible.

South Africa is a middle-income country with a history that resulted in socio-economic class divisions, predominantly along racial lines. While the new democracy has seen the emergence of a more racially integrated middle class, most people in South Africa still live in racially segregated neighbourhoods. The majority of people in South Africa are poor and live in townships, informal settlements and rural areas.

Although HIV in South Africa was initially diagnosed among homosexual males, it is now predominantly found in heterosexual individuals. It has spread throughout the country and affects people at all levels of society. However, the epidemic has mostly affected poor, predominantly black African, communities. These have emerged from a period of political struggle, violence, unrest and economic disruption into a new dispensation, only to be

faced with the ravages of the HIV epidemic. This epidemic is changing the face of society, causing a loss of active, working young adults, a burgeoning population of orphaned or otherwise affected children and potentially serious impacts on the economy.

At a personal level, HIV impacts on individuals, families and communities, which exist within particular contexts shaped by the socio-political environment. HIV is an infectious disease, for which there is currently no cure. Its predominant mode of transmission is through sexual contact, both heterosexual and homosexual (a fact that brings significant prejudice to the fore). At an individual level, psychosocial and physical factors interact. Besides its systemic effects, HIV affects the brain, through direct central nervous system (CNS) infection with HIV and other opportunistic infections (An & Scaravilli, 1997). The psychosocial impact of the disease in South Africa generally occurs in the context of poverty and disadvantage. Until the recent roll-out of antiretroviral treatment, a diagnosis of HIV in South Africa was a death sentence. Despite the current optimism resulting from the recent availability of antiretroviral medications, people continue to die daily and the reality of long-term/life-long treatment of this incurable disorder in large numbers of people in the country has not yet been fully realised.

HIV infection is a condition where the mental health of the infected individual cannot be ignored. International research shows significant mental disorder in people with HIV (Ciesla & Roberts, 2001; Israelski, Prentiss & Lubega, 2007). While Highly Active Anti-Retroviral Treatment (HAART) has saved many from imminent death, and has changed HIV infection into a chronic ñmanageableò disease, international literature indicates that significant mental disorder and suffering persists (Green & Smith, 2004) in people living

with HIV, and ongoing intervention by mental health professionals is still needed. Despite a limited amount of research in this area, this is also likely in developing countries.

Health services in South Africa are planned and implemented according to the premise that most people will access healthcare through the district health care service (Owen, 1995). Primary healthcare services in South Africa currently deal with a significant workload (Day & Gray, 2006). A shortage of human resources is a serious problem and working conditions are very difficult in many areas. It is not surprising that mental healthcare is sidelined in such a situation, when mental illness is not seen to contribute directly to mortality, considerable stigma surrounds mental illness, and its management is believed to be labour-intensive, requiring more time of health workers than physical healthcare does.

Mental health services in South Africa are also inadequate and inequitably distributed (Thom, 2004). In 1994 the country inherited a vertical, primarily custodial, mental health system. The challenge has been to develop a community-based mental health service with initial access to mental healthcare through primary healthcare services (primary mental healthcare) and with provision of the ñleast restrictive care possibleò according to the Mental Health Care Act, No 17 of 2002 (South Africa, 2002). In addition, as well as acute and other specialized inpatient services, more specialized secondary-level community mental health services are needed to support primary mental healthcare services and to coordinate the management of the large numbers of people with serious and chronic mental illness who will no longer be institutionalized for life, and to be a referral resource for primary healthcare services. While the more developed provinces such as Gauteng, Western Cape and KwaZulu-Natal have established secondary-level community mental

health services, less developed provinces rely on primary healthcare services with a limited amount of specialist outreach from inpatient psychiatric facilities.

1.2 Motivation for the study/description of the problem

While international literature on mental disorders in HIV-infected individuals, in particular depression and anxiety, in developed countries abounds, the information on the situation in developing countries is limited. With Sub-Saharan Africa forming the current epicentre of the epidemic ((UNAIDS/WHO, 2006a:2), accurate estimations of the burden of mental disorder in HIV infected individuals are needed. This research project aims to highlight the need for mental health services for people with HIV, in terms of both the quantity and the type of services and to suggest the most cost-effective models for such service-provision. An exploration of factors which may increase the risk of mental disorder, particularly depressive and anxiety disorders, or protect an individual from such conditions would facilitate early identification and intervention and development of preventive interventions to improve mental health in HIV-infected individuals.

1.3 The study context

This study was conducted in Wellness clinics linked to the Perinatal HIV Research Unit and in the Nthabiseng HIV clinic at Chris Hani Baragwanath Hospital (CHB), Soweto. The Perinatal HIV Research Unit (PHRU) was initially established as a research unit in 1996 (Perinatal HIV Research Unit, 2005) to study the impact of HIV and potential interventions in pregnant women and their offspring. Its range of activities was subsequently extended to include prevention of mother to child transmission, voluntary counselling and testing. These are available to everyone. Also included are management of HIV infection in a wide range of people regardless of age or sexual orientation, clinical trials of antiretroviral

medication, wellness clinics, TB treatment, HIV vaccine testing and preventive work to keep people HIV negative.

The PHRU headquarters are based at the Chris Hani Baragwanath Hospital in Soweto, Johannesburg. The PHRU established its first ñWellnessò clinic at the Chris Hani Baragwanath Hospital PHRU site in 2003, before the roll-out of anti-retroviral treatment in the public sector. Additional sites have been established at Weilerôs Farm (in a local authority clinic in an informal settlement south of Johannesburg) at Tintswalo Hospital, Acornhoek in Mpumalanga province (in partnership with the Rural AIDS Development and Action Research (RADAR) programme, and in the Mopani Health District in Limpopo province. These wellness clinics provide a package of services to people from the time of diagnosis of HIV-status. This includes family planning, education on HIV infection, treatment of sexually transmitted infections, TB treatment, nutritional advice, and immune status monitoring. Psychosocial support is provided by HIVSA, a partnering non-governmental organisation, which runs support groups and provides some individual counselling. The clinics generally manage people in the early stages of infection, who are asymptomatic. The aim is to keep these individuals as well as possible for as long as possible. Once a patient becomes immune-compromised or develops AIDS-defining illnesses, and antiretroviral treatment becomes necessary, the person is referred to a suitable treatment point. Before the government roll-out of anti-retroviral treatment, a minority of people could access treatment in the private sector (those who had medical aid insurance or could afford private treatment). The only other access to treatment was through clinical trials. In the early stages, many of these trials used monotherapy, with resultant resistance and implications for treatment later on.

Since the government roll-out was initiated, between April 2004 and April 2005, the Nthabiseng HIV clinic at Chris Hani Baragwanath Hospital has been providing anti-retroviral treatment and, more recently, some of the community health centres in Soweto have also started providing comprehensive HIV/AIDS care, including Anti-Retroviral Treatment (ART). Patients attending PHRU or Weilerôs Farm wellness clinics at the time of this study could be referred to these sites for antiretroviral (ARV) treatment. The ARV roll-out in Mpumalanga province was not as far advanced as in Gauteng and, at the time of data collection, ARV treatment was still available only through clinical trials being conducted at the Wellness clinic site.

The Nthabiseng HIV clinic at CHB has been managing people with HIV infection since the early years of the epidemic. Inpatient and outpatient units at the hospital are the primary referral sources for this clinic, one of the ART sites in Gauteng Province. Thus patients attending this clinic are generally symptomatic. Newly referred patients are initially assessed and staged. Patients requiring ARV treatment are worked up medically and counselled before initiation of treatment.

Overall, the patients attending the wellness clinic at PHRU, Chris Hani Baragwanath (CHB) Hospital, are healthier than those attending the HIV clinic at CHB. However, this is not the case at Weilerôs Farm and Tintswalo, where access to health services is limited.

The data for this study were collected from November 2004 to November 2005. The roll-out of HAART in South Africa began in earnest during this one-year period. This provided a unique opportunity for describing psychopathology pre-HAART and for further studies to track the process as it unfolds. The primary purpose was to identify those at risk of

mental disorder and those needing psychiatric treatment and determine how that treatment could be provided.

1.4 Purpose of study

The aim of the study was to try to find answers to the following questions:

1. Are mental disorders, especially depression and anxiety, common in HIV-infected individuals and are they more common than in the general population in South Africa?
2. Are there particular risk factors associated with the development of these mental disorders (especially depression and anxiety)?
3. Are there any mitigating factors that could protect the HIV-infected individual from developing a mental disorder, particularly depression or anxiety?

1.5 Specific objectives

Primary objectives

These were:

1. To determine the occurrence of mental disorders in general, and depressive and anxiety disorders in particular, in HIV-infected individuals attending selected HIV-treatment facilities in South Africa;
2. To compare the occurrence with similar and existing studies of the prevalence of mental disorders, in particular depressive and anxiety disorders, in the general population in South Africa;
3. To explore factors that may predispose to, or mitigate against the development of mental disorders (in particular depressive and anxiety disorders) in HIV-infected individuals.

Secondary objective

The secondary objective was to use the information obtained from this study to make recommendations on appropriate models of care for depressed HIV-infected individuals.

1.6 Outline of study

This thesis describes current international thinking in the field of depression and anxiety related to HIV-infection. It highlights postulated risk and protective factors and outlines the importance of these disorders in terms of their impact on HIV-infected individuals. The literature review focuses particularly on research conducted in Sub-Saharan Africa. The findings of this research project are discussed in the context of existing knowledge and recommendations are made for further research and for interventions to address the burden of depressive and anxiety disorders in HIV-infected individuals.

The intention of this study is to inform an area of HIV-research that has until now not been explored to any great extent in South Africa in order to provide healthcare professionals working in HIV-treatment facilities with more in-depth knowledge of the mental health needs of HIV-seropositive individuals, thereby enabling them to provide more holistic care for their patients. It is hoped that some of the systemic issues around integrating mental healthcare into general healthcare services will also be addressed.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter reviews the literature on depressive and anxiety disorders in HIV-infected individuals, with particular reference to the context of the HIV epidemic in Sub-Saharan Africa. Relevant literature regarding prevalence of these disorders, their impact, and possible risk and protective factors is also reviewed.

2.2 The HIV pandemic

2.2.1 The global HIV epidemic

Acquired Immune Deficiency Syndrome (AIDS) is a relatively new and unique disease. It was first described in America, in 1981, after a number of young, previously healthy men with homosexual orientation developed pneumocystis carinii pneumonia (PCP) and subsequently died. All had developed severe immunodeficiency which led to the development of opportunistic infection with PCP. Soon afterwards, in central Africa, healthcare workers noted a new fatal disease causing severe weight loss and diarrhoea, which came to be called ñSlims Diseaseò. This was also due to immune-deficiency and it was present in heterosexual people. More and more people began to develop this illness and other conditions associated with immune-deficiency. In September 1983 scientists isolated the human immunodeficiency virus (HIV) and found this to be the cause of this new disease, which they called AIDS (Broder & Gallo, 1984).

Some 25 years later, millions of people have become infected world-wide and AIDS has become the worldôs most serious public health problem. Sub-Saharan Africa (including South Africa) has one of the most severe HIV/AIDS epidemics in the world.

Current global statistics show that an estimated 39.5 million people were living with HIV/AIDS in 2006, of which 37.2 million were adults, and 17.7 million were women. It is estimated that a total of 4.3 million people were newly infected, and 2.9 million people died of AIDS in 2006 (UNAIDS/WHO, 2006a:1).

The profile of HIV infected people in the developed world continues to represent predominantly marginalised groups in society. These include the original population; men who have sex with men (MSM), as well as ethnic minorities, migrants from the developing world, refugees, the homeless (and often mentally ill) and the poor (Green, et al., 2004).

The profile of HIV-infected people in the developing world is much broader. All social strata are affected, although HIV predominantly affects the poor and disadvantaged (who are the majority in these societies). In particular, it affects women on the basis of their biological vulnerability and their social and economic disempowerment in the developing world (Evian, 2000: Chapter 2).

During the past two years, the number of people living with HIV increased in every region of the world. The most striking increases occurred in East and Central Asia and in Eastern Europe. Globally, and in every region, more adult women (15 years or older) than ever before are now living with HIV (UNAIDS/WHO, 2006a:1). Sub-Saharan Africa continues to bear the brunt of the global epidemic. An estimated 24.7 million people in Sub-Saharan

Africa were living with HIV at the end of 2006: 63% of the total global infected population. Approximately 2.8 million additional people were infected with HIV during that year (UNAIDS/WHO, 2006a:2). About 2.1 million people in Southern Africa are estimated to have died of AIDS in 2006. To date, more than twelve million children in Africa have been orphaned by AIDS (UNAIDS/WHO, 2006b: Chapter 4). Globally, one third (32%) of all people with HIV live in Southern Africa, and 34% of all deaths due to AIDS in 2006 occurred there (UNAIDS/WHO, 2006a:3-5).

With the advent of highly active anti-retroviral therapy (HAART), the outcome of HIV diseases in the developed world has changed. Mortality has decreased, and HIV infection has become a chronic ñmanageableò disease. There is, however, considerable morbidity and, as HAART does not rid the body of infection, it is necessary to remain on HAART indefinitely to maintain full viral suppression. The long-term outcome is complicated by side-effects from medication and treatment-resistance (Panther & Libman, 2005).

2.2.2 The HIV epidemic in Africa

The extent of the AIDS crisis is only now becoming clear in many African countries, as increasing numbers of people with HIV are becoming ill. In the absence of massively expanded prevention, treatment and care efforts, the AIDS death toll in sub-Saharan Africa is expected to continue to rise. Indications are that the impact of the AIDS epidemic on these societies will be felt most strongly in the course of the next ten years and beyond. Its social and economic consequences are already widely felt, not only in the health sector but also in education, industry, agriculture, transport, human resources and the economy in general, and it threatens to undermine the gains in development that were underway before the epidemic.

Prevalence is the number of individuals in a population that are affected by a particular disease at a point in time. It is influenced by the number of new cases as well as by the number of deaths. If the time that a person is infected and survives is increased, this will increase the prevalence. Therefore if more people with HIV survive longer due to HAART, the prevalence of the disease will not necessarily decrease, unless the number of new infections is also significantly reduced

Overall, rates of new HIV infections in Sub-Saharan Africa appear to have peaked in the late 1990s, and HIV prevalence seems to be levelling off, albeit at an extremely high level. Stabilization of HIV prevalence occurs when the rate of new HIV infections is equalled by the AIDS death rate among the infected population. This means that a country with a stable but very high prevalence must be suffering a very high number of AIDS deaths each year. Owing to general population growth, although prevalence remains stable, the actual number of Africans living with HIV is rising.

Both HIV prevalence rates and the numbers of people dying from AIDS vary greatly between African countries and large variations exist between the patterns of the AIDS epidemic in different countries in Africa. In some places the HIV prevalence is still growing, while in others it appears to have stabilized, or even declined (probably due in part to effective prevention campaigns). Others countries face a growing danger of explosive increase (Pembrey, Kanabus & Fredriksson-Bass, 2007).

Antiretroviral drugs (ARVs), which significantly delay the progression of HIV to AIDS and allow people living with HIV to live relatively normal, healthy lives, have been available in wealthier parts of the world since about 1996. Distributing these drugs requires

money, a well-structured health system and a sufficient supply of healthcare workers. Most developing countries have struggled to cope with the increasing numbers of people requiring treatment. Fewer than one in five of the millions of Africans in need of the treatment are receiving it. Many millions are not even receiving treatment for opportunistic infections that affect individuals whose immune systems have been weakened by HIV infection. Nonetheless, the overall situation is slowly improving; the number of people receiving ARVs in Africa doubled in 2005 alone (UNAIDS/WHO, 2006b: Chapter 7).

International support has helped in this, with numerous governments and international organizations encouraging progress. In 2003 the World Health Organisation (WHO) initiated the ñ3 by 5ò programme, which aimed to have three million people in developing countries receiving ARVs by the end of 2005. While this target was not reached, a number of African nations made substantial progress under the scheme. A substantial number of people needing ART initiated treatment in Sub-Saharan Africa in 2006, and by the end of December 2006, it was estimated that more than 1.3 million people were receiving treatment (representing about 28% of the treatment need) (WHO, 2007). The latest international target, ñAll by 2010ò, is aiming at universal access to treatment by 2010 (WHO, 2006). Under this programme, it is hoped, considerable progress will be made in Africaôs fight against AIDS.

The major challenges to successfully dealing with the AIDS epidemic are poor healthcare infrastructures, a shortage of healthcare professionals, and the need to ensure the ongoing supply of sufficient quantities of medications. This is critically important because once an individual starts to take ART it must be taken lifelong. Because the risk of resistance is so

high with sub-threshold blood levels of ARV drugs, an interruption in the supply of ARVs to a health service can have very serious consequences.

2.2.3 The HIV epidemic in South Africa

The first case of AIDS was identified in South Africa in 1982. The first infections occurred amongst men who had sex with men (MSM), but it rapidly became a predominantly heterosexual disease. The most rapid increase in South Africaôs HIV prevalence took place between 1993 and 2000, during which time the country was focusing on major political changes. While the attention of South Africans, and the worldôs media, was focused on the political and social changes occurring in the country, HIV was rapidly becoming more widespread (Pembrey, 2007).

Antenatal seroprevalence has been monitored nationally since 1990, when it was found that 0.8% of pregnant women were HIV-positive (National Department of Health, 2000). In 2005 the antenatal seroprevalence was 30.2% (National Department of Health, 2006). The Nelson Mandela HSRC 2005 national household survey of HIV seroprevalence (Shisana, Rehle & Simbayi, 2005) estimated the overall national seroprevalence to be 10.8%. Women between the ages of 15 and 49 years were found to have the highest prevalence (29.5%). It was also noted that the incidence of new HIV infections in the 15 to 24 years age group was eight times higher in females than in males (6.5% vs. 0.8%).

South Africa is currently experiencing one of the most severe AIDS epidemics in the world. By the end of 2005, approximately five and a half million people were living with HIV in South Africa and almost 1 000 AIDS deaths were occurring every day (UNAIDS/WHO, 2006b: Annexure 2).

It is thought that almost half of all deaths in South Africa, and 71% of deaths among those aged between 15 and 49, are caused by AIDS (Dorrington, Johnson & Bradshaw, 2006). As well as the death and suffering that HIV has caused at individual and community levels, South Africaôs AIDS epidemic has also had a substantial impact on the countryôs overall social and economic progress:

- Average life expectancy in South Africa is now 54 years ï without AIDS, it is estimated that it would be 64. Over half of 15 year olds currently are not expected to reach the age of 60 (Centre for Actuarial Research, 2006).
- Between 1990 and 2003, a period during which HIV prevalence in South Africa increased dramatically, the country fell 35 places in the Human Development Index, a global directory that ranks countries according to how developed they are (UNAIDS/WHO, 2006b:Chapter 4).
- Hospitals are struggling to cope with the number of HIV-related patients requiring care. In 2006 a leading researcher estimated that HIV-positive patients would soon account for 60-70% of medical expenditure in South African hospitals (Inter Press Service News Agency, 2006).
- Schools have fewer teachers because of the AIDS epidemic. In 2006 it was estimated that 21% of teachers in South Africa were living with HIV (UNAIDS/WHO, 2006b: Chapter 4).

Antiretroviral treatment became available in the public sector in March 2004, and by March 2005 at least one service point for AIDS related care and treatment had been established in all of the 53 districts in the country (Pembrey, et al., 2007). Recent statistics indicate that by the end of 2006, some 200 000 people (28% of those in need of it) were on

anti-retroviral treatment in South Africa, almost half of them receiving treatment through the private sector or non-governmental organisations (NGOs) (WHO, 2007; Johnson & McLeod, 2007).

2.3 Psychosocial factors in HIV infection

Because of the severity of the disorder, HIV has an impact on any individual who receives a positive diagnosis. The ramifications of a positive diagnosis are many for any individual. It is a serious, life-threatening disorder. Elizabeth Kubler-Ross (1969) and others (Byock, 1996) described the stages that people go through when facing death or bereavement. As part of this process, individuals may experience depressive and anxiety symptoms. The considerable stigma surrounding HIV infection because of the mode of transmission makes it difficult for infected individuals to obtain support in their time of need. It challenges intimate relationships with issues of fidelity and trust that lie at the heart of such relationships. The consequences may be loss of relationships and even, domestic violence. Within the family, partners and children may be infected and many people within one family may die. This results in further losses in terms of childcare, employment, income and often, of the home, for the remaining members of the family. Because sexuality and death are such taboo subjects in most cultures, it may be difficult for individuals and families to address the issues with openness and honesty. This may result in complicated bereavement, anger, distrust and sadness.

Therefore, most individuals diagnosed as HIV-infected could be expected to experience psychological distress. There is no doubt that part of comprehensive HIV treatment should include the provision of emotional or psychological support to all those who are infected. However, differentiation between an expectable and transient reaction in the face of

adversity and a mental disorder requiring an additional psychological or psychiatric intervention is also necessary.

There has been much speculation on the role that mental disorders play in the spread of HIV. It is suggested that people with mental disorders may be more at risk of acquiring the disease as a result of risky sexual behaviour. Evidence from the United States of America indicates that people with severe mental illnesses are at greater risk because of their particular vulnerability (Cournos & McKinnon, 1997). Recent evidence from South Africa shows that depressive and anxiety disorders play a role in the development of risky sexual behaviour (Smit, Myer & Middelkoop, 2006), possibly as a result of lack of concern for the future, or even suicidal ideation. These issues are not within the scope of this thesis, and the primary focus will be on the consequences of HIV infection in terms of depressive and anxiety disorders.

2.4 Depressive disorders in HIV-infected individuals

2.4.1 Introduction

Depression may range from transient feelings of depression as a reaction to life events along a spectrum to a serious life-threatening illness. There are no clear-cut distinctions along this spectrum and to determine the presence of a depressive disorder, psychiatric classification systems depend upon the accumulation of signs and symptoms, as well as intensity, duration and impact of symptoms on functioning.

2.4.1.1 Depressive symptoms vs. depressive illness

Differentiation between feelings of depression/depressive symptoms and a depressive illness is important but is not always clear, particularly in the presence of a medical illness,

where physical symptoms can confound the diagnosis. However, it is clear that depressive symptoms are common in people who are infected with HIV, as they are in other serious medical conditions (Rodin & Voshart, 1986; Israelski, et al., 2007). These symptoms may be a result of biological factors, as well as psychosocial factors that reflect the meaning that a serious medical illness has to a particular individual. Ultimately, differentiation between depressive symptoms and a depressive disorder may not be very important, although the treating clinician must be aware of both. Determining the appropriate type of intervention needed is more important. In some cases, it may be sufficient for the clinician to listen and support; in others, psychotherapy may be the treatment of choice, whereas antidepressant medication, admission to hospital, or even electro-convulsive therapy (and a combination of psychosocial interventions) may be necessary in cases of a serious depressive illness.

2.4.1.2 Interpreting results of prevalence studies of depressive disorders in HIV-infected individuals

Many prevalence studies use screening tools and rating scales (often in the form of self-report questionnaires), because they are quick and easy to administer. However, caution needs to be exercised when interpreting the results of studies that use these instead of diagnostic instruments, as they are likely to overestimate the prevalence of disorders.

2.4.1.3 Depressive disorders in the general population

Over the past fifty years prevalence rates of mental disorders across a range of countries have been studied many times. Studies conducted in the 1970s and 1980s emphasised the uniformity of the prevalence of serious mental disorders across countries and cultures (Harding, De Arango & Baltazar, 1980). This was found to be particularly true for serious

disorders such as schizophrenia, although it was also noted that the presentation and outcome of schizophrenia differed across countries and cultures. It has since been determined that (unipolar) depressive disorders are the commonest mental disorders[1] across the globe and that their prevalence has increased over the years (Lopez, Mathers & Ezzati, 2006). Whether this increase is due to an increase in reporting or whether there is a genuine increase is uncertain. However, the recent World Mental Health (WMH) survey of common mental disorders (which excluded psychotic disorders and disorders of cognitive impairment) in a range of countries (Demyttenaere, Bruffaerts & Posada-Villa, 2004) has highlighted an important fact: the current prevalence of mental disorders, including depression, varies widely across countries. The disorders included in this study were: mood, anxiety, substance use and impulse control disorders, and they were classified as serious, moderate or mild in terms of severity. The prevalence of any disorder in the study in Shanghai was 4.3%, while in the United States of America it was 26.3%. The prevalence in Nigeria (the only African site included) was 4.7%. Prevalence rates in Europe varied considerably by country, as did other sites in the Americas. On average, the rates in Asia, the Middle East and Africa were the lowest, Europe had intermediate rates and the Americasô rates were the highest. The prevalence of mood disorders reflected the same patterns. This study also pointed out that access to treatment is not necessarily determined by severity of disorder, and that this may be dependent on other factors, including social class and healthcare system.

One key issue likely to be raised concerning this apparent disparity in prevalence levels of mood and anxiety disorders across the globe is the role of cultural and linguistic issues in diagnosis and how accurate diagnostic tools developed in Western countries are in

[1] Unipolar depressive disorders are the third most common cause of disability in high income countries, and the seventh most common cause of disability in low and middle income countries.

detecting these disorders. Recent ethnographic research in Uganda has confirmed that a syndrome equivalent to the DSM diagnosis of major depressive disorder is described by local inhabitants in that country (Wilk & Bolton, 2002). However, the ways in which different populations express mental disorders may differ, and diagnostic instruments may not always be sensitive to the different idioms used to describe such phenomena. This continues to pose a major challenge in the field of psychiatric epidemiology.

2.4.1.4 Depressive disorders in medically ill populations (including those with HIV infection)

That depression is common in medically ill populations has been established by numerous research studies (Koenig, Cohen & Blazer, 1993). Studies have shown that up to one third (33%) of medical inpatients report mild or moderate depressive symptoms and one fourth (25%) may suffer from a depressive syndrome (Rodin, et al., 1986). However, much confusion exists regarding the actual prevalence of depressive disorders in the context of a medical illness. This is partly because physical symptoms of the medical illness may overlap with neuro-vegetative features of a depressive disorder and, thus, confound diagnosis, leading to an overestimation of the prevalence of depressive disorders in this population. On the other hand, presentation of symptoms that are not considered core features of depressive illness (for example, unexplained or excessive pain or somatisation) may result in under-diagnosis. Research findings in this area are difficult to interpret and do not provide firm evidence, as a result of differing methodologies, definitions of ñcasenessò, selection bias, the heterogeneity of populations studied (different medical illnesses), the absence of control groups, the subjective nature of reporting symptoms of depression, and the transient nature of depressive symptoms.

Koenig, George and Peterson (1997) demonstrated some of these difficulties when they examined and compared rates of depression, correlates, and course of symptoms in medically ill hospitalized elderly people through use of different diagnostic schemes [inclusive ï including all symptoms meeting criteria for a major depressive episode, etiologic ï excluding disorders due to a general medical condition, substitutive ï substitution of other psychological or cognitive symptoms for physical symptoms ï combinations of these approaches were also tested]. They found that the prevalence of major depression in a medically ill in-patient population (over the age of 60 years) varied from 10% to 21%, depending on diagnostic scheme and, similarly, minor depression varied from 14% to 25%.

The diagnostic strategy that best distinguished a severe and persistent major depression was the exclusive-etiologic approach (elimination of anorexia and fatigue from the list of DSM criteria for major depressive disorder; elimination of a depressive disorder that is clearly due to a general medical condition [an organic mood disorder]). However, this strategy missed 49% of patients with major depression identified by the inclusive approach, almost 60% of whom continued to experience persistent symptoms of depression many weeks after discharge. It was thus concluded that diagnostic strategy affects rates of major and minor depression, with about a twofold difference between the extremes. Therefore, diagnostic strategy should be chosen on the basis of the specific goals and purposes of the examiner. While the exclusive-etiologic approach identifies the most severe and persistent depressions, the inclusive approach is the most sensitive and reliable one and is an intermediate predictor of persistent depression.

Ultimately, it may be difficult to distinguish primary from secondary depressive disorders, but research shows that treatment of both with antidepressant medication is helpful (Rodin, et al., 1986). It is, however, important to identify a mood disorder secondary to a general medical condition, where treatment of the medical condition will result in improvement in the depressive disorder. Discriminating symptoms found to be useful in diagnosing a depressive disorder in the presence of medical illness include: suicidal feelings, sense of failure, and feeling of being punished, diminished social interest, crying, indecision and dissatisfaction.

Other diagnoses with depressive symptoms to consider in the context of a medical illness include adjustment disorder with depressed mood, dysthymic disorder and dementia. Suicidal behaviour and refusal of medical treatment is also common in the presence of serious medical illnesses. There are numerous issues to consider in this situation, but one should always consider the possibility of the presence of a treatable depressive disorder.

Therefore, depression is common in the medically ill as an affective experience, a symptomatic complaint or a clinical syndrome. It may occur in association with or as part of the individual response to the physical and psychological calamity of illness. The concept of depression as a ñpsychobiological final common pathwayò (Akiskal & McKinney, 1975) is particularly relevant in this population. The primary challenge is to detect a treatable psychiatric disorder and understand the personal meaning of illness for each individual.

2.4.2 Prevalence of depressive disorders in HIV-infected individuals

Much of the discussion above has relevance when considering depressive disorders in HIV-infected individuals. There are numerous confounding factors in making a diagnosis

of depressive disorder in an HIV-infected individual, including psychological reactions to the illness, physical symptoms common to both HIV disease and depressive disorder, and common symptoms in HIV dementia and depressive disorders.

2.4.2.1 International prevalence studies of depressive disorders in HIV-infected individuals

These studies can be divided into those conducted from 1982 to 1996, the period before highly-active anti-retroviral treatment (HAART) became available, and from 1997 to 2007, the period of wide availability of HAART in the developed world. In this context, before 1997, HIV infection was a fatal disease; it was a new disease, occurring predominantly in already highly-stigmatised individuals in the developed world.

Studies from 1982 to 1996

It is important to note that most studies during this period were conducted in clinic settings (HIV-treatment sites) or advertised for participants as a recruitment strategy (Williams, Rabkin & Remien, 1991). Some used screening instruments and rating scales (Brown, Rundell & McMains, 1992), not clinical diagnostic assessments, and therefore reported only on depressive symptoms or drew inferences about the rates of depressive disorders (Kelly, Murphy & Bahr, 1993a).

Most of the research during this period was conducted in the United States of America, followed by Europe (including the United Kingdom). Most of the studies show a high prevalence of depressive symptoms (Williams, et al., 1991) and, in some cases, depressive disorders in HIV-infected individuals (Atkinson & Patterson, 1992). However, in studies that compared HIV-seropositive individuals with matched HIV-seronegative controls, most

showed that there was a high lifetime prevalence of depressive disorders in both the affected individuals and the controls (Rosenberger, Bornstein & Nasrallah, 1993). The conclusion drawn from these findings was that HIV infection was occurring in groups of individuals already at high risk of depressive disorders ([MSM], and intravenous drug users [IDUs]). A study of 75 haemophiliac men (Dew, Ragni & Nimorwicz, 1990), some of whom had been infected through blood transfusion, showed higher depression, anxiety and anger scores in those who were HIV-seropositive than in those who were HIV-seronegative. The individuals more likely to have problems were those who had a past history of psychological or psychiatric difficulties. This was a small sample, with even smaller sub-samples and no diagnostic interviews were done (the symptom-90 checklist was used), so caution needs to be exercised in drawing conclusions from this study.

During this period very limited studies were conducted in the developing world. One, by Belec, Martin and Vohito (1989) in the Central African Republic, in 1989, on hospitalised HIV-infected patients found no evidence of depressive disorder. It is however, noteworthy that these were patients in the terminal stages of HIV-infection. As this was a hospitalised sample of ill patients, it is not comparable with the research population of studies in the developed world at the time, which predominantly comprised outpatients receiving primary care services for HIV-infection.

Between 1994 and 1996 the results of the World Health Organisationôs multi-national study on prevalence of neuropsychiatric disorders were published (Maj, Janssen & Starace, 1991; Sebit, 1995; Maj, 1996). This was the first multi-national study conducted in all the areas of high HIV-prevalence at the time (1990 to 1991). The study sites included sites in North America (Los Angeles, USA), two sites in Africa (Nairobi, Kenya) and (Kinshasa,

Zaire), Asia (Bangkok, Thailand), South America (Sao Paulo, Brazil) and Europe (Munich, Germany). Study populations at each site represented at-risk groups for HIV in that particular country. Thus, the research populations in the two African sites consisted of heterosexual subjects; the North American, South American and European sites, consisted of MSM and minority groups and in Munich, a disproportionate number of haemophiliacs. The Bangkok site group consisted predominantly of injection drug users (IDUs). Results published in 1994 and 1996 reported on five sites (excluding the USA site).
Subjects were recruited from primary care facilities at all sites, and HIV-negative controls were included for comparison purposes. The structured Composite International Diagnostic Interview (CIDI), which uses algorithms for psychiatric diagnosis according to the International Classification of Diseases, 10th Revision (ICD-10), was used. (Results were also reported for DSM111-R disorders). Subjects were also rated according to the Montgomery-Asberg Depression Scale (MADRS) in terms of severity of depressive symptomatology. The interviews were conducted by qualified psychiatrists, who had been trained in administration of this structured interview with good inter-centre and intra-centre reliability (Maj, Janssen & Satz, 1991).

The findings reported current and lifetime prevalence of a depressive episode. It is worth noting that the prevalence of current and lifetime depressive disorders in HIV-negative controls varied considerably between centres (from 0% in Munich, Kenya and Kinshasa to 7.8% in Sao Paulo, Brazil), indicating, as in the WMH study (Demyttenaere, et al., 2004), that the prevalence of depressive disorders in the populations studied varied across the globe. Prevalence rates of a current depressive episode in symptomatic HIV+ subjects ranged from 4% in Munich to 21% in Bangkok. While all sites demonstrated a higher prevalence of current depressive disorder in HIV+ subjects than in HIV- subjects, the only

sites showing a statistically significant difference between symptomatic HIV+ and HIV- subjects were Bangkok and Sao Paulo. Across all sites the mean global score on the MADRS was statistically significantly higher in symptomatic seropositive individuals than in seronegative controls. The overall prevalence of lifetime mental disorders was not significantly increased in HIV-seropositive individuals (asymptomatic or symptomatic), compared to HIV-seronegative controls.

This was the first study of depressive disorders in HIV-infected outpatients in Africa. The only conclusion drawn regarding the African centres was that the symptomatic stages of HIV infection were associated with an increased prevalence of depressive symptoms. How much of the depressive symptomatology could be explained by transient psychological reactions to the diagnosis is not clear. Participants were tested for HIV-status as part of the study, and in these cases interviews were conducted only one month after post-test counseling had been completed. Therefore some of their depressive symptomatology may have been part of an adjustment reaction to the diagnosis of HIV infection.

This study therefore did not confirm a statistically significant increase in the prevalence of depressive disorders in HIV-infected individuals (except in Bangkok) compared to HIV-negative controls, but the extent of depressive symptomatology was statistically significantly increased in HIV-infected individuals. It also demonstrated the same variability in prevalence of depressive disorders across the globe.

International research since 1997

Many of the studies conducted in the United States of America and Europe since 1997 have continued to show a high prevalence of depressive disorders in HIV-infected

individuals and to display many of the methodological difficulties outlined above. The demographics of the disease have changed, in that more women and some heterosexual men are now becoming infected (Catalan, Meadows & Douzenis, 2000; Morrison, Pettito & Ten Have, 2002). HIV-infection, however, occurs more commonly in marginalised communities who have inadequate access to social resources; including healthcare (African-Americans, Hispanics/Latinos, refugees, the mentally ill, the homeless and the poor) (Green, et al., 2004). Many of these groups already have an increased risk of depressive disorders due to socio-economic factors, so it is again difficult to tease out depressive disorders that are specific to HIV-infection itself.

One of the most cited studies in the field of HIV depression research is the meta-analysis conducted by Ciesla, et al. (2001). In their review, they outlined how studies determining the prevalence of major depressive disorder in HIV-infected individuals showed varying results and noted that the findings were inconclusive. This, they suggested, was largely due to small sample sizes and methodological difficulties. In order to obtain a sufficiently large sample, 10 studies were selected for meta-analysis. Those which they included all had an HIV-negative control group. All determined Major Depressive Disorder (MDD) by means of a diagnostic interview (not self-report or rating scales) using DSM-111 or 1V criteria and assessed current (1-6 months) rates of MDD and/or dysthymic disorder. If a study was longitudinal, data from the first assessment was used and study subjects were not recruited through the mental health system (which would have biased results). The study subjects included MSM, heterosexual men and women and injection drug users.

Three separate statistical analytical techniques were used and all three meta-analytic techniques showed a highly significant relationship between MDD and HIV-positive

status. The frequency of MDD was nearly twice as high in HIV-positive subjects as in HIV-negative comparison subjects. There was no association with sexual orientation or disease stage in infected individuals. The risk of depression was apparent in both symptomatic and asymptomatic HIV-positive individuals. It is noteworthy that, in six of the studies the study population was MSM, in one study the population was IDUs, and only two had study populations of men and women. These studies were all done in developed countries, except for the one conducted by Maj et al. (1991).
No compelling evidence of increased risk of dysthymic disorder was found. (Fewer studies have been conducted on this disorder, which has a lower prevalence and is a less severe condition. Moreover, it can be even more difficult to differentiate between HIV disease and dysthymic disorder.)

This meta-analysis was conducted rigorously, using a number of differing statistical methods in a large sample, and it provides the strongest evidence thus far, that HIV-positive individuals, compared to HIV-negative individuals in the same population, are at an elevated risk of developing major depressive disorder. The authors noted that determining attribution of symptoms to depression or HIV disease requires considerable clinical skill.

Another oft-cited study was that by Morrison et al. (2002). This reported on rates of depressive and anxiety disorders in women with HIV in the U.S.A. The Structured Clinical Interview for DSM-1V was used to assess depressive and anxiety disorder diagnoses. Symptoms of depression and anxiety were evaluated according to the Hamilton Depression and Anxiety rating scales. The rate of current major depressive disorder was four times higher (19.4%) in HIV-seropositive women than in HIV-seronegative women (4.8%).

Mean depressive symptom scores on the HAM-D also were significantly higher in the HIV-infected women than in comparison subjects (mean = 8.7 compared to mean = 3.3). Some of the limitations of the study include the recruitment process, confounding physical symptoms and the fact that the study site was in rural Florida in the United States, so its findings are not necessarily generalisable. On the other hand, the strengths of the study include the comprehensive nature of the assessment process using structured and standardized psychiatric instruments and consensus diagnoses, as well as the exclusion of subjects with substance use disorders, which can be a major confounding factor in research in this field.

2.4.2.2 Prevalence of depressive disorders in HIV-infected individuals in Sub-Saharan Africa, including South Africa

Research on prevalence rates of depression in HIV-infected individuals in Africa and South Africa is limited: besides the study by Belec et al. (1989) and the WHO study mentioned above, only a handful of research studies have been published.

An interesting study was conducted by Carson, Sandler and Owino (1998), who examined a population of working adults in Western Kenya. This was a cross-sectional study, with subjects and raters both blind to HIV status, to assess psychiatric morbidity associated with HIV. Subjects were recruited from an occupational health clinic for statutory annual health checks of workers in the food industry. Psychiatric interviews and neuropsychological tests were conducted. Of 230 subjects, 34% were HIV-positive. Women had a higher infection rate than men, and those who worked as bargirls or were divorced, widowed, or separated were particularly at risk of HIV infection. The study reported only psychiatric symptoms as assessed by the Clinical Interview Schedule (CIS), which reported symptoms of depression

in 12% of HIV-positive individuals and 8% in HIV-negative individuals (not statistically significant), and a manifest abnormality of ñbeing depressedò in one HIV positive individual, and no manifest abnormality of ñbeing depressedò in any HIV negative individuals (statistically significant with a Fisherôs exact test p-value = 0.02). ñSlownessò and ñlack of spontaneityò were other manifest abnormalities noted in HIV positive individuals and not in HIV negative individuals. These could indicate early cognitive impairment or depression. There were no substantial differences in psychiatric morbidity or neuropsychological functioning between the HIV-positive and HIV-negative subjects. Some problems related to the study were: the small number of participants; a significant refusal rate regarding entering the study, of individuals at high risk of HIV-infection; the loss of a large number of blood specimens; various other logistical difficulties. The methodology of this study differed from previous research in that participants were asymptomatic (working, and therefore healthier overall than many other study populations) and unaware of their HIV status, and interviewers were also blinded to the subjectsô HIV status, so this study was perhaps better able to provide information on the biological effects of HIV without the variables of psychosocial reactions to knowledge of HIV status. Studies of the prevalence of Depressive disorders in HIV in sub-Saharan Africa are noted in the table below.

Table 2.1 Studies of prevalence of Depressive disorders in HIV-infected individuals in sub-Saharan Africa

Researcher	Country	Year published	Methodology	Results
Sebit (1995)*	Zaire (DRC) and Kenya	1995	Diagnostic interview (CIDI) HIV-negative controls	No statistically significant increase in depressive disorders; generally low prevalence of depressive disorder
Sebit, Tombe and Siziya (2003)	Zimbabwe	2003	Diagnostic interview (MINI) HIV-negative controls	71.3% of HIV-positive individuals had a psychiatric disorder vs. 44.3% in HIV-negative individuals (no separate information on

				depressive disorder)
Stranix-Chibanda, Chibanda and Chingono (2005)	Zimbabwe	2005	Screening instrument (Shona SSQ) HIV-negative controls	17% of all women attending a VCT clinic had psychological morbidity. No statistically significant difference between those who were HIV-positive and those who were HIV-negative
Kahazura, Bunnell and Moss (2006)	Uganda	2006	Screening instrument (CES-D) No control group	47% of 1 017 HIV-infected individuals had a CES-D score $\geq$ 23 (significant depression).

*This study was part of the WHO study described by Maj et al. (1991) earlier and describes the results for the two African centres

These studies appear to show the same inconsistent findings overall between HIV-positive and HIV-negative individuals. The same methodological difficulties abound. However, in contrast to the WHO study (Sebit, 1995), the others show a significant prevalence of mental disorder, in both infected and uninfected individuals in Africa. This may be a reflection of the burden of depressive disorders on the continent. This is important, considering the lack of access to treatment, which was highlighted in the WMH study (Demyttenaere, et al., 2004). Therefore, if countries respond to the need for treatment of mental disorders in the context of HIV, this may result in increasing access to mental health treatment for the general population overall.

It is also worth noting that the prevalence of depressive disorders in both HIV-positive and HIV-negative individuals is higher in these studies than that found in the African site (Nigeria) in the World Mental Health survey (Demyttenaere, et al., 2004). It is unclear whether these differences can be wholly accounted for by methodological differences, or whether the prevalence of depressive disorders varies considerably in different places in Africa; for example, community prevalence studies of common mental disorder in Uganda, conducted in 1979 and 2004, showed high prevalence rates (Orley & Wing, 1979; Bolton, Wilk & Ndogoni, 2004), as have similar studies conducted in South Africa (see below).

Studies of prevalence of depressive disorders in HIV in South Africa are noted in Table 2. These studies all show high prevalence rates of depressive disorders in the study populations. The numbers of patients in these studies were low (between 90 and 130). In addition, all these samples were from hospital infectious diseases clinics treating people with HIV infection, before the availability of HAART in the public sector, and were likely to be weighted with people in the later stages of the infection. It is also not known how long the participants had been aware of their HIV status and whether recent diagnosis of HIV status influenced reporting of depressive symptomatology. Also, none of these studies used HIV-seronegative controls to compare prevalence rates.

Table 2.2 Studies of prevalence of Depressive disorders in HIV-infected individuals in South Africa

Researcher	Year published	Methodology	Results: prevalence of MDE
Bganya (1999) (Gauteng)	1999 (MMed)	Screening (Beck Depression Inventory) + unstructured clinical interview	38%
Els, Boshoff and Scott (1999) (Free State)	1999	Mini International Neuropsychiatric Interview (MINI)	35%
Olley, Gxamza and Seedat (2003) (Western Cape)	2003	MINI (baseline of cohort; within 6 months of HIV-diagnosis)	34.9%
Olley, Seedat and Stein (2006) (Western Cape)	2006	MINI (6-month follow-up of cohort)	26%

The Nelson Mandela/Human Sciences Research Council (HSRC) HIV Household Survey (2005) (Shisana, et al., 2005) noted that mental health in people living with HIV/AIDS was an unexplored area. The survey included some screening questions probing the mental health of respondents who knew their HIV status. It was found that 41% of those who were

HIV-positive felt sad, empty and depressed, while these feelings were present in 29.6% of HIV-negative respondents. Overall, the rates of sleeping, eating and anxiety problems were higher in HIV-positive respondents. While these results were not prevalence rates of depressive or anxiety disorders, they suggest that these are likely to be quite high. Studies of prevalence of mental disorders in more general populations in South Africa are listed in the table below.

Table 2.3 Studies of prevalence of mental disorders in general populations in South Africa

Study name	Year	Site	Methodology	Result
Thom et al. (Thom, Zwi & Reinach, 1993)	1993	Urban Primary Care clinic	SRQ + PSE	10% (anxiety and depression)
Rumble et al. (Rumble, Swartz & Parry, 1996)	1996	Rural community in Western Cape	SRQ + PSE	27.1% (most anxiety and depression
Bhagwanjee et al. (Bhagwanjee, Parekh & Paruk, 1998)	1998	Rural community in KwaZulu-Natal	SRQ + clinical interview	23.9% (anxiety and depression)
Pillay et al. (Pillay & Kriel, 2006)	2006	District-level services ï hospital and CHC	Screening instrument	21% depression
SASH Study (Stein et al, 2007)	2007	Country wide community prevalence study	CIDI (12-month and lifetime)	4.5% 12- month (mood disorders) 9.8% lifetime (mood disorders)

The studies conducted in rural community settings found very high levels of both depression and anxiety (reported together). The study by Thom et al. was conducted in a primary care setting and results pertain to that population and not to the general population. The study by Pillay et al reported on women only, and covers a selected sample of women attending clinical psychology services in an urban district health service in KwaZulu-Natal. Because the participants were in mental health referral centres, rates of depression and

anxiety were likely to be higher than in the general population or in primary care settings. A recent survey linked to the World Mental Health Survey, the SASH study (South African Stress and Health Survey) (Williams, Herman & Kessler, 2004), aimed to produce community prevalence figures for mental disorders in South Africa. The focus of this study was on consequences of apartheid violence, torture and trauma. The SASH study used the CIDI as its diagnostic tool. The findings of this study were released in October 2007, in a policy brief of the South African Medical Research Council (MRC). The 12-month prevalence rate for mood disorders was 4.5% and the lifetime prevalence rate was 9.8% (Stein, Seedat & Herman, 2007). No separate findings were noted for people in relation to their HIV-status.

These studies show a great variability in prevalence rates. The SASH study was conducted across the country with representative samples from all provinces. It provides the most recent evidence of prevalence rates of mental disorders in the general population in South Africa. The findings from South African studies of HIV-infected individuals (in clinic settings) appear to show an increased prevalence of depressive disorder (26% to 38%) in these populations compared to the prevalence in the general population in this most recent study (4.5%).

2.4.3 Possible risk factors for depressive disorder in HIV infected individuals

2.4.3.1 Biological factors

Recent research into the pathophysiology of depressive disorder suggests a complex interaction between genetic factors (Levinson, 2006), early adversity (Pollak, 2005) and psychosocial stressors (Akiskal, 1985; Caspi, Sugden & Moffitt, 2003), which results in functional (and possibly structural) changes in the areas of the brain responsible for mood

regulation and emotions. Neuroimaging studies of depressed patients have shown several abnormalities of regional cerebral blood flow and glucose metabolism (a surrogate of neuronal function) in various brain regions, including the limbic cortex, the prefrontal cortex, the anterior cingulate cortex, the hippocampus and the amygdala) (Kalia, 2005). Recent research has also demonstrated the complex interaction between the central nervous system, endocrinological and immunological systems in the genesis, maintenance and resolution of depressive disorder (Leonard, 2001). It has also been suggested that antidepressants play a role in recovery from depressive illness through neurotropic and neuroplastic effects (structural remodelling) (Lanfumey & Hamon, 2005) on the brain. Genetic factors (for example, those which regulate the production of brain-derived neurotropic factor (BDNF) are also involved (Hashimoto, Shimizu & Iyo, 2004) and may explain the variability in response to antidepressant medication. It is suggested that vulnerability to, or recovery from depressive illness is mediated through the balance between neurotoxins and neurotropic factors (Kalia, 2005).

Age and gender are thought to play a role in increasing the risk for depressive disorders. Older age is associated with an increasing risk, while female gender is associated with an almost two-fold increase in risk. Whether this is a result of biological or social factors or a combination of both is not clear (Kaplan, Sadock & Grebb, 1997:522).

HIV infection leads to a range of antiviral responses in the body, including the production of virus specific antibody, but the major response is in cell-mediated immunity (Cann, 2007). Because the virus infects and damages these very cells in the body, this leads to dysregulation of many aspects of immune response, including defective antibody and T-cell responses to new antigens and decreased natural killer (NK) cell responses (Mavilio,

Benjamin & Daucher, 2003). During the antiviral response, and as a result of damage to cells involved in cell-mediated immunity, toxic substances are released, which damage immune cells both systemically and within the central nervous system. While the CD4 count is the standard clinical marker of disease progression in HIV-infection, there are effects on other cells within the psychoneuroendocrinological and psychoneuroimmunological systems that are not usually measured in the clinical setting. However, in research settings, these effects have been detected even when CD4+ cell numbers are normal, but become more marked as CD4+ cell numbers decline.

It is now known that HIV is commonly found in the Central Nervous System and that the virus has a direct effect on CNS structures (An & Scaravilli, 1997). It has been shown that pro-inflammatory cytokines, free radicals and other neurotoxins released from glial cells play a role in damaging neurons and ultimately resulting in neuronal death (Merrill & Chen, 1991).

Without the support of glial cells, and with the release of neurotoxins, neurons are damaged or destroyed. HIV is thought to invade the subcortical areas and can destroy the basal ganglia, thalamus and temperolimbic structures. While these changes have been directly linked to HIV-associated cognitive/motor complex disorders (HIV-associated dementia complex and Minor Cognitive Motor Disorder), it is also thought that damage in these areas can result in new-onset depression (Martin, Tummala & Fernandez, 2002) as well as mania or psychosis.

Because of the effects of HIV infection discussed above, there has been considerable study of the association between depressive disorder and clinical indicators of HIV infection.

Stage of illness and association with depressive disorder

Many studies show an association between current HIV symptoms and the presence of depressive disorder (Catalan, Klimes & Day, 1992; Maj, 1996). Most do not confirm a relationship between depressive disorder and HIV disease stage (Ciesla, et al., 2001). However, some have shown an association between the earlier stages of infection and depressive disorders (Els, et al., 1999; Olley, et al., 2003). This may be related more to the time from diagnosis when a study is done than to the HIV infection itself, since it is known that the immediate period after diagnosis is a period of high risk for psychological distress. An interesting finding by Lyketsos, Hoover and Guccione (1996) in a prospective follow-up study was that a significant rise in depressive symptoms occurred in the 18 months prior to the onset of clinical AIDS, but this finding has not been replicated.

CD4 count and association with depressive disorder

Research on the association between CD4 count and depressive disorder has focussed largely on the impact of depressive disorder on CD4 count as a factor in disease progression (Ickovics, Hamburger & Vlahov, 2001; Ironson, OõCleirigh & Fletcher, 2005). Most studies showing an association between depressive disorder and a decrease in CD4 count or other immune-status markers have been prospective cohort studies which found that the deterioration of immune status is a consequence of depressive disorder, and not that a low CD4 count is a cause of depressive disorder. Two studies in Africa have explored this association. Both were cross-sectional studies, and were therefore subject to limitations. The study by Moosa, Jeenah and Vorster (2005), in South Africa, found no association between CD4 count and depressive symptomatology on the Beck Depression Inventory (with a cut-off score of 10 or more being indicative of possible depressive

disorder). On the other hand, the study by Kahazura et al. (2006) did find a statistically significant association between CD4 counts less than 100 cells/ml and the presence of a probable depressive disorder (cut-off on the Centre for Epidemiological Studies ï Depression Scale of 23 or more). However, due to its cross-sectional design, this study was still not able to conclude whether a low CD4 count is a cause or a consequence of depressive disorder.

Other biological causes of depressive disorders in HIV-infected individuals

Besides the direct effects of HIV CNS infection, other opportunistic infections and conditions, substance use disorders, as well as medication used in the treatment of HIV infection (HAART), opportunistic infections, co-infections and associated conditions may also produce depressive disorders (secondary to a general medical condition or substance). Of these, the conditions most commonly associated with depressive disorders are: substance use disorders; toxoplasmosis; herpes zoster and varicella virus infections; hepatitis C co-infection, as well as its treatment with Interferon-gamma (Jones, Ferrando & Talal, 2004); some of the antiretrovirals used in treatment (zidovudine, efavirenz) (Halman, Bialer & Worth, 2002); CNS malignancies (Stolar, Catalano & Hakala, 2005).

The impact of anti-retroviral medication on depressive disorders

As noted above, some antiretroviral medications have been implicated in the development of neuropsychiatric syndromes, including depressive disorders. However, longitudinal follow-up studies on the relationship between HAART and depressive disorders found that HAART appears to decrease depressive disorders overall (Judd, Cockram & Komiti, 2000; Low-Beer, Chan & Yip, 2000; Rabkin, Ferrando & Lin, 2000; Alciati, Starace & Scaramelli, 2001; Starace, Bartoli & Aloisi, 2002; Chan, Orlando & Joyce, 2003). There also appears to be a reverse effect, with evidence that individuals with depressive disorders

have inferior virologic and clinical responses to HAART and, once treated for depression, this response improves (Pence, Miller & Gaynes, 2007).

2.4.3.2 Past psychiatric history and family psychiatric history

Several studies describing prevalence and risk factors of depressive disorder in HIV infected individuals have found that a previous personal history of depressive disorder (Dew, et al., 1990; Perry, Jacobsberg & Fishman, 1990; Brown, et al., 1992; Catalan, et al., 1992; Rosenberger, et al., 1993; Rabkin, Ferrando & Jacobsberg, 1997), substance abuse or dependence (Brown, et al., 1992), or a family history of mental disorders (Dew, et al., 1990) increases the risk of developing a depressive disorder in the context of HIV infection. Whether this reflects a biological predisposition or vulnerability is unclear, but it does suggest that the host response to a severe psychosocial stressor (knowledge of HIV infection) is compromised by earlier events, and that genetic and biological factors listed above play a role in this.

2.4.3.3 Personality characteristics

It has also been shown that low self esteem (Catalan, et al., 1992), poor sense of mastery (Dew, et al., 1990), avoidant or disengaged personality styles, insecure or anxious attachment and levels of perceived stress increase the likelihood of an HIV-infected individualõs developing a depressive disorder. Whether these characteristics are biologically or environmentally determined, or not, they are characteristics that predate the onset of HIV-infection, and appear to increase vulnerability to depressive disorders in the context of HIV infection.

The issue of perceived stress is important, as HIV infection is associated with greatly increased levels of stressful life events. Koopman, Gore-Felton and Marouf (2000) examined the relationships of coping, attachment style and perceived social support, to perceived stress within a sample of HIV-positive people. Participants were 147 HIV-positive persons (80 men and 67 women). Multiple regression analysis was used to examine the relationships of total score on the Perceived Stress (PS) Scale with demographic variables, AIDS status, three coping styles, three attachment styles and perceived quality of general social support. PS was significantly associated with less income, greater use of behavioural and emotional disengagement in coping with HIV/AIDS and less secure and more anxious attachment styles. These results indicate that HIV-positive people who experience the greatest stress in their daily lives are those with lower incomes who disengage behaviourally/emotionally in coping with their illness, and those who approach their interpersonal relationships in a less secure and more anxious style. Thus, it is important to consider the psychological meaning of stressful events to a particular individual.

2.4.3.4 Psychosocial factors in the development of depressive disorders in HIV-infected individuals

Most research on the role of psychosocial factors in depressive disorders relates to the study of the impact of stress on individuals. Literature covering the impact of stressful life events and other environmental stressors in the development or precipitation of a depressive illness is extensive (Kaplan, et al., 1997:522). The conclusion is that stressful life events play a role in the genesis of depressive disorders. One of the striking findings of more recent research is that stress, particularly cumulative stress, induces endocrine,

immunological and neurochemical changes in the brain (Leonard, 2001; Dantzer & Kelley, 2007, Gunnar & Ouevedo, 2007).

Infection with HIV results in an individual having to deal with a number of serious psychological issues, including: the impact of the illness on body image; self-esteem; sense of identity; capacity to maintain social, family and marital relationships; facing oneôs own death and the deaths of loved ones. The early months after diagnosis of HIV infection are associated with increased levels of psychological distress, which appears to lessen with time (Lyketsos, Hoover & Guccione, 1996b). However, some individuals remain at risk of developing mental disorders, particularly depressive disorders, both at the time of diagnosis and during all the stages of HIV infection.

Psychosocial factors found to be associated with an increased prevalence of depressive disorders in HIV-infected individuals include: lack of social support, stressful life events (both general events and HIV-related stressors, both past and recent), low income and unemployment, female gender and disability (Dew, et al., 1990; Perry, 1994; McClure, Catz & Prejean, 1996; Rabkin, et al., 1997; Simoni & Ng, 2000; Mello & Malbergier, 2004). Social support is the most commonly mentioned variable in these studies. Of note in South Africa is the research conducted by Olley et al. (Olley, Seedat & Nei, 20040. Female gender, negative life events and disability were the factors found to predict major depression in these studies. [Female gender and negative life events have also been associated with depressive disorders in uninfected samples as well (Piccinelli & Wilkinson, 2000).] This study also noted that the impact of negative life events, rather than the number of such events, predicted major depression, bearing out a previous point that it is not only the amount of stress, but the way that stress is perceived by the individual that is important.

Information on the impact of stigma and discrimination around HIV in South Africa is limited and contradictory, with some authors suggesting that considerable stigma exists and impacts on the mental health of HIV-infected individuals (Simbayi, Kalichman & Strebel, 2007), while others emphasise the changes in societyôs response and the importance of avoiding stereotyping of responses when the reality of the overwhelming numbers of people affected by the epidemic means that more and more people are called to care (Jewkes, 2006).

2.4.3.5 Possible protective factors in HIV-infected individuals that could prevent development of depressive disorders

An aspect that has received little attention relates to the factors associated with resilience in patients with HIV infection and those which may protect them from depressive disorders and/or disease progression. Much of the literature on stressful and negative life events and perceived stress suggests that less vulnerable individuals are less likely to develop depressive disorders, and that psychological diatheses moderate the impacts of life events.

Simoni and Cooperman (2000), in their study of women living with HIV/AIDS in New York City, found that while there were considerable severe stressors (both past and present) in this group, participants also reported considerable strengths, including high levels of spirituality, mastery and HIV-related social support. Multivariate analyses indicated that these resources were generally associated with less depressive symptomatology.

The impact of disclosure on mental health has also not been explored to any great extent in South Africa; nor has the impact of pre- and post-test counselling in protecting individuals from mental disorder been explored.

2.4.4 The impact of depressive disorders on HIV-infected individuals

2.4.4.1 Depressive disorder and disease progression

Research into the impact of stress and depressive disorders on physical health indicates a close relationship between psychological factors, neurological pathways and the immune and endocrine systems (Kiecolt-Glaser & Glaser, 1991; Kemeny, Solomon & Morley, 1992). In terms of HIV infection, considerable research exploring the impact of stress, depression and anxiety on HIV-illness progression has been done (Coates, Stall & Ekstrand, 1989; Leserman, Jackson & Petito, 1999; Farinpour, Miller & Satz, 2003). In addition, in recent years there has been a focus on the impact of anti-retroviral medication on psychiatric symptomatology (see Section 2.4.3.1) and the impact of mental disorders on treatment response to HAART (Pence, et al., 2007). All of this research appears to indicate a close and reciprocal relationship between internal factors and systems, both biological (the brain, endocrine and immune systems) and psychological (coping mechanisms, personality structure and internal brain circuitry affected by early life events, which may predispose or protect against later depressive illness) and external stressful life events. Each individual has various homeostatic mechanisms which interact, with the ultimate aim of survival, and psychiatric disorders as well as HIV infection can be both cause and effect of disruptions in these homeostatic mechanisms.

Both stress and depressive disorders appear to impact on disease progression, either directly through effects on the immune system (Mayne, Vittinghoff & Chesney, 1996;

Ickovics, et al., 2001; Ironson, et al., 2005), or indirectly through poor adherence to medication (Cook, Cohen & Burke, 2002). The studies in this area generally indicate an association between depression and disease progression. However, the mechanisms by which this association is mediated are not clear. There seems to be evidence for mediation through CD4 cell count (Ickovics, et al., 2001; Ironson, et al., 2005), but it is also suggested in some studies that most of these effects are mediated through other cell-lines; in particular, CD8 cells and Natural Killer cells (Evans, Ten Have & Douglas, 2002; Creuss, Douglas & Petitto, 2005). Studies of both psychotropic and psychotherapeutic treatments for depressive disorders have also shown a beneficial effect on disease state immune markers (Antoni, 2003; Burke, Cook & Grey, 2004).

2.4.4.2 Impact of depressive disorders on adherence

Another reason advanced for motivating for the need to identify and treat depressive disorders is the suggested impact of depressive disorders on adherence. It has been proposed that depressive disorders result in decreased adherence as a result of poor motivation, poor organisational capacity, diminished energy, and on the basis of suicidal ideation or behaviour. Several studies have examined this issue.

Two studies published in 2002 do not mention depressive disorders as factors in non-adherence. In a cross-sectional study of a sample of HIV-seropositive patients in Hong Kong, Molassiotis, Nahas-Lopez and Chung (2002) identified predictors of adherence as high self-efficacy, low tension-anxiety scores and low intensity of nausea and vomiting. Murphy, Greenwell and Hoffman (2002) found very poor rates of adherence in a group of HIV symptomatic or AIDS diagnosed women with young children. The major factors associated with non-adherence were alcohol use, perceived stress, having a partner and age

of youngest child, poor self-efficacy to stay with treatment, and poor outcome expectancies regarding the benefits of following the treatment regimen. Neither of these studies specifically mentioned depressive disorder as a possible factor, and whether this was actually investigated is unclear.

A prospective cohort study by Cook et al. (2002) followed HIV-seropositive women from 1996 to 1998 and examined the longitudinal effects of depressive symptoms and mental health quality of life on utilization of HAART among HIV+ women. High levels of depressive symptoms and poor mental health quality of life were found, and they significantly reduced the probability of HAART utilization. Receiving mental health services significantly increased the probability of using HAART. HIV+ women characterized as being in poor mental health were less likely to use HAART, whereas those receiving treatment for mental health difficulties were more likely to use it.

Tucker, Burnam and Sherbourne (2003) used data drawn from the HIV Cost and Services Utilization Study, and showed that HIV-seropositive patients with depression, generalised anxiety disorder and panic disorder were more likely to be non-adherent than those without a psychiatric disorder. Non-adherence was also associated with use of cocaine, marijuana, amphetamines or sedatives in the previous month. Compared with patients who did not drink, those who were moderate, heavy or frequent heavy drinkers were more likely to be non-adherent. These associations could not be explained by demographic, clinical or treatment factors. 19% of the 1910 study subjects screened positive with the CIDI-screen for a probable psychiatric disorder, 14% reported heavy drinking in the past month, and 28% reported other substance use (illicit) or abuse.

Turner, Laine and Cosler (2003), in a retrospective cohort study, using a pharmacy-based measure of adherence and DSM diagnoses, showed that antiretroviral adherence is worse in women than in men, and that depression can influence medication adherence. The study also found that treatment for depression improved adherence in those with depression.

On balance, the evidence seems to show an association between depressive disorders and poor adherence. However, other psychiatric illness (anxiety disorders) and active substance abuse also play a role (Ickovics & Meade, 2002). The literature also shows that treating depressive disorders has a significantly improves treatment adherence in HIV-infected individuals.

2.4.4.3 Suicidal behaviour in HIV-infected individuals

Another reason for actively diagnosing and treating depressive disorders in HIV-infected individuals is the high rate of suicidal behaviour in such individuals (Cote, Biggar & Dannenberg, 1992; Starace 1995), which is similar to that in other chronically medically ill patients (Hughes & Kleespies, 2001). Kelly, Raphael and Judd (1998b) also found increased levels of suicidal ideation in symptomatic HIV-positive men and highlighted the role that multiple psychosocial factors associated with suicidal ideation and attempted suicide play in this population. A 2001 Komiti et al. review (Komiti, Judd & Grech, 2001) noted that most studies had considerable methodological problems (the problems inherent in assessing suicidal ideation and completed suicide, particularly in retrospective studies), and that longitudinal studies of a wider range of affected groups were needed. No information is available on suicide related to the HIV-infected in Sub-Saharan Africa although it is needed to improve care to this group.

Other factors besides depressive disorders play a role in producing suicidal behaviour; in particular, substance abuse. To control for the impact of substance use disorders, Roy (2003) studied a series of 149 HIV-seropositive substance-dependent patients, to identify other risk factors. Almost half the group had attempted suicide. Significantly more female than male patients attempted suicide, had a family history of suicidal behaviour, reported childhood trauma, scored significantly higher for neuroticism, had experienced significantly more comorbidity with depression, and had received antidepressant medication. This study indicated that past, as well as more recent risk factors were involved in producing suicidal behaviour. The challenge for the clinician is to intervene, particularly with recent and current risk factors. High risk periods for suicidal behaviour in the course of HIV infection have been identified as the months immediately following diagnosis and periods of evident disease progression.

2.5 Anxiety disorders

2.5.1 Introduction

Anxiety disorders in HIV-infected individuals have received far less attention in the literature than depressive disorders, possibly because anxiety symptoms are regarded as expectable normal reactions to the stress of being HIV-infected. Furthermore, anxiety is often part of a complex symptom picture that frequently includes mood disorders and substance use disorders. This co-morbidity makes diagnosis of ñpureò anxiety disorders difficult. There are also many general medical factors and substance related factors that may cause anxiety disorders. Other viral opportunistic infections, medication side-effects, vitamin deficiency states and substance-related withdrawal states are common causes of anxiety disorders secondary to general medical conditions.

2.5.2 Methodological issues

The same issues regarding anxiety symptomatology vs. disorder, as in depressive disorders, are evident and create methodological difficulties. In addition, the nature of anxiety disorders is continually under review. Confusion surrounds differentiation of trait anxiety (a personality characteristic) from state anxiety (a disorder). There is considerable overlap between symptoms of generalised anxiety disorder and depressive disorders, as well as in genetic loading for both disorders, and it has been suggested that these may be the same disorder expressed with slightly different phenomenologies (Breslau, 1985). On the other hand, anxiety disorders as a group may be disparate, with different genetic underpinnings and psychosocial correlates (Stein, 2006).

This is reflected in methodological issues. Current diagnostic psychiatric systems tend to use a stepwise approach to diagnosis; thus before a diagnosis of a generalised anxiety disorder is made, a depressive disorder would generally be excluded (anxiety symptoms affect as many as 90% of all depressed patients), as would a substance-related disorder or a disorder due to a general medical condition (according to DSM1V-TR criteria).

ñStressò is a common term used to describe a number of different events or mental states. These include the normal stress of living, ñabnormalò stressful/negative life events or traumatic events, and individualsô reactions to stress/difficulties in their lives. Recent literature on stress and coping has highlighted the difference between perceived and objective stress, suggesting that individuals may react differently to the same stressful event, depending on their individual histories (including genetic factors, personality factors and early experience of adversity). There are also anxiety disorders that are classified as acute stress disorders and post-traumatic stress disorder (PTSD).

Post-Traumatic Stress Disorder is of interest to many researchers in the field of HIV psychiatry. It has been postulated that it is common in HIV-infected populations, both as a result of learning of oneôs HIV-status and because individuals may be infected through rape and assault, which in themselves are traumatic. A significant amount of controversy exists in the literature regarding post-traumatic stress disorder as a diagnosis, and there has been considerable research on its biological, personality and psycho-social correlates. Concern has been expressed over possible over-diagnosis of this disorder for the purposes of insurance claims. This has led to caution in terms of defining traumatic events that could result in PTSD. The controversy has extended to debate on whether a diagnosis of HIV is in itself a traumatic event.

2.5.2.1 Interpreting research findings on anxiety disorders in HIV-infected individuals

The same issues regarding screening instruments, diagnostic interviews and rating scales discussed in the section on depressive disorders pertains to the diagnosis of anxiety disorders. The CIDI, MINI, SCAN and SCID are all diagnostic instruments that can be used to diagnose anxiety disorders. There are screening instruments and rating scales for specific anxiety disorders such generalised anxiety disorder, post-traumatic stress disorder, obsessive compulsive disorder and panic disorder. It is important to use these instruments for the correct purposes and to interpret research findings with an awareness of what exactly is being reported depending on the instruments that are used in the research.

Common screening instruments used in anxiety disorders research include general questionnaires like the General Health Questionnaire (GHQ), the Self-Reporting Questionnaire (SRQ) and the Symptom-90 checklist. In addition, screening instruments for specific anxiety disorders have been developed. The PTSD-checklist ï civilian version has been commonly used in studies of PTSD in HIV-infected individuals. Researchers report a

high correlation between the cut-off (44) on this checklist and DSM-diagnostic criteria for this disorder (Dobie, Kivlahan & Maynard, 2002).

Rating scales which are primarily used for rating the severity of a disorder and tracking changes over time, are also commonly used in studies to determine the levels of anxiety symptomatology. The Hamilton Anxiety Rating Scale for Generalised Anxiety Disorder is one such tool.

2.5.3.2 Anxiety disorders in the general population

The WMH study (Demyttenaere, et al., 2004) again showed a wide range of prevalence rates of anxiety disorders across countries and continents. The prevalence rates of anxiety disorders (all disorders) diagnosed with the CIDI-12-month instrument ranged from 2.4% in Shanghai to 18.2% in the United States of America. The site in Africa (Nigeria) reported a 12-month prevalence of 3.3% for all anxiety disorders.

Recent prevalence studies on PTSD in the United States are noted in the table below.

Table 2.4 Studies of prevalence of Post-Traumatic Stress Disorder in the United States of America

Authors	Country	Methodology	Prevalence
Koopman, Gore-Felton and Azimi (2002)	USA	no control group; screening tools ASD PTSD	 31.3% 40%
Martinez, Israelski and Walker (2002)	USA	No control group; screening tool PTSD	 42%
Israelski et al. (2007)	USA	primary care; no control group; screening tool PTSD ASD	 34% 43%

These studies report very high prevalence of Acute Stress Disorder and Post Traumatic Stress Disorder. The studies all used self-report screening instruments, the Stanford Acute Stress Reaction Questionnaire and the PTSD Checklist-Civilian Version. Although researchers argue that these are valid instruments correlating well with the DSM diagnoses, results should be treated with caution, particularly in countries where the scale has not been validated in terms of factors and cut-off score. The studies noted above lacked HIV-seronegative control groups, so it is not possible to comment on the prevalence rates reported in these studies.

2.5.3.3 Anxiety disorders in medically ill populations

The differential diagnosis of anxiety symptoms in medically ill populations includes disorders secondary to a general medical condition, substance-induced anxiety disorder, adjustment disorder with anxious mood, generalised anxiety disorder, panic disorder, specific and social phobias, obsessive compulsive disorder and post-traumatic stress disorder. Anxiety symptoms and anxiety disorder have been estimated to occur in 5% to 20% of medical inpatients and 4% to 14% of medical outpatients (Skodol, 1999). These estimates do not distinguish between anxiety symptoms and anxiety disorders, nor between the various causes of anxiety in the medically ill.

2.5.3 The prevalence of anxiety disorders in HIV-infected individuals

Prevalence data on anxiety disorders in this population are limited and often of questionable value. Studies often do not separate anxiety disorders from other mental disorders, but merely report on high rates of ñmental disorderò or ñdepression and anxietyò. As with depressive disorders, there are many methodological problems (small samples, selected groups, measuring and reporting of symptoms and not syndromes). Study

design may limit the usefulness of information as, for example, retrospective cross-sectional studies often do not address the issue of whether anxiety preceded or followed HIV infection. There is, therefore, a very wide range of reported rates of anxiety disorders (5% to 40%) in HIV-infected individuals (McDaniel & Blalock, 2000).

2.5.3.1 International prevalence studies of anxiety disorders in HIV-infected individuals

Early studies in the developed world showed that lifetime prevalence rates of anxiety disorders in HIV-seropositive and matched HIV-seronegative controls were similarly high, suggesting that individuals at risk for HIV infection were also at risk for anxiety disorders. The only statistically significant difference in prevalence rates between HIV-seropositive individuals and HIV-seronegative controls in these studies is in adjustment disorder with anxious mood in the study by Dew, Becker and Sanchez (1997).

The table below outlines studies that have used diagnostic instruments and control groups to make (current) anxiety disorder diagnoses.

Table 2.5 International studies of the prevalence of anxiety disorders in HIV-infected individuals

AUTHOR	Country	Methodology	Prevalence	
			HIV+	HIV-
Williams et al. (1991)	USA	control group; SCID (total anxiety disorders)	2%	0% (ECA: 4.7%)
Brown et al. (1992)	USA	control group (ECA); SCID (total anxiety disorders)	12.9%	4.8%
Rosenberger et al. (1993)	USA	control group: SCID (total anxiety disorders)	10%	10%
Dew et al. (1997)		Prospective cohort study; control group; SCID		
Baseline data	USA	GAD lifetime prevalence	15%	8.8%
Baseline data	USA	GAD current prevalence	2.4%	1.9%
Baseline data	USA	Adjustment disorder with anxious mood:	23.4%	11.3%

Rabkin et al. (1997)	USA	control group: SCID (total anxiety disorders)	14%	8%
Bing, Burnam and Longshorgshore (2001)	USA	HIV Cost and SUS; CIDI screen (12-month version) GAD Panic Attack	 15.8% 10.5%	
Morrison et al. (2002)	USA	control group: SCID	10.8%	6.5%

The most recent controlled study with rigorous methodology was conducted by Morrison et al. (2002). The findings were that 10.8% of HIV-positive women had an anxiety disorder (diagnosed with the SCID), whereas 6.5% of HIV-negative women had such an anxiety disorder. This difference was not statistically significant. However, levels of anxiety symptoms were higher in HIV-positive women than in HIV-negative women (using the Hamilton Anxiety Rating Scale) and the difference was statistically significant. The most common anxiety disorder in HIV-positive women was social phobia and in HIV-negative women it was generalised anxiety disorder. Again, it was not noted how long the participants had been aware of their HIV-status, and whether this had an impact on anxiety symptoms.

2.5.3.2 Prevalence studies in Africa and South Africa

Studies conducted in Africa are even more limited than in the developed world. Some results of research conducted at sites in Africa are listed in the table below.

Table 2.6 Studies of the prevalence of anxiety disorders in HIV-infected individuals in sub-Saharan Africa

AUTHOR	Country of study	Methodology	Prevalence	
			HIV+ve	HIV-ve
Maj et al. (1994)	Multi-national	control group: CIDI	1-2%	1-2%

Carson et al. (1998)	Kenya	control group: CIS worry symptoms (no anxiety disorders)	13%	12%
Els et al. (1999)	South Africa	no control group; MINI Panic disorder Agoraphobia Social phobia GAD PTSD	 37% 9% 15% 21% 6%	
Olley, Zeier and Seedat (2005)	South Africa	no control group; MINI PTSD (Baseline)	 14.8%	
Olley et al. (2006)	South Africa	cohort study; MINI at 6 month follow-up PTSD	 20%	

Only the Carson et al. and Maj et al. studies used HIV-seronegative controls, and these reported low rates of anxiety disorder in both groups and no difference between HIV-seropositive and HIV-seronegative individuals. The studies in South Africa show much higher prevalence rates for all the anxiety disorders reported but none of these studies had control subjects. Comparison of the reported rates of PTSD in the American and South African studies shows that rates in the American studies are higher. The American studies used a screening tool, whereas the South African ones used a diagnostic instrument. Whether this explains the difference in rates or reflects a true variation in rates of PTSD is unclear. Studies in both countries need to be conducted using the same diagnostic instrument and using control groups, to compare with general population prevalence rates.

Some studies of the prevalence of anxiety disorders in the general population in South Africa have already been discussed in the section on depressive disorders (see the table below). The recent SASH study showed a 12-month prevalence rate of 8.1% and lifetime prevalence rate of 15.8% for anxiety disorders in South Africa. Of interest in this study is that, despite high rates of exposure to psychological trauma in the study sample, the rates of PTSD were found to be low.

Table 2.7: Studies of the prevalence of anxiety disorders in general population in South Africa

Study name	Year	Site	Methodology	Result
Thom et al. (1993)	1993	Urban Primary Care clinic	SRQ + PSE	2% (anxiety disorders)
Rumble et al. (1996)	1996	Rural community in Western Cape	SRQ + PSE	27.1% (most anxiety and depression
Bhagwanjee et al. (1998)	1998	Rural community in KwaZulu-Natal	SRQ + clinical interview	23.9% (anxiety and depression)
Pillay et al. (2006)	2006	District level mental health services ï hospital and CHC	Screening instrument	10% anxiety
SASH Study. Stein et al (2007)	2007	Country-wide community prevalence study	CIDI (12-month and lifetime prevalence)	8.1% 12-month 15.8% lifetime

Summary

International studies of anxiety disorders in HIV-infected individuals show great variability and while there is some evidence of an increased prevalence of anxiety disorders in these individuals, compared to individuals in the general population, the variability in prevalence rates across countries and differing methodologies make it difficult to conclusively state that this is the case. The same conclusion applies to studies conducted in African and South African settings. While there is considerable variability in prevalence rates of anxiety disorders in the general population, it appears from the most recent study (Stein, et al. 2007), that anxiety disorders are common. The prevalence of anxiety disorders in HIV-infected individuals in studies conducted in South Africa is also high, but there does not appear to be a statistically significantly higher prevalence in this population compared to the general population.

Therefore, the conclusion from this review must be that while anxiety disorders are common in HIV-infected individuals and should be a focus of attention, current evidence

does not show that they are more common than anxiety disorders in matched HIV-seronegative controls or in similar medically ill populations.

2.5.4 Risk factors for anxiety disorders in HIV-infected individuals

As with depressive disorders, in the recent past, considerable research has been carried out on the psychobiology of anxiety disorders. Investigations into genetic factors, psychoneuroendocrinological responses, brain development and plasticity are attempting to elucidate factors responsible for the development of anxiety disorders. The outcomes of these investigations again suggest that the development of anxiety disorders involves a complex mix of genetics, early brain development, early adversity, and current psychosocial stressors. Stein (2006) suggests that anxiety disorders can be conceptualised in terms of a ñfalse alarmò, mediated by specific neurocircuitry, with a particular evolutionary origin for specific anxiety disorders, and that Serotonin-Specific Reuptake Inhibitors (SSRIs) and Cognitive Behaviour Therapy (CBT) appear to normalise ñfalse alarmsò, possibly by inducing brain changes.

Westermann, Sirois and Shultz (2006) explored the interaction between brain development and cognitive development in terms of the role that experience (environmental influences) and innate maturational factors play in development. A number of authors have explored the issue of trait anxiety and Pollak (2005) suggests that trait anxiety is related to adversity in early development, and that these experiences effect structural brain changes. Van Eck, Berkhof and Nicolson (1996) studied salivary cortisol levels and explored the effects of perceived stress, traits, mood states and stressful daily events on these levels. The findings were that distress reflected by mood states was associated with higher cortisol levels and stressful daily events increased cortisol secretion. Perceived stress, anxiety and depression

did not increase reactivity, but there was reduced habituation to recurrent events in subjects scoring high on these traits. The conclusion reached was that mood appears to play a mediating role in the relationship between stressful events and cortisol secretion. Schlotz, Schulz and Hellhammer (2006), in recent work using salivary cortisol levels, showed that subjects scoring high on trait anxiety seem to process stress-relevant information in a way that amplifies the association between performance pressure and cortisol levels. These studies suggest that longstanding traits of anxiety develop as the brain develops and they are accompanied by biological changes. These long-term changes may make individuals more vulnerable to stress and the development of anxiety disorders later in life.

Many authors have commented on the role of stress in the genesis of anxiety disorders, explaining how stress is necessary for survival, but that repeated stress increases the risk of physical and mental health problems especially during periods of rapid brain development. Gunnar and Ouevedo (2007) also outlined the critical role of social regulation and the importance of individual differences.

Research into Post Traumatic Stress Disorders highlights that not all people who experience traumatic events develop PTSD (Keane, Marshall & Taft, 2006). There is a striking individual variation in emotional and neurobiological responses. Cognitive appraisal and coping factors may explain differences in neuroendocrinological stress response and development of this disorder (Olff, Langeland & Gersons, 2005).

Suggested risk factors for PTSD in HIV include: more physical symptoms, more pre-HIV trauma, less perceived social support, more perceived stigma, and more negative life events. Katz & Nevid (2005) found three individual predictors for PTSD in HIV infected

individuals: total impact of negative life events; total stigma score; total number of physical symptoms. Stigma was found to be the strongest individual predictor. Social support in this study failed to moderate relationships between PTSD symptoms and HIV symptoms and negative life events.

Kelly et al. (1998a) explored the issue of PTSD as a response to HIV infection: in a small sample of MSM, 30% met criteria for PTSD in response to the diagnosis of HIV. PTSD was associated with other mental disorders, especially first onset major depression after diagnosis of HIV status and was significantly associated with a past history of PTSD before HIV, other pre-HIV mental disorders and neuroticism traits. While the authors suggest that a PTSD response to HIV diagnosis or any other life-threatening illness has clinical validity, the small sample size and the confounding variables in this study are problematic. The strongest predictor of PTSD post-HIV diagnosis was a past history of PTSD, which may suggest that particular individuals are more at risk of developing the same pattern of illness when faced with a new stressor, and not necessarily that the stressor *per se* is of sufficient severity to produce PTSD. While this is in keeping with the current understanding of PTSD, it is precisely this approach that has caused the controversy in psychiatric circles regarding PTSD.

2.5.5 The impact of anxiety disorders in HIV-infected individuals

What impact anxiety disorders have on HIV-infected individuals and whether there is an impact in terms of disease progression, adherence to treatment, suicide and/or quality of life needs clarification.

Leserman, Whetten and Lowe (2005) explored the impact of recent stressful events, trauma and PTSD on biological markers as well as physical functioning and healthcare utilisation in HIV-seropositive individuals in the ñCoping with HIV/AIDS in the South-East study ï CHASE Studyò. Results of 611 interviews showed that patients with more lifetime trauma, stressful events and PTSD symptoms reported more bodily pain and poorer functioning. Trauma and PTSD symptoms predicted an increase in healthcare utilisation, but this was not explained by CD4 count or viral load.

2.5.5.1 Impact on disease progression

The impact of stress on disease progression has already been discussed in the section on depression and disease progression. Research into the impact of anxiety disorders on progression is limited and the findings do not confirm a direct association between specific anxiety disorders and disease progression. Perry, Fishman and Jacobsberg (1992) found no association between emotional distress and biological markers of progression. One study, by Kimerling, Calhoun and Forehand (1999), found a high prevalence of traumatic stressors and PTSD in their small sample of HIV-seropositive women. In this study, traumatic stressors were significantly associated with lower CD4 to CD8 ratios at 1-year follow-up and those with PTSD symptoms as well had an even lower CD4/CD8 ratio.

2.5.5.2 Impact on adherence

A number of studies have shown an association between specific anxiety disorders and adherence and, therefore, an indirect effect on disease progression (Tucker, et al., 2003). In addition to the study by Tucker et al. (2003), Boarts, Sledjeski and Bogart (2006) found that PTSD had a negative impact on adherence, and Delahunty, Bogart and Figler (2004)

found an association of PTSD with worse adherence but also found lower morning salivary cortisol levels and **higher** CD4 counts.

2.5.5.3 Impact on suicidal behaviour

The impact of psychiatric disorders in general on suicidal behaviour in HIV-infected individuals has been discussed in the section on Depression. Although anxiety disorders have been associated with an increased prevalence of suicidal behaviour, it is difficult to separate these disorders from mood and substance use disorders in the affected individuals and it would appear that the latter two diagnoses have a particularly strong association with suicidal behaviour in this group.

2.5.6 Impact of mental disorders on quality of life

In terms of the impact of depressive or anxiety disorders on quality of life in HIV-infected individuals, the evidence is not specific for these disorders, but it is nevertheless likely that it is significant. Hays, Cunningham and Sherbourne (2000) reported on findings of the HIV Cost and Services Utilisation Study, which found that emotional well-being was significantly worse in HIV-infected individuals than in the general population and in other chronic disease populations (except for depression). There was no difference across the stages of the disease, but HIV-related symptoms were strongly associated with poor physical and mental health.

2.6 Conclusion

From the studies reviewed, it appears that depressive disorders in HIV-infected individuals internationally and in South Africa are a significant problem and that HIV-infection (or knowledge of HIV status) probably does increase the risk of developing a depressive

disorder, although the risk is probably similar to the risk in other chronically medically ill individuals. Whether or not there is actually an increased risk in HIV-infected, compared to non-HIV-infected individuals, the burden of depressive disorder is high in this group of individuals, and warrants treatment. Important risk factors for depressive disorders in HIV-infected individuals, which have been identified in the literature, include: the individualôs clinical condition, their past psychiatric history, other co-morbid mental disorders such as substance abuse, the level of psychosocial stress to which they are exposed, a lack of social support and the individualôs particular coping style. There has been little research in terms of protective factors, but it has been suggested that personality characteristics, levels of spirituality and good social support may be important protective factors. The impact of depressive disorders on disease progression, adherence and suicidal behaviour is highlighted as an important reason why these disorders should be identified and treated.

Evidence from prevalence studies of anxiety disorders is variable; few rigorously conducted studies have been conducted, and these do not show a significant difference between HIV-seropositive and HIV-seronegative individuals, although there appears to be a significant difference in levels of anxiety symptoms. The results are confounded by differing approaches to diagnosis and the considerable overlap of symptoms of anxiety disorders and depressive disorders. As with depressive disorder, the variability of the prevalence of anxiety disorders in both infected and uninfected populations across continents and countries is noted. The literature on risk factors for anxiety disorders in HIV-infected individuals emphasises the impact of psychosocial stress and the interaction of stress (both early in life and in adulthood) on neurobiological pathways that predispose the individual to anxiety disorders. The research on protective factors is extremely limited and is often linked with depressive disorders. A review of the literature indicates that the

impact of anxiety disorders on HIV-infected individuals is considerable in terms of adherence (and thus indirectly on disease progression), suicidal behaviour and quality of life.

Therefore, depressive and anxiety disorders are common in HIV-infected populations. There is a wide variability in prevalence rates, some of which may be a reflection of methodological differences, or the variability in prevalence rates in general in community studies and primary care populations across the globe. While evidence exists that these disorders are at least as common in HIV-infected individuals as in people with other chronic diseases, it has not been proved that people with HIV-infection suffer greater emotional distress than people with other chronic illnesses.

The information on prevalence, risk and protective factors in HIV-infected individuals in South Africa is limited. The aim of the current study was to explore some of these areas.

CHAPTER 3

METHODOLOGY

3.1 Study design

This was a cross-sectional, descriptive-analytic study.

3.1.1 Study population

The study population was as follows:

1. All HIV-seropositive individuals attending HIV-wellness clinics run under the auspices of the Perinatal HIV research unit of the University of the Witwatersrand at the following sites:
    a. Chris Hani Baragwanath Hospital, in Soweto, Johannesburg, Gauteng
    b. Weilerôs Farm, an informal settlement south of Johannesburg, Gauteng
    c. Tintswalo Hospital in Limpopo Province. (During the study period, this area was incorporated into Mpumalanga Province).
2. All patients attending the Nthabiseng HIV-clinic at Chris Hani Baragwanath Hospital. When the study started, the clinic included a general clinic on a Wednesday, where patients who were newly referred to the clinic, and those who did not yet qualify for anti-retroviral treatment, were seen. Patients receiving anti-retroviral treatment were seen on all other days of the week once the anti-retroviral treatment roll-out was initiated (April 2005).

3.1.2 Inclusion criteria

- All HIV-seropositive individuals over the age of 18 years attending the various clinics.
- Willingness to be screened and interviewed.

3.1.3 Exclusion criteria

Any patient reluctant to participate in the study was excluded. An unforeseen exclusion criterion was that the potential participant was a prisoner. A number of prisoners attend the HIV clinic at Chris Hani Baragwanath Hospital for treatment. Prisoners can be included in research studies only with the consent of the head of Correctional Services. If a certain randomisation number had been allocated to a prisoner on a particular day, it was óskipped outô and an additional randomisation number was used. The same strategy was used in the rare case that a particular individual selected by the randomisation strategy was not willing to participate.

3.1.4 Sampling and Randomisation

A randomisation strategy was used to select participants in the study on each day of interviews. On each clinic day, patients were given a number according to their place in the queue (this is a normal routine at the clinics). Random numbers were computer-generated and potential participants were selected using these numbers. The total number of numbers for each day was estimated based on knowledge of the daily patient load at each clinic. The number of patients attending each of the sites daily varied according to the site. During the year of data collection, the number of patients attending PHRU Wellness clinic at Chris Hani Baragwanath Hospital was limited to a maximum of thirty patients a day. The clinics at Weilerôs Farm and Tintswalo saw fewer patients (about 10 to 20 per day). The numbers of patients attending the HIV clinic at the hospital ranged from 40 to 80 per day. Randomisation sheets were produced by the statistical department at the Peri-Natal HIV

Research unit, taking into account the varying daily attendance at each site. Therefore, for a busy day at Nthabiseng Clinic, random numbers were generated from a list of 1 to 60. On a quiet day in Tintswalo, random numbers were generated from a list of 1 to 10.

3.2 Measurements

3.2.1 Interview for obtaining demographic information and exploring risk and protective factors

A semi-structured interview was conducted with all participants to explore factors that may have been associated with the presence of a mental disorder in general or a more specific depressive or anxiety disorder. Some factors postulated as protecting individuals from these disorders were also explored. The following factors were considered:

- Demographic variables: age, gender, level of education, employment status, relationship status, household situation (financial status)
- Clinical indicators of HIV disease stage: WHO Clinical Stage, CD4 count, presence of other medical conditions
- Treatment with anti-retroviral medication
- Duration of knowledge of HIV status
- The amount and quality of voluntary counseling and testing
- Utilisation of support groups
- Impact of disclosure
- Impact of stigma/discrimination
- Feelings of isolation
- Religious faith as a coping mechanism
- Significant losses/bereavement

- Other significant psycho-social stressors
- Past history of psychiatric disorder
- Past or present substance use disorder

The role of personality and coping style were not explored, as this would have lengthened the interview considerably.

3.2.2 Screening for psychiatric disorder

Patients recruited for the study were screened, using the overview from the Structured Clinical Interview for DSM (SCID) non-patient, primary care version (First, Gibbon & Spitzer, 2002). This tool includes a screen for psychosis, but lacks a screen for cognitive disorders associated with HIV, so in addition, the International HIV Dementia Scale (IHDS) was used to screen for possible cognitive impairment.

3.2.3 Diagnostic interview

The research version of the SCID, non-patient, primary care version, with psychotic screen (First, Gibbon & Spitzer, 2002) was then used to interview participants who screened positive for a possible mental disorder. The interviews were conducted in English. Where the study subject was not fluent in English, the research assistant translated during the interview.

3.2.4 Rating of severity of disorder

All patients identified as suffering from a current depressive disorder were rated using the Montgomery-Asberg Depression Rating Scale (MADRS) to describe the severity of the depressive disorder (Montgomery & Asberg, 1979). The MADRS is a more preferable measure of depression than the Hamilton Depression Rating Scale in people with co-morbid physical illnesses, as it depends less on somatic symptoms of depression, which

could be confounding factors in this context (Khan, Broadhead & Kolts, 2004). All patients identified as suffering from a generalised anxiety disorder were rated using the Hamilton Anxiety Rating Scale (HAM-A) to describe the severity of the anxiety disorder (Bruss, Gruenberg & Goldstein, 1994).

3.2.5 Staging of HIV infection

Information regarding the staging of HIV-infection for every participant was obtained from the clinical file by the investigator, as was any relevant information regarding physical illnesses, laboratory investigations and medication that the subject was receiving. The staging was at the time of the interview, based on information in the file as well as the current history of the individualôs condition obtained from the participant.

3.3 Statistical considerations

The expected occurrence of depressive and anxiety disorders in this population ranges between 10% and 40% (from international literature). The conservative approach to determining the sample size was to consider an expected outcome of 40%. In order to detect an occurrence of 40% (with an accuracy of 7%), at the 95% confidence level, a sample of 180 was necessary (Elashoff, 2003). In addition, various variables (see section 2.4) were explored in terms of their relation to depression and anxiety. No more than 12 variables were expected to enter into a multivariate analysis. Hence, the suggested sample size of 10 to 15 subjects for every variable studied was met. Variables entered into multivariable analysis were those significant at a 0.20 level of significance in a univariate analysis.

The study sample therefore had to include a minimum of 180 people from the study sites. As outlined in the table below, 302 subjects were enrolled and interviewed.

Table 3.1 Study sample

Sample	PHRU	Weilers	Tintswalo	Nthabiseng Bara Gen	Nthabiseng Bara ARV	Total
Target sample	90	30	30	30		180
Actual Sample	111	41	30	60	60	302

3.4 Preparatory work

3.4.1 Planning the questionnaire

Initial planning work was done in collaboration with Professor Melvyn Freeman of the Human Sciences Research Council, who was engaging in a similar study. The two researchers developed an initial questionnaire exploring risk and mitigating factors together. The research assistant for this study, a trained psychiatric nurse with extensive experience, conducted interviews for Professor Melvyn Freeman prior to the initiation of this study. From this work, it was possible to revise the questionnaire used in this study in terms of the way in which questions were asked and the content of some of the questions. During this phase significant issues in relation to the quality of pre-test counseling were raised. As a result, an additional interview schedule was developed, which was administered to a sub-sample of study subjects. This interview explored various aspects of pre-test counseling.

Professor Melvyn Freeman also conducted individual semi-structured interviews with/of a number of HIV-positive individuals who were involved with an NGO in Grahamstown. A review of the information obtained from these interviews confirmed that the most significant issues raised had been included in the questionnaire for this study.

In addition, a focus group discussion with staff working in the wellness clinic at the PHRU at Chris Hani Baragwanath Hospital was facilitated by the investigator and research assistant. The aim this discussion was to inform staff of the purpose and methodology of the study, and to obtain information regarding their perceptions of the prevalence of psychiatric disorder in their clinic, the possible presenting symptoms and risk and mitigating factors. The information obtained from this discussion confirmed that relevant factors were to be explored. The discussion also highlighted the fact that the practitioners working in this service are very aware of the mental health issues related to HIV, but are often at a loss about to how to deal with these issues. The information obtained from this discussion was presented in poster form at the International AIDS Impact conference in Cape Town in April 2005.

3.4.2 The diagnostic interview

Considerable time was spent in exploring issues surrounding psychiatric diagnosis and research methodology in psychiatry. Various psychiatric diagnostic instruments were considered before the SCID was selected as the most appropriate for the purposes of this study.

In a research setting, the presence or absence of a mental disorder needs to be established according to internationally agreed-upon criteria. It should also be possible to make comparisons between various studies of the same disorder. Therefore, a structured approach, using standardised criteria for particular disorders, needs to be applied.

As evident from the literature review, considerable confusion exists regarding psychiatric diagnoses in research, and conclusions are sometimes drawn regarding psychiatric

diagnoses from studies that use screening instruments or rating scales. In a research context, when being particular about standardised diagnoses is required, it is necessary to consider the difference between screening tools, diagnostic instruments and rating scales.

Screening tools are used to identify/elicit disorders in a large population. They need to be easy and quick to administer and they need to detect all possible cases of disorder. They therefore need to be highly sensitive to the possible presence of disorder, but there should also be a number of ñfalse positivesò detected (not very specific). Examples of screening tools for depression are the Self-Reporting Questionnaire (SRQ) (Cherian, Peltzer & Cherian, 1998), the General Health Questionnaire (GHQ) (Schmitz, Kruse & Heckrath, 1999), the Centre for Epidemiological Studies ï Depression subscale (CES-D) (Radlof, 1977; Cheng & Chan, 2005), and the Prime-D (Fisher & Copenhaver, 2006).
A consideration of the CES-D highlights some of the difficulties involved in using screening tools in research studies. The original screening tool is a 20-item self-report measure, which includes screening for cognitive and affective symptoms as well as somatic symptoms of depressive disorder. Somatic symptoms are confounders in the presence of physical illness. Therefore, an alternative CES-D 10-item scale which excluded these symptoms was subsequently developed. The CES-D reports current symptomatology for the past seven days.

That the duration diagnostic criterion for DSM1VR Major Depressive Disorder is the presence of symptoms for at least two weeks already indicates the problems intrinsic to using this instrument to make a diagnosis. In a 1985 validation study (Breslau, 1985) comparing diagnoses made with the Diagnostic Interview Schedule (DIS), which at the time was considered the ñgold standardò psychiatric interview schedule determining

Research Diagnostic Criteria and Feighner Criteria (equivalent to DSM111 diagnostic criteria), it was found that the CES-D did not discriminate adequately between major depression and generalized anxiety disorder. It was also found that it had high sensitivity but low specificity (in keeping with the purposes of a screening tool) and ñhighò scores on the CES-D should be considered a reflection of depressive symptomatology, which cannot be equated with a clinical diagnosis of major depressive episode (MDE). The CES-D has been used in a number of studies on depression in HIV. Both the 20-item and the 10-item scales have been used. A significant problem when comparing studies in this field using this tool is the variation in cut-off scores and their definitions: some researchers use a cut-off of 16 or more as equivalent to a major depressive disorder, whereas others have defined this as ñprobable depressionò and others use a cutoff of 23 or more for MDE for the 20-item scale. One study by Cheng suggested a cutoff of 12 for the 10-item scale (Cheng, et al., 2005). Of note is that the 20-item CES-D has been validated in South Africa (Pretorius, 1993) and used in a recent study in HIV-positive mothers to assess depressive symptomatology (Swartz, Brandt & Dawes, 2005).

Rating scales: once a diagnosis has been made, these are used to determine the severity of the disorder in question, and to track response or progression longitudinally. Examples of rating scales include the Beck Depression Inventory (Storch, Roberti & Roth, 2004), the Hamilton Anxiety and Depression Rating Scales (Bagby, Ryder & Schuller, 2004), and the Montgomery-Asperg Depression Rating Scale (Montgomery, et al., 1979).

Diagnostic instruments make a diagnosis of a mental disorder. These are usually structured clinical interviews. Examples include the Diagnostic Interview Schedule (DIS) (Robins, Helzer & Croughan, 1981), the Structured Clinical Interview for DSM (SCID) (Segal,

Hersen & Van Hasselt, 1994), the Composite International Diagnostic Interview (CIDI) (Kessler & Ustün, 2004; Haro, Arbabzadeh-Bouchez & Brugha, 2006), the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing, Babor & Brugha, 1990) and the Mini International Neuropsychiatric Interview (MINI) (Sheehan, Lecrubier & Hairnet-Sheehan, 1998). Some of the differences between these instruments are outlined in the table below.

Table 3.2 Diagnostic instruments used in psychiatric epidemiological studies

Diagnostic instrument	Administered by:	Training	Diagnoses	Analysis
SCID	Clinician	Self-guided with user's guide and videos	Current and lifetime (DSM)	Computerised or manual
CIDI	Lay person	Structured training	1-month, 12-month and lifetime versions (ICD)	Computerised only
MINI	Clinician	Self-guided	Current (DSM)	Manual
SCAN	Clinician	Structured	ICD	Comp/manual

The SCAN developed from the Present State Examination (PSE) (Wing, Cooper & Sartorius, 1974), which the investigator had used in previous epidemiological research. However, this instrument only produces diagnoses of the subject's current mental state and not life-time diagnoses. Since a key question in the research was the relationship between the stage of HIV infection, knowledge of diagnosis and psychiatric disorder, it was important to be able to make diagnoses across the subject's lifetime. In addition, the SCAN now requires intensive training by an accredited SCAN trainer. There are none in South Africa. Analysis of data is by a computer programme, which involves considerable expense. The SCAN was therefore not suitable for the purposes of this study.

The CIDI is an interview schedule that can be administered by trained non-clinicians. It is recognized by the WHO as a user-friendly and appropriate interview schedule that can be used in a range of settings in order to conduct epidemiological research on mental

disorders. It has been used in a number of epidemiological research studies conducted recently by the WHO, including one such study in South Africa, the SASH study (Williams, et al., 2004). However, no-one is not allowed to use this instrument without training by the developers of the CIDI at the University of Michigan. Again, the results are analysed by a computer programme. The difficulties around obtaining permission to use the CIDI and the training and expense involved resulted in a decision not to use it. It is to be noted that the SCID was used in the South African SASH study to validate the CIDI.

The Mini International Neuropsychiatric Interview (MINI) is a shortened mental state examination that takes a trained clinician 15 minutes to administer. It is user-friendly and available in the public domain and does not require any additional training in order to be able to administer it. However, it also does not test for lifetime depressive disorders (only for recurrent major depressive disorder if there is a current major depressive episode), lifetime anxiety or substance use disorders. It also lacks a category for depressive disorders that do not meet criteria for a Major Depressive Episode, or for adjustment disorders.

The Structured Clinical Interview for DSM-1V-TR Axis 1 Disorders (SCID)

The SCID (First, et al., 2002) is a structured clinical interview that can be used to assess mental disorders and provide diagnoses according to the definitions and criteria of the fourth edition (revised) of the American Psychiatric Associationôs *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) (American Psychiatric Association, 2000). The SCID has been used in a variety of countries, cultures and settings (Wilson & Young, 1988; Buntting & Wessels, 1991; Williams, Spitzer & Gibbon, 1992). It is administered by a clinician or trained mental health professional who is familiar with the DSM-IV classification and diagnostic criteria (American Psychiatric Association, 2000).

The SCID has a research version and a clinical version. It consists of an overview section that allows the participant or patient to describe current and past psychiatric symptoms, and the researcher/clinician to explore the significance of such symptoms. The remainder of the SCID has a modular design which enables the researcher or clinician to eliminate consideration of major diagnostic classes that are irrelevant to their purposes.

The research version of the SCID is more comprehensive than the clinician version, but is designed to be used flexibly, depending on the circumstances of the individual study. The SCID is considered the gold standard in terms of making DSM research diagnoses and has been validated for use in both community and clinical populations in a range of countries and contexts (Segal, et al., 1994). Most other diagnostic instruments are validated by comparing them to the SCID (Haro, et al., 2006). Using the SCID, it is possible to obtain current and lifetime diagnoses. [Lifetime diagnoses include the diagnosis of a mental disorder at any time up to one month before the administration of the interview.]

The schedule is available from the developers, together with an 11-hour training programme on video. While a computer programme is available for analysis of results, this can also be done by the researcher, using a simple spreadsheet and statistical package.

Of the versions of the SCID, that chosen for this study was the primary care version, which is used in non-psychiatric (primary care) treatment settings. It includes a screen for psychotic disorders. The SCID was considered to be the most suitable diagnostic instrument as it is an appropriate instrument for experienced clinicians to use, training is accessible and not too expensive; it is available without undue regulation, has been well-

tested in many settings and is considered to be the gold standard in terms of psychiatric research interviews.

V-codes:

The SCID also generates V-codes as listed in the DSM classification. These are conditions that are not psychiatric disorders, but they are significant in that they often nevertheless require a mental health intervention. Examples of V-codes include bereavement and problems in interpersonal relationships (partner relational problem, parent-child relational problems.

3.4.3 The International HIV Dementia Scale

The SCID does not include any assessment of cognitive functioning. However, none of the other interview schedules listed above do this either. In order to cover this area, the International HIV Dementia Scale was used to screen for possible dementia due to HIV disease. This screening instrument has been found to have good sensitivity and adequate specificity in study populations in both the United States of America and Uganda in Africa (Sacktor, Wong & Nakasujja, 2005). See Appendix 2.

3.5 Logistics

3.5.1 Responsibilities of investigator

Training and preparation for data collection

The principal investigator and the study coordinator/research assistant were trained in administration of the SCID. The principal investigator also familiarised the research assistant with the complete interview schedule (semi-structured and diagnostic interviews), so that the interviews could run smoothly when translated/assisted by the professional

nurse/study coordinator. The research assistant also received training in GCP principles, recruitment procedures and collection of clinical data from the clinical records. The investigator supervised the research assistant throughout the study.

Information and training regarding the study was also provided for the clinicians/health workers at the study sites, as well as appropriate interventions (and referral resources) for patients who were identified to be in need of mental health intervention.

Preparation for data collection

The investigator prepared the case-report form (CRF) and the interview schedules in liaison with staff involved in data management at the PHRU. The CRF was prepared in a way that allowed scanning of the forms into a database. Quality control checks were then routinely completed to ensure that data entered was correct.

Data collection

The investigator and the study coordinator/research assistant were responsible for obtaining informed consent from each subject, for conducting the interviews and completing the case report form (CRF).

Data management and analysis

The data management department at the PHRU entered CRFs into a database and provided quality control over the data. Assistance with analysis of the data was obtained from the Epidemiology Data Centre of the Faculty of Health Sciences, University of the Witwatersrand, and the Biostatistics Unit of the Medical Research Council of South Africa.

3.5.2 Responsibilities of staff

A research assistant/study co-ordinator, Ms Dumi Masondo, was appointed to assist with the study. She is a trained professional nurse with a qualification in psychiatric nursing. The study co-ordinator was responsible for co-ordinating the study, liaising with clinical staff at the various study sites, recruiting study subjects according to the randomization strategy, assisting in obtaining informed consent for the study, collecting clinical information from the subjectsô clinical records and for assisting with translation for the principal investigator during interviews. She also assisted with the keeping of the study records, together with the data management department, and ensured proper data control procedures. Clinical staff working in the study sites worked closely with the investigator and the study co-ordinator.

3.6 Time schedule

1. The research protocol was submitted to the Postgraduate Committee in September 2003. Revisions were required, which included changing the psychiatric screening and diagnostic interview, improving the randomisation strategy and clarifying the rating scale for depression, which was to be used in the study. The committee finally approved the protocol on 20 October 2004.
2. The research protocol was submitted to the Committee for Research on Human Subjects (medical) in September 2003 and the committee approved the study. Amendments to the protocol were submitted to the committee in August 2004 and these were approved by the chairperson of the committee on 24 August 2004.
3. Approval from authorities at the various institutions was obtained. This included approval from the hospital management of Chris Hani Baragwanath Hospital,

Tintswalo Hospital, the Johannesburg Metro District Health Service, and the provincial health departments of Gauteng and Limpopo/Mpumalanga.

4. Preliminary exploratory work was conducted from September 2003 to September 2004.
5. Preparation of research instruments took from February 2004 to September 2004.
6. Preparation of protocols and referral resources for clinical staff and orientation of clinical staff to the study took place from July to October 2004.
7. Data collection was done from November 2004 to November 2005
8. Results were analysed and the thesis was written up between January 2006 and January 2008.

3.7 Data management and analysis

Data capture was carried out by data management staff of the Peri-Natal HIV Research Unit at Chris Hani Baragwanath Hospital. Analysis was done by the investigator, with assistance from Dr Piet Becker from the Medical Research Council and Mr. Eustacius Musenge from the Epidemiology Data Centre at the Faculty of Health Sciences. The Enterprise Guide for SAS Version 3 (SAS Version 9.1) (SAS institute inc., 2007) and STATA (Statacorp, 2007) were both used for the statistical analysis of the data. Univariate logistic regression analysis to identify significant risk and mitigating factors for mental disorders was carried out. Further multivariate analysis was undertaken only on those variables that were significant at a < 0.2 level of significance.

3.8 Resources

This study was conducted with financial support from the Division of Psychiatry of the University of the Witwatersrand, USAID (through its funding of the Perinatal HIV

Research Unit of the University of the Witwatersrand and the Human Sciences Research Council (Social Aspects of HIV/AIDS). Additional funding was obtained from the National Research Foundation (NRF) (through a Thutuka Grant to the investigator) in 2005 and 2006. The Biostatistics Unit of the Medical Research Council and the Epidemiology Data Centre of the Faculty of Health Sciences, University of the Witwatersrand provided assistance with statistical analysis of the research.

3.9 Ethical and legal considerations

The study was introduced at all the study sites by clinicians working at these sites. In order to ensure confidentiality of HIV status, clinical staff advised patients of the study before they were approached by the researchers. Only patients who agreed to be approached were included in the recruitment process. All participants were clearly informed about the purpose of the research. Furthermore, they were provided with an opportunity to decide whether or not they wanted to participate in the study.

3.9.1 Risks and benefits

There were no risks associated with the study. The benefit was that early intervention and treatment was offered to individuals with a positive psychiatric diagnosis.

3.9.2 Privacy and confidentiality

Every effort was made to keep all patient information private and confidential. Participants were assigned study numbers to identify them in the study, and were not identifiable by name on the data collection forms. All source data remains in secure sites at the Peri-Natal HIV Research Unit or at the study sites. All staff involved in the research followed standard procedures (both in operation at the sites, and in relation to mental disorders) to

ensure confidentiality. These were described to the staff in the information sessions held before the study commenced.

3.9.3 Compensation

Participants did not receive any financial compensation for taking part in the study. However, their transport and refreshment costs were reimbursed. Each participant at the study sites in Gauteng received R30. The issue of this payment at Tintswalo generated some concern amongst the staff and directors of the service. Thirty rand in a poverty-stricken rural context was considered a perverse incentive and the staff there was opposed to our providing the participants with this amount of money. They felt that it could create conflict within the patients, particularly those who were not selected in the randomisation process. It was finally agreed that the money allocated for payment to the study subjects each day would be pooled and a meal for all the patients attending the clinic that day was provided out of this fund. It was felt that all the patients contributed to the study, either by participating directly or by waiting longer than usual for service as a result of staff involvement in the research.

3.9.4 Conflicts of interest

There were no conflicts of interest in this study.

3.9.5 Informed consent

Written informed consent was obtained for all aspects of this study. This included consent to access the participantsô clinical records, and also included consent from all staff participating in the focus group discussion.

The information letter and consent form was read, explained and given to individual participants. The investigator ensured that the participant understood the information, the potential risks and benefits, confidentiality and privacy issues.

If a potential participant was unable to give informed consent, s/he was to be included only if a responsible escort was in a position to give proxy consent. This did not happen with any of the participants who were interviewed. A number of participants were unable to read or write. In these cases, with the participantsô agreement, their consent was witnessed by an independent person.

3.9.6 Follow-up for mental disorders

All study subjects were informed of the availability of treatment for psychiatric disorders. The staff working at the study sites received some training and information regarding the management of common mental disorders. Study subjects were encouraged to discuss any concerns with their treating clinicians. Possible treatments included medication, psychotherapy, counselling or involvement in a support group and/or referral to a specialised mental health service. These were offered singly or in combination. Protocols for the use of anti-depressant medications available on the primary level Essential Drugs List (EDL) in Gauteng and Limpopo were provided at the study sites. Criteria for referral to a psychiatrist/mental health service were also provided.

Participants identified as needing a mental health intervention, (or who needed attention for a physical disorder, including possible HIV dementia) were referred to the clinician who was primarily responsible for their treatment. If this clinician could manage the problem, no further action was taken. However, where the researcher felt that the

participant needed a specialist mental health referral, this was discussed with the responsible clinician and the researcher made a referral to the nearest mental health service. A copy of the referral letter was inserted into the participantôs clinical record.

Contingency plans were discussed beforehand with regard to a possible situation where the investigator might be urgently concerned about the mental condition of a study subject. It was agreed that she would ask the subject if she could inform the treating clinician of her concern and ensure that the subject was seen by a clinician who could take over the management of the mental disorder. If the study subject refused such referral or treatment and the investigator remained concerned, the investigator would then inform the head of the HIV service, or the delegated responsible person, immediately and a joint decision would be made regarding the management of the individual. It could have become necessary in such a case for the principal investigator/head of the HIV-service to identify the subject in order to ensure that the subject received the necessary intervention and for procedures in terms of mental health legislation to be followed. The training of the study co-ordinator and the input provided to the clinical staff working at the study sites covered these aspects, and they were given information regarding management of common mental disorders, indications for referral to a mental health service and a list of referral resources. The mental health service, in the district health service and at the hospitals, was also informed of the study, and the possibility of referrals for emergency management. However, no subject required urgent psychiatric intervention and no-one refused referral to a mental health service when this was suggested.

3.9.7 Ethical approval

This study was approved by the University of the Witwatersrand Human Research Ethics Committee (Medical) on 26 September 2003, with a further approval of an amendment to the protocol on 24 August 2004 (Protocol Number: 03-09-51; ref R14/49 Thom)

3.10 Critique of study methodology

Because this was a cross-sectional descriptive analytic study, it was able to provide a picture of participantsô lives at a particular point in time. For collecting data on current mental status, this is adequate, but a richer and probably more accurate picture would have been obtained in a prospective longitudinal study. The recent report by Swartz et al. (2005), which (amongst other things) explored the mental health of young HIV-seropositive mothers, exemplifies how such research could be done. In terms of exploring risk and protective factors, again, a more comprehensive assessment would have been obtained using a longitudinal study design, with more qualitative research methods. These are, however, labour- and time-intensive, so the methodology was chosen as above. These factors must, however, be borne in mind when considering the results of the study.

Much of the literature in the area of HIV and mental disorders reports on psychiatric symptomatology as well as disorders. For example in the WHO study (Maj et al, 1994)), in addition to using the CIDI to make a diagnosis of a depressive disorder, the MADRS was administered to all participants to generate rates of depressive symptomatology. In this study the MADRS was completed only for those participants who were identified as having a depressive disorder. This gave an indication of the range of severity of these depressive disorders. Using the MADRS in all participants gives an indication of the extent of depressive symptomatology in all participants. It is not clear how useful assessing

symptomatology is. On the one hand, it can identify individuals who are distressed but who do not meet criteria for a depressive disorder. On the other hand, one would expect that there should be an association between depressive disorder and higher scores on a rating scale, so that outlining the extent of depressive symptomatology is not likely to add much information about the participants. In addition, rating symptomatology in this manner gives a result at a particular point in time, i.e. at the time of the interview, and is dependent on the individualôs feelings at that particular point in time, which may be transitory. How useful this is in terms of assessing an individualôs need for intervention is debatable.

There has been considerable research examining the influence of language and culture on the diagnosis of disorders; particularly, depressive and anxiety disorders (Swartz, 1998). While understanding of these disorders has advanced from biological, psychological and social perspectives, the question remains as to whether mental disorders and diagnostic criteria are standard across cultures. Both quantitative epidemiological studies and qualitative ethnographic research can contribute to our understanding of these disorders across cultures. This research is based on the premise that depressive and anxiety disorders (and other mental disorders) do exist in all cultures and can be diagnosed through using standardised diagnostic instruments. Recent ethnographic research in Africa has provided interesting evidence of this in the area of depressive disorders and the HIV epidemic (Wilk, et al., 2002). While there are valid concerns about using a categorical approach to diagnose mental disorders in people who are individuals, in differing cultural contexts, the DSM or ICD systems, imperfect as they are, provide the best approach available thus far, in terms of comparing disorders across studies.

CHAPTER 4

RESULTS

Three hundred and two interviews were conducted as set out in the table below.

Table 4.1: Breakdown of participants by site

Site name	Site number	Number of interviews
Wellness PHRU	1	111
Wellness Tintswalo	2	30
Nthabiseng General clinic CHB	3	60
Nthabiseng ARV clinic CHB	4	60
Wellness Weilerôs Farm	5	41
Total		302

4.1 Demographic characteristics of study sample

Just over seventy percent (70.2%) of the participants were female and 29.8% were male. The mean age of the study sample was 36.3 years, with a range from 19 to 63 years. Just over sixty percent (60.6%) of the participants described themselves as currently single, divorced or widowed and 39.4%, as married or in a long-term relationship. Most (83.11%) of the participants had children, with a mean number of children (alive) of 1.92.

Only 17% of the study sample had completed secondary education. Unemployment in the study sample was high: almost seventy percent (69.87%) of the participants were unemployed; 19.87% were in part-time employment, self-employed or had ñpiece jobsò and 10.26% were in full-time employment. Forty percent (40%) of the participants felt that they had insufficient financial income to provide for even the most basic needs (food and clothing), while 47% of the participants felt they had just enough funds to provide for basic needs alone. Only 13% felt they were able to afford most of the important things in their households. While there may have been some reporting bias in this subjective reporting,

the findings did indicate that the study population came from a socially deprived and disadvantaged sector of the population.

4.2 Clinical characteristics of the study sample

Clinical stage

At the time of their interviews, seventy-two percent of the participants were in WHO Clinical Stage 1 or 2, and 28% were in Stage 3 or 4.

CD4 count

Two hundred and seventy-three participants had at least one CD4 count recorded in their clinical files. The mean for the most recent CD4 count of these participants was 243 cells/ml. One hundred and fifty-four (51% of the total sample) and 56.4% of those who had a CD4 count (n=273) had a count of <200 cells/ml. This indicates the minimum number of participants who qualified for HAART at the time of the study. (Participants who did not yet have a CD4 count result may also have had a count < 200 cells/ml.)

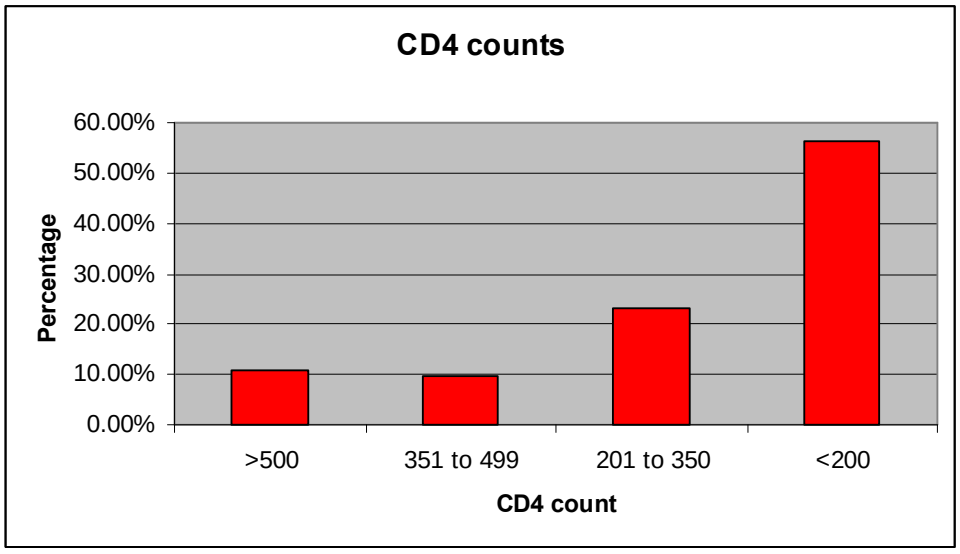


Figure 4.1: Percentage of participants in each CD4 count category

Viral load

Ninety-nine participants had a recorded viral load. Ninety-four of these participants were patients at the HIV clinic at Chris Hani Baragwanath Hospital. The mean viral load was 1,128,938 copies/ml, with a range from 25 copies/ml to 50 million copies/ml.

Anti-retroviral therapy

Seventy participants (23.18%) of the total sample had started anti-retroviral therapy at the time of their interview. This is in contrast to the 154 (51%) of participants who qualified for anti-retroviral therapy at the time of their interview. Ninety percent of the participants receiving ART were attending the HIV clinic at Chris Hani Baragwanath Hospital.

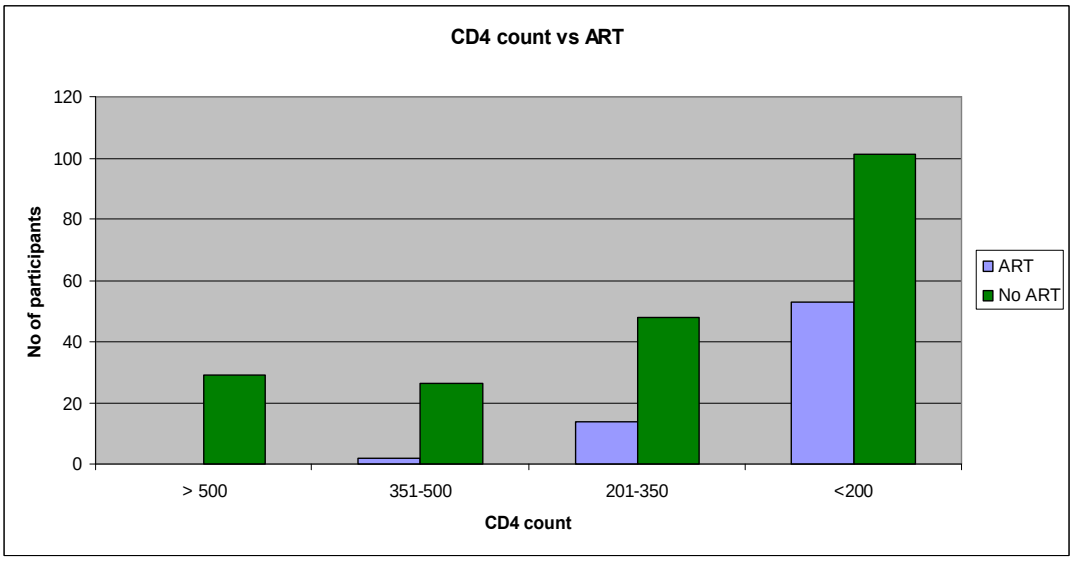


Figure 4.2: Number of participants on ART by CD4 count category

From the table above, it can be seen that only about a third of participants with a CD4 count of < 200/ml were on HAART at the time of their interview. Many of these were waiting to start treatment. From the table it can be seen that a number of individuals were on HAART and had CD4 counts > 200 cells/ml. These were individuals who had been on treatment for some time, and is probably an indication of their response to treatment.

Table 4.2: Viral load by ART

ART	N	Mean viral load (copies/ml)	Range (copies/ml)
Not on ART	43	1 420 026	4 000 to 50 million
On ART	56	905 425	25 to 22 million

The difference in mean viral load between those on ART and those not on ART was not statistically significant. This was to be expected, since many participants had only recently commenced ART and data on duration of ART treatment was not obtained.

This information may not be that useful, since there may be a number of reasons for a high viral load. It would have been more useful to identify those on HAART with an undetectable viral load as a measure of the success of treatment.

Medical conditions in addition to HIV infection

Over 40% of the study sample (n=127; 42.05%) had, in addition to HIV infection, at least one other medical condition. Almost 75% (74.02%) of these could be directly related to HIV infection. The most common opportunistic condition was tuberculosis.

4.3 Demographic and clinical characteristics of participants by site

Table 4.3: Summary of demographic and clinical characteristics by site

	Site 1 PHRU	Site 2 Tintswalo RADAR	Site 3 HIV CHB General (Wed)	Site 4 HIV CHB ART	Site 5 Weilerôs Farm	Total
Participants (n)	111	30	60	60	41	302
Gender M:F (%)	15: 85	30: 70	37: 63	48: 52	32: 68	30: 70**
Mean Age (yrs)	32.8	39.7	38.7	39.1	35.8	36.3**
Relationship status single: in relationship (%)	60: 40	60: 40	58: 42	57: 43	71: 29	61: 39
Mean No of children (n)	1.8	2.9	2.0	1.5	2.0	1.9
Household situation: Cannot afford basics (%)	34	50	30	32	76	40**
Employment status: Unemployed (%)	60	80	77	68	80	70**
Part-time employment (%)	30	17	8	18	15	20
Full-time employment (%)	10	3	15	13	5	10
Level of education Completed secondary education (%)	28	7	13	13	7	17**
Clinical stage 1 (%)	55	13	18	23	51	37**
Clinical stage 2	35	20	37	45	27	35**
Clinical stage 3	10	64	33	20	20	23**
Clinical stage 4	0	3	12	12	2	5**
Mean CD4 (cells/mm3)	356	285	140	132	260	243**
CD4 < 200 (%)	26	40	80	82	39	51**
Number on ART (%)	1	13	27	78	5	23**
Medical condition (%)	28	20	63	52	51	42**

** Statistically significant difference between sites ($p<0.05$)

* Some significance ($p<0.2$)

Notes:

1. Overall, there was a statistically significant difference in gender ratio, mean age, level of education, employment status and household situation between sites ($p<0.05$). There was no significant difference in relationship status or in the mean number of children between sites.
2. There was a statistically significant difference in clinical stages at the different sites with more people being in Stage 1 at the PHRU and Weilerôs Farm sites ($p<0.05$).
3. There was also a statistically significant difference in mean CD4 count at the different sites ($p<0.05$). Participants at the Nthabiseng HIV clinics at Chris Hani Baragwanath Hospital had significantly lower mean CD4 counts than those at the other three sites.
4. Significantly more participants at the Nthabiseng sites and at Weilerôs Farm had concurrent medical conditions than those at PHRU or Tintswalo. The Nthabiseng general HIV clinic had the most participants with a medical condition.

In general, participants attending PHRU Wellness clinic were more likely to be female, and in the earlier stages of HIV infection, with a higher mean CD4 count and fewer associated medical conditions.

Participants at Tintswalo hospital were older than those at the other sites, were predominantly female, were less educated, had more children and were predominantly in the later clinical stages of HIV infection, although they had an intermediate mean CD4 count.

Participants at both the Nthabiseng clinics at Chris Hani Baragwanath Hospital were also generally older and there were more males attending at this site than at any of the other sites. In general, more participants had a higher level of education, were employed (either full-time or part-time) and were better-off financially than those at the other sites. They were, however, more medically ill, with more associated medical conditions and the lowest mean CD4 counts, although fewer participants were in Stages 3 and 4 than at the Tintswalo Hospital site.

The Weilerôs Farm site had the most participants with low levels of education, who were single and considered themselves the worst off in terms of financial status. Gender ratio and clinical indicators were intermediate between the Nthabiseng clinics and Tintswalo Hospital.

4.4 Demographic and clinical characteristics by gender

Females were in the majority in the sample. There were statistically significant gender differences in age, levels of education and relationship status ($p<0.05$). Females were

generally younger (mean age 34.9 years vs. males mean age 39.5 years; $p<0.0001$), better educated and more likely to be in a relationship than males in the sample.

There was also a statistically significant gender difference in clinical stage ($p=0.0155$): females were more likely to be in Stage 1 or 2 of HIV infection. The difference in mean CD4 count between genders was also statistically significant ($p=0.0003$). The mean CD4 count in males was 167 cells/ml and in females it was 274 cells/ml.

4.5 Occurrence of mental disorders in the study sample

Although the primary focus of this study was on depressive and anxiety disorders, other mental disorders were found in the participants, which could have been confounders or contributors to the occurrence of depression and anxiety. For example, substance use disorders are commonly associated with mood and anxiety disorders, and medical conditions can also produce organic mood and anxiety disorders. The sample was therefore analysed for the presence or absence of a current and lifetime mental disorder or a V-code.

The mental disorders included in the analysis were:

1. Mood disorders
2. Anxiety disorders
3. Substance use disorders
4. Adjustment disorders
5. Mental disorders secondary to a general medical condition (including HIV/AIDS) or substance use
6. Psychotic disorders (screen on SCID)

7. Possible Dementia due to HIV disease (screen with International HIV Dementia Scale and make a clinical diagnosis)

Although diagnosed separately, adjustment disorders were regarded as depressive disorders and are included in the discussion about these disorders.

4.5.1 Current mental disorders

Almost one third (94) of participants (31.13%) had at least one current mental disorder and fifty-five (18.21%) had a V-code only. Forty-three participants had two current mental disorders, and 3 participants had three current mental disorders.

4.5.2 Lifetime mental disorders

One hundred and twenty-one (40.07%) participants had evidence of at least one mental disorder at some stage in their lives (up to one month prior to interview). Forty participants had a second lifetime disorder and six participants had a history of three lifetime disorders. Thirteen (4.3%) participants had a lifetime history of a V-code.

Figure 4.3: Current mental disorder and V-codes

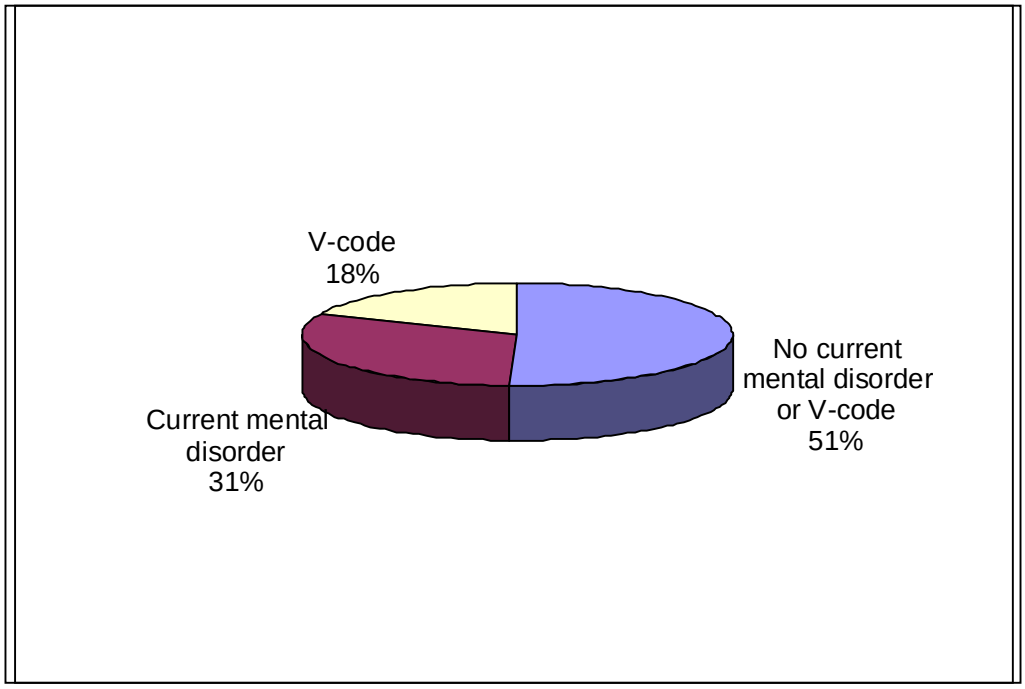


Figure 4.4: Lifetime mental disorders and V-codes

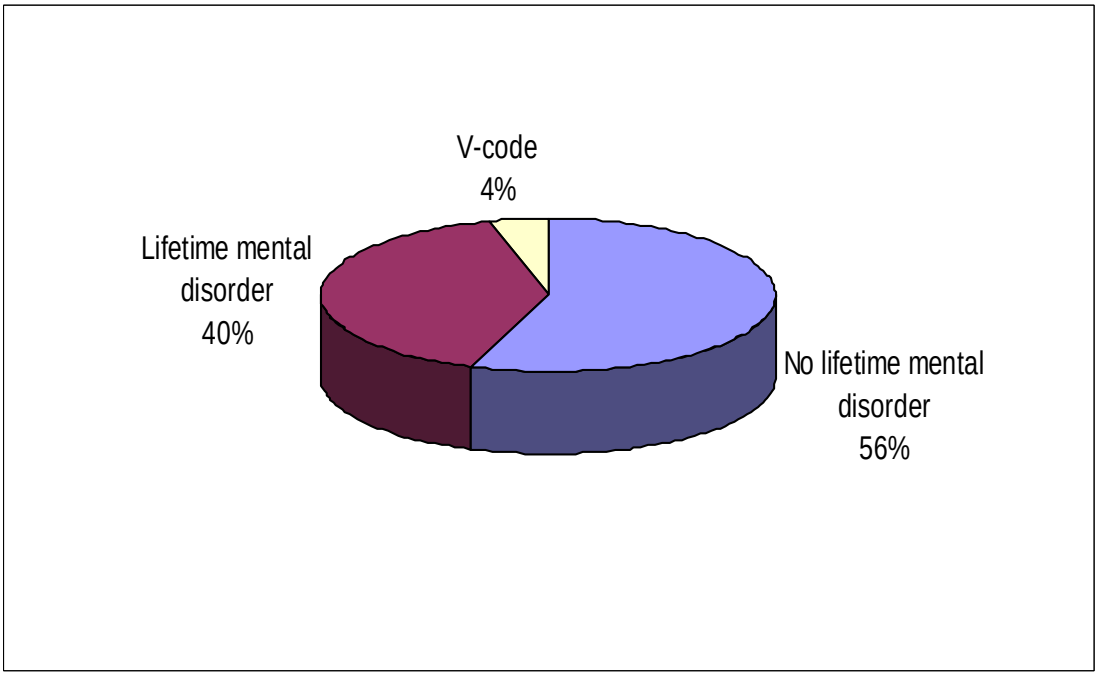


Table 4.4: Breakdown of mental disorders (current and lifetime) by diagnostic groupings

	Current mental disorders		Lifetime mental disorders	
Diagnostic grouping	No	Percentage of total participants (n=302)	No	Percentage of total participants (n=302)
Mood disorder	34	11.26%	48	15.89%
Anxiety disorder	12	3.97%	11	3.64%
Adjustment disorder	20	6.62%	0	0%
Substance use disorder[2]	23	7.62%	56	18.87%
Dementia (HIV)	11	3.64%	11	3.64%
Organic mental disorder ï other (delirium, dementia, mental disorder secondary to general medical condition or substance use)	3	9.93%	5	1.66%
Psychotic disorder	14	4.64%	12	3.97%
Other mental disorder	0	0%	1	0.33%
V-code	76	25.17%	21	6.95%

4.5.3 Relationship of lifetime mental disorders to diagnosis of HIV infection:

Of the 121 participants with at least one lifetime mental disorder, 86 (28.48% of the total sample) had the onset of at least one mental disorder prior to knowledge of their HIV status.

Table 4.5: Relationship of lifetime mental disorder to HIV diagnosis

Relation to HIV diagnosis	Frequency	Percent	Cumulative Frequency	Cumulative Percent
No mental disorder[3]	181	59.93	181	59.93
Lifetime mental disorder prior to HIV diagnosis	86	28.48	267	88.41
Lifetime mental disorder since HIV diagnosis	35	11.59	302	100.00

[2] Many participants had more than one comorbid substance use disorder. See section on substance use disorders

[3] Participants may have had a V-code

The remaining 35 participants with a lifetime mental disorder had no history of a mental disorder prior to receiving their diagnosis of their HIV status. This constituted 11.59% of the total sample, and consisted of participants primarily with dementia due to HIV disease and depressive disorders.

Table 4.6: Breakdown of primary lifetime mental disorder into categories

Primary lifetime mental disorder	Total	Percent	Pre-HIV diagn.	Percent	Post-HIV diagn.	Percent
Dementia due to HIV disease	7	5.8%	0	0%	7	20%
Mood disorder	48	39.7%	22	25.6%	26	74.2%
Psychotic disorder	9	7.4%	8	9.3%	1	2.9%
Anxiety disorder	7	5.8%	6	7.0%	1	2.9%
Substance use disorder	45	37.2%	45	52.3%	0	0%
Organic mental disorder ï other	5	4.1%	5	5.8%	0	0%
Total	**121**	**100.00%**	**86**	**100.00%**	**35**	**100.00%**

This does not include the substantial number of V-code diagnoses that were related to the knowledge of a positive diagnosis of HIV infection. The most common mental disorder prior to diagnosis of HIV infection was a substance use disorder. The most common mental disorder after diagnosis of HIV infection was a mood disorder

4.5.4 Individual groups of disorders

4.5.4.1 Mood disorders

Current depressive disorder

A total of 34 participants had a diagnosis of a current mood disorder. One was diagnosed with a Bipolar Disorder in remission. The remaining 33 (10.92%) had a depressive disorder. In addition, 18 (5.96%) participants received a diagnosis of an adjustment disorder with mixed anxiety and depressed mood or depressed mood. (One participant received a diagnosis of adjustment disorder with disturbance of conduct, and one had an

adjustment disorder with anxiety only.) Thus, 16.88% of the participants had a current depressive disorder. Twenty-five (8.28%) participants were suffering from depressive symptoms related to a recent bereavement. (None of these participants met criteria for a depressive disorder.) Incorporation of all these diagnoses gives a total of 25.16% of participants who had depressive symptomatology that met criteria for a mental disorder or a V-code. (Participants diagnosed with schizoaffective disorder were classified as primarily having a psychotic disorder and were not included in the analysis of mood disorders.)

Fifteen participants (4.96%) met criteria for a diagnosis of a current Major Depressive Episode. Four of these had evidence of a general medical condition that could have contributed to their mood disorder. In one of these cases, the episode appeared to be related to antiretroviral medication (efavirenz). Sixteen participants (5.29%) had depressive symptoms that did not meet criteria for a Major Depressive Episode, but could be classified as depressive disorder Not Otherwise Specified (NOS). Three of these had evidence of a co-morbid medical condition that could have contributed to the mood disorder and in another three there was evidence of a substance use disorder that could have contributed to the mood disorder. Two participants met criteria for a current dysthymic disorder.

Table 4.7: Current depressive disorders

Current Diagnosis	Freq	%	Cum Freq	Cum %
Major depressive episode	11	3.64	11	3.64
MDE secondary to GMC	4	1.32	15	4.96
Dysthymic disorder	2	0.66	17	5.62
Depressive disorder NOS	10	3.31	27	8.93
Mood disorder secondary to GMC (not MDE)	3	0.99	30	9.92
Substance-induced mood disorder	3	0.99	33	10.92
Adjustment disorder with depressed mood or mixed anxiety and depression	18	5.96	51	16.87
Total depressive disorders	**50**	**16.87**		
Bereavement symptoms	25	8.28		
Total depressive syndromes	**75**	**25.16**		
Bipolar disorder in remission	1			

Severity of depressive disorders

MADRS scores were obtained only for those participants who met DSM1V criteria for a depressive disorder (including adjustment disorder with depressed mood). The mean MADRS score for these participants was 31, with a range from 11 to 57.

Lifetime depressive disorders

Forty-eight participants (15.89%) had a lifetime history of a depressive disorder. Thirty-one (10.26%) of these had a lifetime history of at least one major depressive episode. In 19 (61.3%) of these participants, the onset of the first major depressive episode occurred after the diagnosis of HIV infection was made. Fifteen participants had a lifetime history of at least one depressive episode that did not meet full criteria for a major depressive episode (Depressive Disorder NOS). Seven (46.67%) of these participants had their first depressive episode after the diagnosis of HIV infection was made. Overall, there is no statistically significant difference in the number of participants who developed a lifetime depressive disorder before or after the diagnosis of HIV infection. More participants with a lifetime

major depressive disorder developed this after diagnosis of HIV infection compared to before the diagnosis, but the difference is not statistically significant.

Table 4.8: Lifetime depressive disorders

Lifetime Diagnosis	Total No.	%	Pre-HIV diagnosis	%	Post-HIV diagnosis	%
Major depressive episode	31	10.26%	12	3.97%	19	6.29%
Depressive disorder NOS	15	4.97%	8	2.65%	7	2.32%
Dysthymic disorder	2	0.66%	2	0.66%	0	0
Total	**48**	**15.89%**	**22**	**7.28%**	**26**	**8.61%**
Bipolar disorder	1		1		0	

4.5.4.2 Anxiety disorders

Twelve participants received a diagnosis of a current anxiety disorder (including one participant with a diagnosis of adjustment disorder with anxiety). In three of these participants there was a co-morbid mood disorder. The following anxiety disorders were diagnosed:

Table 4. 9: Current anxiety disorders

DIAGNOSIS	NO.	%
POSTTRAUMATIC STRESS DISORDER	3	0.99%
GENERALISED ANXIETY DISORDER	3	0.99%
SOCIAL PHOBIA	2	0.66%
PANIC DISORDER	1	0.33%
ANXIETY DISORDER NOS	2	0.66%
ADJUSTMENT DISORDER WITH ANXIETY	1	0.33%
TOTAL	12	3.96%

Eleven participants had a lifetime diagnosis of an anxiety disorder. The following anxiety disorders were diagnosed:

Table 4.10: Lifetime anxiety disorders

DIAGNOSIS	NO.	%
POST-TRAUMATIC STRESS DISORDER	7	2.31%
GENERALISED ANXIETY DISORDER	0	0%
SOCIAL PHOBIA	2	0.66%
PANIC DISORDER	2	0.66%
TOTAL	11	3.63%

The only lifetime anxiety disorder that occurred after the diagnosis of HIV infection, was in one participant who developed a panic disorder without agoraphobia after the diagnosis of HIV infection was made. Another participant, with a lifetime history of panic disorder, did not meet criteria for a current panic disorder, but did have a current major depressive episode.

4.5.4.3 Adjustment disorders (see under depressive and anxiety disorders)

As outlined in the section on depressive disorders above, most participants with adjustment disorders had mixed mood and anxiety symptoms. A strong relationship was found between severity of psychosocial stressors and the presence of an adjustment disorder but there was no relationship between recent diagnosis of HIV and the presence of an adjustment disorder (p=0.3). It appears that other psychosocial stressors (besides knowledge of HIV status) were largely responsible for the development of adjustment disorders.

4.5.4.4 Substance use disorders

Fifty-seven participants (18.87% of the total sample) met criteria for a lifetime substance use disorder, while only 23 (7.62%) of these participants were diagnosed with a current substance use disorder. Presuming that reporting on current substance use disorders is accurate, this indicates a significant reduction in the occurrence of substance use disorders (two sample test of proportion; $p<0.0001$).

Table 4.11: Breakdown of current substance use disorders

Substance use disorder	**No.**	**Percentage**
Alcohol abuse and dependence only	17	73.91%
Cannabis only	2	8.70%
Alcohol and cannabis	3	13.04%
Other substances only	1	4.35%
Total participants with current substance use disorder	**23**	**100.00%**

Table 4.12: Breakdown of lifetime substance use disorders

Substance use disorder	**No.**	**Percentage**
Alcohol abuse only	27	47.39%
Alcohol abuse and dependence only	18	31.58%
Alcohol and cannabis	7	12.27%
Cannabis abuse only	1	1.75%
Polysubstance abuse or dependence	4	7.01%
Total participants with lifetime substance use disorder	**57**	**100.00%**

4.5.4.5 Dementia due to HIV disease

The International HIV Dementia Scale has been validated as a screening tool for HIV dementia across cultures (Sacktor, et al., 2005). Using this scale, 57 (18.87%) participants scored 10 or less on the IHDS, which has been suggested as the cut-off score for possible HIV dementia. Eleven of these (3.64%) participants received a clinical diagnosis of HIV dementia (based on a clinical assessment of neurocognitive impairment in keeping with a subcortical dementia, using a brief ñbedsideò neuropsychological and clinical examination). The SCID does not contain a module for assessing dementia. No neuropsychological testing was done. Participants who scored 10 or less on the IHDS should have had a more thorough neurological and neuropsychological assessment but this was not part of the scope of this study. It is possible that a more comprehensive clinical assessment and formal neuropsychological testing in these participants may have found evidence of dementia or less severe neurocognitive impairment in these participants. Some of these participants were already on HAART, while others were to due to start treatment soon as a result of their low CD4 counts.

4.5.4.6 Psychotic disorders

Fourteen (4.64%) of the participants had evidence of a current psychotic disorder. Six of these participants had a history and evidence of a primary psychotic disorder (schizophrenia or schizo-affective disorder), with onset prior to diagnosis of HIV infection. The other participants had clinical presentations in keeping with substance-induced psychotic disorders and/or psychotic disorders due to a general medical condition. The general medical conditions involved included: HIV (Stage 3 or 4, or low CD4 count), tuberculosis and temporal lobe epilepsy.

Twelve participants had a history of a past psychotic episode. Six of these were the participants noted above, who had a chronic primary psychotic illness. The other participants had presentations in keeping with substance-induced psychotic disorders and/or psychotic disorders due to a general medical condition.

4.5.4.7 V-codes

Seventy-two participants (25.49% of the total study sample) had one or more V-code diagnosis made. Of these, fifty-five (18.21%) only had a V-code diagnosis (i.e. no additional mental disorder), while 17 had a mental disorder and one or more V-code diagnosis.

Table 4.13: The breakdown of V-code diagnoses

Diagnosis	No.	% of total sample (n=302)
Bereavement symptoms	29	9.60%
Parent-child relational problem	6	1.99%
Partner relational problem	29	9.60%
Relational problem NOS	2	0.66%
Sibling relational problem	7	2.32%
Other	4	1.32%
Total	77	25.49%

4.5.5 Relationship between mental disorders and site

Despite significant demographic and clinical differences between sites, there were no statistically significant differences in current or lifetime mental disorder, current or lifetime depressive disorder, and current or lifetime substance use disorders between sites.

Table 4.14: Occurrence of mental disorders by site

	Site 1 PHRU	Site 2 Tintswalo RADAR	Site 3 HIV CHB General (Wed)	Site 4 HIV CHB ART	Site 5 Weiler's Farm	Total
Current mental disorder (%)	27	37	37	25	39	31
Current depressive disorder (%)	18	13	17	17	15	17
Current substance use disorder (%)	7	7	7	7	20*	9*
Lifetime mental disorder (%)	35	43	50	40	37	40
Lifetime mental disorder onset after HIV diagnosis (%)	11	17	22	5	5	12
Lifetime depressive disorder (%)	19	13	20	12	7	16
Lifetime depressive disorder onset after HIV diagnosis (%)	9	7	15	5	5	9

Although not statistically significant, the following was noted:

1. Current mental disorder, current substance use disorder and lifetime substance use disorder were highest at Weilerôs Farm.
2. The general Nthabiseng clinic had the most lifetime mental disorders and the most lifetime depressive disorders.

There were also no statistically significant differences between sites in terms of the cut-off score for dementia on the IHDS although there was a marginally significant trend to there being fewer participants at the PHRU site who screened positive for a possible dementia (p=0.0948).

4.5.6 Relationship between mental disorders and gender

The association between gender and mental disorder was explored in some detail.

Current mental disorders by gender

Although not statistically significant, males were found to have more current mental disorders than females had in this study (males: 35.56% vs. females: 29.25%). There were also slightly more current depressive disorders in males (16.98% vs. 15.56%). Significantly more males than females had a current substance use disorder (16.67% vs. 5.19%) ($p=0.0011$).

Lifetime mental disorders by gender

No significant gender difference was found in the rates of lifetime mental disorder. There were significant gender differences in the rates of lifetime depressive disorder ($p<0.0005$). As expected from general prevalence studies, depressive disorders were more common in females than in males. Also, as expected, there were statistically significant gender differences in lifetime substance use disorders (males > females) ($p<0.0001$)

4.6 Suicidal ideation or behaviour

Current suicidal ideation or behaviour

Twenty-six participants (8.61% of the study sample) had suicidal ideation when interviewed. Of these, 19 reported thoughts of suicide but no serious plan to attempt it, and 7 reported that they had a plan for attempting suicide. These participants were all referred to the nearest mental health service for assessment and intervention. None were considered to be at immediate risk of attempting suicide.

Relationship between current suicidal ideation and current mental disorder

There was a statistically significant relationship between the presence of suicidal ideation and the presence of a current mental disorder (p=0.0008) and a current depressive disorder (p<0.0001). Participants with a current mental disorder were 4 times more likely to express suicidal ideation and those with a current depressive disorder were 5 times more likely to express suicidal ideation than those without a current mental or depressive disorder (p < 0.0001). There was also a statistically significant relationship between current and past suicidal ideation (p=0.0181). Participants with past suicidal ideation were twice as likely to express current suicidal ideation as those without past suicidal ideation.

Past suicidal ideation or behaviour

Sixty-eight participants (22.52% of the study sample) reported previous suicidal ideation or behaviour on one or more occasion (total 90 episodes). Of these, 44 participants had experienced suicidal thoughts only, 16 had developed plans to attempt suicide, but had not carried them out, and 8 had attempted suicide at least once in the past. In total there were 10 suicide attempts in these 8 participants. Five participants had made a serious suicide attempt, while the other three had made what were considered to be 5 para-suicide attempts.

From the table below it can be seen that more than two-thirds (69%) of past episodes of suicidal ideation were related to HIV diagnosis.

Table 4.15: Reasons given for past suicidal ideation or behaviour

REASON	**No.**	**% (of all episodes of past suicidal ideation)**	
At time of HIV diagnosis	34	37.78%	68.89% (due to HIV diagnosis
Change in stage of HIV illness	7	7.78%	
Other related to HIV diagnosis or infection	21	23.33%	
Unrelated to HIV diagnosis or infection	28	31.11%	
Total episodes	90	100%	

Relationship between past suicidal ideation, lifetime mental disorder and lifetime depressive disorder

A statistically significant association was found between past suicidal ideation and lifetime depressive disorder. Lifetime mental disorder and lifetime substance use disorder were not significantly associated with past suicidal ideation, although there was a trend for lifetime mental disorder to be associated with past suicidal ideation. When adjusted for mental disorder and substance use disorder, participants with lifetime depressive disorder were seven times more likely to have had past suicidal ideation (adjusted odds ratio = 7.3).

4.7 Postulated risk and mitigating factors in the study sample

Besides demographic and clinical variables, the following factors were hypothesized to be potential risk or mitigating factors in the development of current depressive or anxiety disorders. A description of the study population in terms of these factors follows.

Time since informed of HIV status

More than half the participants (56.95%) had known their HIV status for a year or more at the time of their interview.

Mode of transmission

Most (91.06%) of the participants reported that they had become infected with HIV through consensual sexual intercourse with a regular or a casual partner.

Why an HIV test was done

The most common reasons for having an HIV test were: as a result of falling ill with a condition likely to be related to HIV-seropositive status (58.8%); receiving antenatal care

(17.61%); concern regarding HIV status (14.62%). As expected, the majority of participants at PHRU were tested while receiving antenatal care, while the most common reason for having an HIV test at the other sites was a result of having a medical illness. While Tintswalo and Weilerôs Farm are Wellness clinics, they were then the only HIV treatment sites available to the population in those areas, so people who were medically ill made use of these sites.

Voluntary counselling and testing

Fifty (16.56%) participants stated that they had received neither pre- nor post-test counselling.

Pre-test counselling

Seventy-five (24.85%) participants stated that they had not received pre-test counselling before having an HIV-test. Of the 227 participants who did receive pre-test counselling, 184 (81.06%) considered the pre-test counselling helpful in terms of coping with receiving a positive HIV diagnosis.

Post-test counselling

One hundred and fourteen (37.42%) participants stated that they had not received any post-test counselling. Of the 188 who did, 159 (84.57%) considered the post-test counselling to be helpful in terms of coping with receiving a positive HIV diagnosis.

Use of support groups

One hundred and twenty-four participants (41.06% of the total sample) had been in a support group with other HIV-seropositive individuals since being diagnosed with HIV infection. Seventy-one (23.5% of the total sample) participants were still in a support

group at the time of their interview. One hundred and nineteen (95.97%) of the 124 participants attended a support group more than once, and 106 (85.48%) attended a support group for more than a month. Eighty-three (66.94%) of the participants who attended a support group found being in the group very helpful in terms of coping with their diagnosis.

There was a statistically significant association between helpfulness of support groups and the number of times ($p<0.0001$) and length of time ($p=0.01$) an individual attended a support group.

Disclosure

Two-hundred and seventy (89.70%) of the participants had disclosed their HIV-status to someone outside the health service. They were most likely to disclose their status to their partners, siblings, relatives, friends, mothers and other people whom participants knew to be HIV positive. Most participants found it helpful to disclose their status to someone.

Two-hundred and thirty six participants (78.15%) were in a relationship when they were informed of their HIV status. One-hundred and seventy-six (74.58%) of these informed their partners of their HIV status. In 28 (15.91%) cases the disclosure caused that relationship to break up.

Being open regarding HIV status

Of note is the response to the question about being totally open about HIV status. Of the participants, 256 (84.77%) indicated that they were not totally open about their status, but chose carefully to whom to disclose their status. However, all of the 46 (15.23%)

participants who indicated that they were totally open about their status felt that this helped them cope with their status.

Involvement in organisations for people living with HIV/AIDS

Only 16 participants reported that they were involved in such organisations. Examples were the TAC, PLWA and community-based self-help and support groups. All but two felt that their involvement helped them cope with their diagnosis/infection.

Role of religion/faith in coping with HIV status

More than half the participants described themselves as being very religious and almost two-thirds stated that their faith was very helpful to them in terms of coping with their HIV status.

Experience of discrimination as a result of HIV status

Almost a quarter of the participants (75 participants or 24.83% of the study sample) claimed that they had been discriminated against as a result of their HIV status. The types of discrimination experienced included labelling, avoidance and verbal abuse. Of those who had experienced discrimination, 58.66% felt that this had had considerable negative effects on their ability to cope.

Feelings of isolation

A small number of participants (38, or 12.58% of the sample) described feeling isolated from other people as a result of their HIV status. Almost equal numbers of participants (43 to 44% each) felt that the diagnosis had made no difference or that they had become closer to others. There were problems related to the way in which this question was interpreted.

In many cases the researcher felt that when participants said they were closer to others, what they actually meant was that they preferred to spend time with people because it made them feel less alone, and that they were able to forget their HIV status while in the company of others. It is possible that these individuals still had internal feelings of isolation, and used the company of others to alleviate this feeling. However, those who answered that they had become isolated did describe internal feelings and behaviours of isolation and confirmed that this change had happened since they had been informed of their HIV status.

Duration of attendance at current clinic

The mean duration of attendance at the current clinic was 12 months, with a range from 0 to 99 months.

Antiretroviral therapy

One-hundred and fifty-four (56.41%) of those who had a recent CD4 count (n=273) had a count of <200 cells/ml. This indicates the minimum number of participants who should have been on HAART at the time of the study.

Seventy participants (23.18%) were on anti-retroviral treatment. The mean CD4 count in participants on HAART was 146, with a range from 2 to 484 cells/mm3, and 53 (75.71%) had a CD4 count < 200cells/ml.

Ninety-seven participants had a CD4 count < 200 cells/ml and were not on ART at the time of interview. Of these, 89 (91.75%) said they would take ART if it was offered to them.

Reactions to not being on ART

It was possible to give more than one response to this question. Sixteen participants gave two responses. It should be noted that in response to this question more participants said that they had joined an activist or advocacy group, than in the prior question related to having joined an activist organisation.

Table 4.16: Reactions of participants who were not on ART and who qualified for treatment

Reaction	Frequency	Percentage
Angry	9	8%
Depressed/ anxious	23	20.4%
Activist	24	21.2%
No effect	37	32.7%
Other	20	17.7%
Total	113	100.00%

Almost half the participants who responded to this question were unhappy about their lack of access to ART, while the other half had no problem with their current lack of access. This included those who responded ñotherò to the question. Eighteen of these participants were due to start ART within the next month, and 2 participants had only recently been diagnosed HIV positive and were happy to wait a while before starting ART. From this it can be concluded that most of the participants thought that ART would help in managing their disease.

Eight participants, who should have been on ART according to their CD4 counts, stated that they would not take ART at that stage. The reasons given were: a lack of information about the medications, fear of side effects, feeling healthy at the time, and concern regarding the commitment to taking medication for the rest of their lives once started on treatment.

Death of others as a result of AIDS

Almost half the sample, 141 (46.36%) participants, had experienced the death due to AIDS of at least one person who was close to them.

Effect of deaths due to AIDS

Of the participants who had experienced AIDS-related bereavements, 102 (72.86%) felt that these deaths had had a major impact on their ability to cope with their own illness.

Other losses in the past year

Sixty-nine participants (22.85%) had experienced bereavement (the death of a close relative or friend) in the past year, and 14 had been bereaved more than once in that period. Forty-four (63.76%) felt that this had had a major impact on their ability to cope. These deaths were not AIDS-related, as far as could be ascertained.

Levels of psychosocial stress

Levels of psychosocial stress were determined in each participant and an estimation of severity was made. This was dependent on the type and number of stressors. Thirty percent of participants had no additional stress besides knowledge of HIV status. Fifty-five percent had what was considered to be mild additional stress, and 8% had moderate or severe additional stress.

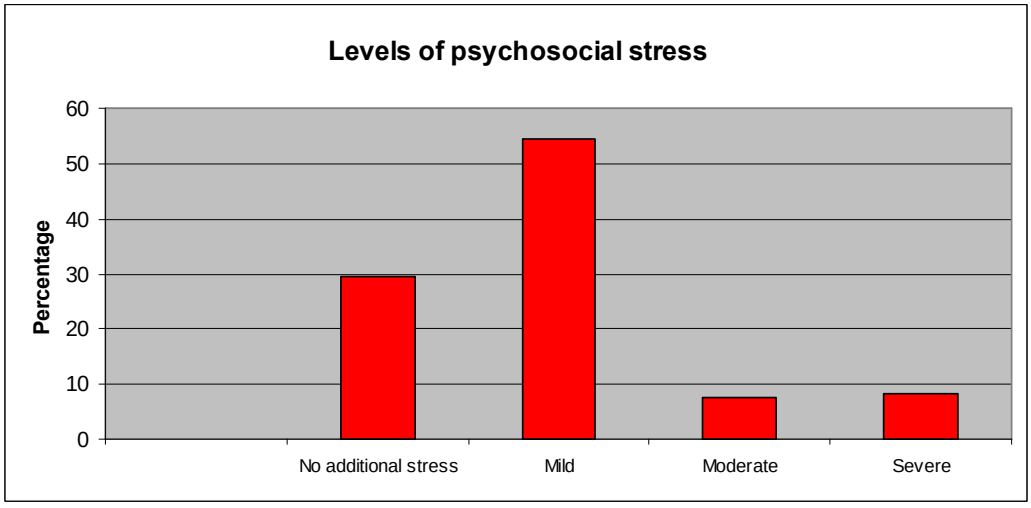


Figure 4.5: Levels of psychosocial stress in participants

4.7.1 Site differences between psychosocial variables

There were no significant differences between sites in terms of the following psychosocial variables: time since diagnosis, being open regarding HIV status, experiencing discrimination, experiencing losses in the past year (excluding AIDS-related deaths).

There were significant differences in the following variables:

1. Why HIV test done ($p<0.0001$): most participants at PHRU were tested during antenatal care;
2. Pre-test counselling ($p<0.001$): at Tintswalo Hospital 43% did not have pre-test counselling;
3. Post-test counselling ($p=0.02$): at Weilerôs Farm (56%) and at Nthabiseng ART (43%) did not have post-test counselling;
4. No pre- or post-test counselling ($p=0.003$): Tintswalo Hospital and Nthabiseng ART had the most participants who claimed they had had neither pre- nor post-test counselling at the time that they were informed of their HIV test results;

5. Support groups ï yes (p<0.0001): Tintswalo Hospital had most support group members. This probably reflects selection bias, since interviews were conducted on days that support groups met and more than half the participants at PHRU had been, or were, in support groups;
6. Disclosure (p<0.0001): all (100%) participants at Nthabiseng ART had disclosed their status to someone (This probably also reflects selection bias) and the lowest levels of disclosure were at Weilerôs Farm;
7. Disclosure to partner at time of diagnosis (p=0.03): the lowest levels of disclosure were at Tintswalo Hospital and the highest were at PHRU;
8. Religious belief (p=0.0012): more participants at Weilerôs Farm described themselves as not at all religious (34%) than at the other sites;
9. Experiencing AIDS-related deaths (p=0.05): participants at Weilerôs Farm had experienced the smallest number of such deaths (24%) in close family or friends (At all the other sites, between 40% and 50% of participants had experienced such deaths);
10. Psychosocial stress (p<0.0001): Nthabiseng general clinic had the most participants with no additional psychosocial stress (52%) and PHRU had the most participants with moderate to severe stress (34%).

4.7.2 Analysis of variables related to current mental disorder and current depressive disorder

Analysis of possible risk and protective factors was carried out for current mental disorders in general and for current depressive disorders in particular. Since the occurrence of anxiety disorders was so low, it was unlikely that anything of significance would be found. Therefore, analysis of risk and mitigating factors was not carried out for anxiety disorders.

Appendix 1 outlines the univariate analysis of postulated risk or mitigating factors outlining the odds ratios and tests of statistical significance for current mental disorder and current depressive disorder.

Univariate analysis

On univariate analysis, the following variables were found to be statistically significantly associated with a **current mental disorder** (with a p value of $\leq$ 0.05):

1. Clinical stage of HIV disease;
2. Presence of a medical condition
3. Lack of a strong religious belief
4. Psychosocial stress (mild or severe)
5. A lifetime mental disorder at any time up to one month prior to interview
6. A lifetime mental disorder before the diagnosis of HIV infection was made
7. A lifetime depressive disorder at any time up to one month prior to interview
8. A lifetime substance use disorder at any time up to one month prior to interview

There was a marginally statistically significant ($p<0.10$) association between current mental disorder and an individual feeling that they had experienced discrimination as a result of their HIV-status, and feeling that this discrimination had made coping very difficult for them.

On univariate analysis, the following variables were found to be significantly associated with a **current depressive disorder**:

1. Feelings of isolation
2. Increased levels of psychosocial stress (mild, moderate or severe)

3. A lifetime mental disorder at any time up to one month prior to interview
4. A lifetime mental disorder before the diagnosis of HIV infection was made
5. A lifetime depressive disorder at any time up to one month prior to interview
6. A lifetime depressive disorder before the diagnosis of HIV infection was made

There was also a marginally statistically significant ($p<0.10$) association between the number of AID-related bereavements the individual had experienced and the presence of a current depressive disorder.

Multivariate analysis

Variables that reached a level of statistical significance of $p<0.20$ were entered into a backward step-wise multivariate logistic regression and an attempt was made to develop a predictive model for the risk of mental disorder or depressive disorder in the study population based on the postulated risk and protective factors.

The following variables were entered into the multivariate analysis for **current mental disorder:**

- Clinical stage
- Presence of a medical condition
- Time since diagnosis of HIV status
- Disclosure of HIV status
- Impact of discrimination
- Lack of a strong religious belief
- Impact of faith on coping
- Impact of AIDS-related bereavements

- Number of AIDS-related bereavements
- Presence of lifetime depressive disorder at any time up to one month prior to interview
- Presence of a lifetime depressive disorder before the diagnosis of HIV infection was made
- Lifetime history of substance abuse

Although the presence of a lifetime mental disorder at any time up to one month prior to interview, and the presence of a lifetime mental disorder before the diagnosis of HIV infection was made, were statistically significantly associated with a current mental disorder on univariate analysis, these variables were not entered into the logistic regression, as they were considered to be too broad to give a useful result. In addition, the variables of lifetime depressive disorder and lifetime substance use disorder were already entered into the regression analysis, and these specific categories were also subsumed into the category ñlifetime mental disorderò.

The results of the logistic regression analysis showed a statistically significant association ($p \leq 0.05$) between the following variables and the presence of a current mental disorder:

- Clinical stage 3 and 4 (OR = 2.16; p=0.025)
- Presence of additional psychosocial stress (OR = 2.2: p=0.023)
- Feeling that oneôs faith was marginally helpful or not at all helpful in coping with HIV status (OR= 2.3: p=0.044)
- The presence of a lifetime history of a depressive disorder (OR= 2.37: p=0.022)
- The presence of a lifetime history of a substance use disorder (OR= 4.3: p<0.0001)

Of note is that a lifetime history of depressive disorder prior to the diagnosis of HIV infection was not found to be statistically significantly associated with a current mental disorder.

Disclosure of HIV status was found to be statistically significantly protective of having a current mental disorder (OR=0.42; p=0.044)

It was not possible to build a sufficiently robust predictive model using the variables which were identified in this study.

The following variables ($p < 0.2$) were entered into the multivariate analysis for **current depressive disorder:**

- Level of education
- Attending a support group
- Reported experience of discrimination
- Feelings of isolation
- Number of AIDS-related bereavements
- Psychosocial stress
- Lifetime depressive disorder
- Lifetime depressive disorder pre-HIV diagnosis

Although there seemed to be some statistically significant association between employment status and current depressive disorder on univariate analysis, this variable was not entered into the multivariate logistic regression due to the large number of unemployed participants, which would have resulted in skewing of the results of the regression analysis.

Recent viral load was also excluded from the logistic regression due to the small number of participants with a documented viral load, as this again would have had a confounding effect on the regression analysis.

The results of the multivariate analysis showed a statistically significant association ($p<0.05$) between the following variables and the presence of a current depressive disorder:

- Moderate or severe levels of psychosocial stress (OR=5.5; p=0.001
- Lifetime depressive disorder (OR=4.0; p=<0.0001 (again, of note is that a lifetime history of a depressive disorder prior to the diagnosis of HIV-infection was not found to be statistically significantly associated with a current depressive disorder
- Feelings of isolation (OR=3.05;p=0.016)

Being in a support group was found to be protective of the presence of a current depressive disorder (OR=0.48; p=0.043).

Again, it was not possible to build a useful predictive model using the variables which were identified in this study.

4.8 Quality of pre-test counselling

Nineteen participants who had received pre-test counselling were asked additional questions regarding their experience of pre-test counselling. Most pre-test counselling was done by lay counsellors in the patientsô home language. Most people received counselling in a private setting, but some reported interruptions and feeling that other people might overhear what was being said. Half felt that the counsellors did not really understand how they were feeling, and that the counsellors were either in a hurry, not listening or not interested and only seeing the job as a routine task. Some felt that too much emphasis was placed on the negative aspects of a positive diagnosis. Again, half felt that they were not given a chance to ask questions because the counsellors were in a hurry. Most felt that the counsellors did address issues of positive living, but some felt that they only focused on safe sex issues. Interestingly, more participants felt more anxious than less anxious after the pre-test counselling. Although these interviews were too few to provide any meaningful results, they did indicate some of the issues of importance related to pre-test counselling; particularly, the need for counsellors to demonstrate that they have sufficient time available for their clients and regard their task as important and not just a routine job. Increased anxiety after counselling may have been inevitable, as having an HIV test is a stressful experience. It may be more important to ensure that post-test counselling is always available, and that the feelings raised by a positive result are adequately dealt with.

CHAPTER 5

DISCUSSION

This research investigated:

1. The occurrence of depressive and anxiety disorders in HIV-infected individuals attending certain treatment sites in South Africa
2. Whether the results of this study are comparable with those of other studies conducted in South Africa, Africa and internationally
3. Whether there is an increased occurrence of depressive and anxiety disorders in this population of HIV infected individuals compared to the prevalence of these disorders in the general population in South Africa.
4. Whether any aetiological/risk factors or protective/mitigating factors could be identified for mental disorders (and specifically for depressive and anxiety disorders) in the study population

5.1 Important findings

This study was conducted in both primary and tertiary HIV-treatment sites. All previously published studies of HIV-infected individuals in South Africa were conducted at tertiary level outpatient services. The Wellness clinics established under the auspices of PHRU are primarily intended to treat newly diagnosed asymptomatic individuals and maintain their health for as long as possible through primary health care, education, psychosocial support and treatment of sexually transmitted infections and opportunistic conditions. While the clinic population at the Soweto/CHB Wellness site matches this profile, those at Tintswalo and Weilerôs Farm had a considerable number of patients with symptomatic HIV disease.

They were intermediate between PHRU and the Nthabiseng clinics in this regard. It is possible that this was related to access to healthcare in these areas.

5.2 The occurrence of depressive and anxiety disorders in HIV-infected individuals in this study

This study found a considerable burden of mental disorder in the study population. In terms of current mental disorders, the most common disorders were depressive disorders (including adjustment disorders), followed by substance use disorders, psychotic disorders, and equal numbers of anxiety disorders and dementia due to HIV disease. With regard to lifetime mental disorders, substance use disorders were the most common, followed by depressive disorders.

The occurrence of current depressive disorders in this study was 16.87% and that of lifetime depressive disorders was 15.89%. Current anxiety disorders and lifetime anxiety disorders were found in 3.96% and 3.63% of the study population respectively. Therefore, about 20.83% of the participants suffered from current or lifetime depressive and anxiety disorders.

Major depressive disorder was present in just under 5% of the participants at the time of interview, and just over 10% of participants had a lifetime history of a major depressive disorder. Of note is that almost two-thirds of these had their first major depressive episode **after** diagnosis of their HIV status.

Generally, anxiety disorders were not common. There was a range of anxiety disorders, none of which predominated.

5.2.1 Comparison with similar studies in Sub-Saharan Africa, including South Africa

5.2.1.1 Depressive disorders

Other studies conducted in Sub-Saharan Africa, including South Africa, have produced results for current major depressive episode only.

Table 5.1: Studies of depressive disorders in HIV-infected individuals conducted in Sub-Saharan Africa

Researcher	Country	Year published	Methodology	Results
Maj et al. (1994)	Zaire (DRC) and Kenya	1994	Diagnostic interview (CIDI) HIV-negative controls	No statistically significant increase in depressive disorders; generally low prevalence of depressive disorder (0 to5.5%)
Sebit et al. (2003)	Zimbabwe	2003	Diagnostic interview (MINI) HIV-negative controls	Statistically significant difference in prevalence of psychiatric disorder between HIV-positive and HIV-negative (71.3% vs. 44.3%). (No separate information on depressive disorder)
Stranix-Chibanda, Chibanda and Chingono (2005)	Zimbabwe	2005	Screening instrument (Shona SSQ) HIV-negative controls	17% of all women attending a VCT clinic had psychological morbidity. No statistically significant difference between those who were HIV-positive and those who were HIV-negative
Kahazura et al. (2006)	Uganda	2006	Screening instrument (CES-D) No control group	47% of 1017 HIV-infected individuals had a CES-D score >=23 (significant depression).
Bganya (1999)	South Africa (Gauteng)	1999 (MMed)	Screening (BDI) + unstructured clinical interview. No control group	38% major depressive disorder
Els et al. (1999) (Free State)	South Africa	1999	MINI No control group	35% major depressive disorder
Olley et al. (2003) (Western Cape)	South Africa	2003	MINI (baseline of cohort; within 6 months of HIV-diagnosis). No control group	35% major depressive disorder
Olley et al. (2006) (Western Cape)	South Africa	2006	MINI (6-month follow-up of cohort). No control group.	26% major depressive disorder
Thom (Gauteng, Mpumalanga)	South Africa	Current study	SCID MDE. No control group.	5% major depressive disorder
Thom (Gauteng, Mpumalanga)	South Africa	Current study	SCID all depressive disorders. No control group.	16.87% all depressive disorders

The WHO study by Maj et al. in 1994, found prevalence rates of between 0 and 5.5% in HIV-seropositive individuals (asymptomatic and symptomatic) at the two African study sites. The difference between these groups and HIV-negative controls was not statistically significant. The only other African study conducted with a diagnostic interview and with HIV-negative controls was carried out by Sebit in Zimbabwe in 2003. This study reported on psychiatric disorders in general, and not specifically on depressive disorders. This study did, however, find high rates of disorder, and a statistically significant difference between HIV-positive and HIV-negative individuals.

Generally, all the other studies (including all those from South Africa) show much higher rates of MDE than the current study does (26 to 38% vs. 5%). Possible reasons include the use of differing methodologies, different study populations or the existence of other as yet unknown reasons for the variation in results.

Some studies used screening instruments rather than diagnostic interviews, which would result in inflated results. All the studies conducted in South Africa used a diagnostic interview, although Bganya used the Beck Depression Inventory to screen for major depressive disorder and confirmed the diagnosis with an unstructured clinical interview. The other studies in South Africa used the MINI. As was discussed in Chapter 3, while the MINI has been validated against the SCID (Sheehan, Lecrubier, & Hairnet-Sheehan, 1998), it does not provide the range of diagnoses that the SCID does. It also usually takes a trained clinician an average of 15 minutes to administer, whereas the SCID usually takes, on average, an hour to administer. The MINI does not code for sub-syndromal depressive disorders (Depressive disorder NOS), nor for adjustment disorder. This might lead to an expectation that these diagnoses would be excluded when the MINI is used. However, it is

possible that for this very reason the criteria are applied more liberally than with the SCID. It is therefore possible that sub-syndromal depressive disorders were included as major depressive disorder in these studies.

As noted previously, it is difficult to differentiate depressive disorders from early signs of cognitive impairment in HIV-infected individuals. The other studies did not give results for levels of cognitive impairment and no diagnoses of dementia were made. As reported by Ciesla & Roberts (2001), the overlap in symptoms between cognitive impairment, physical illness and depressive disorder in HIV disease makes accurate diagnosis very difficult, particularly within a limited period of 15 minutes. This may, again, have led to over-diagnosis of major depressive episode in these studies. Again, of note, is that these studies were conducted in tertiary infectious diseases clinics, where the levels of confounding cognitive impairment could be expected to be quite high.

Another consideration relates to who conducted the interviews in these research projects. The interviewers in all the studies, except that by Els et al (1999), were trained mental health clinicians. Els used final year medical students trained and supervised in administering the MINI and other instruments used in the research. Interviewers are instructed to use their clinical judgement in administering both the MINI and the SCID. It is possible that the criteria for major depressive disorder were more liberally applied in the studies using the MINI than in the study under discussion, particularly in those using interviewers with less clinical experience, especially considering that there was no other category of depressive disorder allocated for participants with less severe depressive disorders.

Another methodological argument may relate to cultural and linguistic difficulties in making diagnoses of mental disorders in a cross-cultural context. The other studies conducted in South Africa did not comment on this aspect. All these studies, including the current one, were conducted in similar cultural populations. Therefore, the cultural concepts and understandings of depression and anxiety are likely to have been similar across the studies.

With regard to language: in the current study, interviews were conducted by the researcher in English if the participant was fluent in English. However, the research assistant was present during all interviews, which were jointly conducted in the participantôs home language where that person lacked fluency in English. Since the research assistant was also a trained in administering the SCID and was an experienced mental health clinician, the researcher and assistant were able to reach consensus in terms of diagnosis in all cases. It is therefore unlikely that language difficulties affected the accuracy of diagnoses in the current study. There was no comment on this aspect in the other studies.

In terms of the study populations: all the other South African studies were conducted at infectious diseases clinics in tertiary hospitals. The study populations were largely similar in socio-demographic profile to those in the current study. Clinical indicators were also similar, although most of the participants in Bganyaôs study were in Stages 3 and 4 of HIV disease. The study population in Olley et al.ôs baseline study were recently diagnosed (mean of 5.8 months since diagnosis). However, their 6-month follow-up study nevertheless showed significantly more major depressive disorder than the study under discussion did. All these studies had fewer than 150 participants.

Sixty percent of participants in the current study were attending primary care sites. The Nthabiseng clinic at Chris Hani Baragwanath Hospital is a tertiary level infectious diseases clinic, similar to the sites in the other South African studies. Patients attending the tertiary care sites are likely to be more medically ill or to have significant cognitive impairment, and there were significant differences in demographic and clinical variables between sites in the current study. However, no significant difference was found in the occurrence of depressive disorders and major depressive disorders between the sites in the current study. Therefore, while the primary and tertiary level populations may have been different, this is likely to account only partially for the differences in findings between this and other South African studies.

The other studies were conducted before antiretroviral treatment was made available in the public sector, while the current study was conducted during the initiation of this treatment. Very few of the participants in the other studies were on anti-retroviral treatment, whereas almost one quarter of participants in the current study were on anti-retroviral medication. However, univariate and multivariate logistic regression did not find that being on anti-retroviral medication had any significant impact on rates of depressive disorder. Many of the participants had only recently commenced anti-retroviral therapy and it is therefore unlikely that this had yet had an effect. It is possible that participants in the current study had an increased level of hope, which was not present in the previous studies and this may explain to some extent the lower levels of depressive disorder in the current study. However, this is unlikely to completely explain the difference; particularly the difference in occurrence of a serious mental illness like major depressive disorder.

It is therefore possible that some or all of these methodological and contextual issues may have contributed to the differences in the findings between this study and other South African studies. On the other hand, the rates of depressive disorder may simply be different in the populations studied.

5.2.1.2 Anxiety disorders

As stated above, anxiety disorders were not common in the study sample. Less than 4% of the sample had a current and/or a lifetime anxiety disorder. While this result is in keeping with the findings of the WHO study sites in Africa (Maj et al., 1994), this again is in contrast with other studies conducted in similar settings in South Africa. In particular, Els et al. found panic disorder in 37% of their study sample, and generalised anxiety disorder in 21%, while Olley et al. found PTSD in 14.8% at baseline and 20% at 6-month follow-up. Disparities may, again, be due to methodological or study population differences, true differences in rates of the disorders, perceptions of distress or the psychological effects of the anti-retroviral roll-out.

Table 5.2: Prevalence of anxiety disorders in HIV-infected individuals in Africa

AUTHOR	Country of study	Methodology	Prevalence	
			HIV+ve	HIV-ve
Maj et al. (1994)	Multi-national	control group: CIDI (all anxiety disorders)	1-2%	1-2%
Carson et al. (1998)	Kenya	control group: CIS worry symptoms (no anxiety disorders)	13%	12%
Els et al. (1999)	South Africa	no control group; MINI Panic disorder Agoraphobia Social phobia GAD PTSD	 37% 9% 15% 21% 6%	
Olley et al. (2005)	South Africa	no control group; MINI PTSD (Baseline)	 14.8%	
Olley et al. (2006)	South Africa	cohort study; MINI at 6 month follow-up PTSD	 20%	
Thom (current study)	South Africa	No control group; SCID (all anxiety disorders)	3.96%	

5.2.2 Occurrence of mood and anxiety disorders compared to general prevalence studies

Table 5.3: Prevalence rates for mood and anxiety disorders in the general population in South Africa

Study name	Year	Site	Methodology	Result
Thom et al. (Thom, Zwi & Reinach, 1993)	1993	Urban Primary Care clinic	SRQ + PSE	10% (anxiety and depression)
Rumble et al. (Rumble, Swartz & Parry, 1996)	1996	Rural community in Western Cape	SRQ + PSE	27.1% (most anxiety and depression
Bhagwanjee et al. (Bhagwanjee, Parekh & Paruk, 1998)	1998	Rural community in KwaZulu-Natal	SRQ + clinical interview	23.9% (anxiety and depression)
Pillay et al. (Pillay & Kriel, 2006)	2006	District-level services ï hospital and CHC	Screening instrument	21% depression 10% anxiety
SASH Study (Stein et al, 2007)	2007	Country wide community prevalence study	CIDI (12-month and lifetime)	4.8% mood disorder (12-month) 9.8% mood disorder (lifetime) 8.1% anxiety disorder (12-month) 15.8% anxiety disorder (lifetime) 12.9% mood and anxiety disorder (12-month) 25.6% mood and anxiety disorder (lifetime)

Prevalence rates in studies of depressive and anxiety disorders in the general population in South Africa range from 9% to 27%. The most recent estimate of 12-month prevalence rates in South Africa is from the SASH study (Stein, Seedat & Herman, 2007), which reported a prevalence of 12.9% in the general population. While not entirely comparable, the 1-month occurrence rate in this study for the same two disorders was 20.83%.

Study	n	affected	percentage
SASH	4351	561	12.90%
Thom HIV	302	63	20.83%

There is a statistically significant difference in the rates of mood and anxiety disorders between these two studies ($p<0.0001$). The SASH study did not take account of HIV status, and there would certainly have been some HIV+seropositive individuals who participated in this study. It should thus be noted that comparing these two studies is not the same as comparing the current study with an HIV-seronegative control group.

The findings of this current study, in comparison with those in a study conducted by the same researcher using a similar methodology in a very similar study population (a primary care clinic in Soweto) (Thom, Zwi & Reinach, 1993), show a difference in prevalence of depressive and anxiety disorders of 10% vs. 20%. Again this is a statistically significant difference ($p<0.0001$). However, this general prevalence study was conducted in 1991, some 14 years prior to the current study and prevalence levels of depression and anxiety may have changed in that time independent of the HIV epidemic.

Study	N	affected	percentage
Thom PHC	300	30	10%
Thom HIV	302	63	20.83%

5.2.3 Occurrence of other mental disorders in the study

While other mental disorders were not the primary concern of this study, significant findings were also noted with regard to substance use disorders, and to a lesser extent, organic mental disorders, including HIV dementia and psychotic disorders.

Substance use disorders are common in South Africa. Data from the SASH study show a 12-month community prevalence of substance use disorders of 5.8% and a lifetime prevalence of 13.3%. Other data on the prevalence of alcohol abuse and abuse of other substances show that 9.9% of females and 27.6% of males in South Africa can be

considered to be alcohol dependent (National Department of Health, 1998), while the point prevalence of abuse of other substances (cannabis, cocaine, amphetamines, ecstasy and opiates) in South Africa was estimated to be just over 10% (United Nations Office on Drugs and Crime, 2006).

Lifetime occurrence of substance use disorders in the current study was 18.87% and current occurrence was 7.72%. Almost all of this was alcohol abuse and/or dependence, with some cannabis abuse and a very small occurrence of abuse of other substances. These findings are in keeping with the general prevalence rates in South Africa as noted above.

The breakdown of substance use (current and lifetime) is outlined by gender in the table below.

Table 5.6 Current and lifetime substance use

Gender	Lifetime SUD		Current SUD	
	Lifetime SUD**	No lifetime SUD	Current SUD*	No current SUD
Male	36.67%	63.33%	16.67%	83.33%
Female	11.32%	88.68%	5.19%	94.81%

**p<0.0001
*p=0.0011

It can be seen that significantly higher levels of substance use disorder were found in males than in females, in the study population. Again, this is in keeping with findings in the general population. However, there was a significant decline in current substance use disorders compared to lifetime rates in both genders. This could have been due to under-reporting of current substance abuse or it could have been due to a genuine decrease in substance use disorders.

This finding may have implications for HIV-treatment services. It suggests that individuals attending HIV-treatment sites may reduce their use of harmful substances once they know that they are HIV-positive. Alcohol was the most common substance abused in this study. While some individuals on HAART may experience disulfiram-like effects when using alcohol, this is considered rare and not likely to be clinically significant (McDowell, Chittick & Pilati-Stevens et al, 2000). The reduction in substance abuse may have been due to under-reporting of current abuse, or it may have been as a result of knowledge of HIV status alone, as a result of unpleasant side-effects, due to psychosocial interventions that took place at these sites or it may have resulted from a combination of all these factors. This is an area that needs further exploration.

The considerable numbers of participants who screened positive for a **possible dementia** according to the International HIV Dementia Scale is a cause for concern. While most of these participants had a low CD4 count, which would render them eligible for ART (the treatment of choice for Dementia due to HIV disease), some had CD4 counts > 200 cells/ml. While the treatment guidelines in South Africa indicate treatment for any HIV-positive person with an AIDS-defining condition, (of which HIV-associated dementia is one), irrespective of CD4 count, it is unclear whether HIV-practitioners are always aware of this. Dementia due to HIV disease is also difficult to diagnose unless specific assessments are carried out.

One of the difficulties affecting access to appropriate treatment may involve the diagnosis of HIV-associated dementia. The IHDS is a screening tool for HIV dementia, and not a diagnostic instrument. The cut-off suggested by the developers for possible HIV dementia is 10 or less in patients without psychotic or affective symptoms. The mean IHDS score for

the total research population in this study was 11, while the mean score for those who were given a clinical diagnosis was 8.

The diagnosis of HIV-associated dementia is made by thorough clinical assessment. Laboratory and other special investigations may be needed to exclude other causes of cognitive impairment. Sometimes neuropsychological testing may be necessary to confirm the diagnosis. This can be difficult in a resource-constrained environment such as exists in public sector health services in South Africa. However, with judicious use of bedside neuropsychological testing, together with neurological and psychiatric examination, it should be possible to reach a firm diagnosis in most cases.

In 2007, the National Department of Health, Directorate: Mental Health and Substance Abuse invited a task team of public sector psychiatrists to develop recommendations on the prevention, screening and treatment of HIV Associated Dementia (HAD) and related conditions. A draft document was submitted to the National Department of Health SMT working group on the comprehensive HIV and AIDS plan. The recommendation of the task team in terms of diagnosis of HAD as well as other common mental disorders was to use the IHDS as a screening tool, and the modified MINI screen as a screening tool for depression and alcohol use disorders. Dr John Joska of the task team developed an assessment tool for HIV Dementia Case Definition. It was recommended that further research in this area be commissioned by the National Department of Health to ensure that the most effective assessment methods are used in the diagnosis of HIV Associated Dementia.

In terms of **psychotic disorders** noted in this study, a number of participants had chronic psychiatric illnesses that had been present **prior to** diagnosis of HIV infection. Most of the participants with psychotic disorders had a CD4 count of <200 cells/ml and had associated substance use disorders or medical conditions. Only one of these participants was on ART.

Whether any of the psychotic disorders presenting **after** diagnosis of HIV status were true ñnew-onsetò psychoses related to HIV CNS infection, psychotic disorders related to other general medical conditions or primary psychotic disorders is not clear. As with depressive disorders, the natural history of schizophrenia and other chronic psychotic disorders is onset in early adulthood, also the age at which HIV infection is most commonly incurred. This makes it difficult to identify which psychotic disorders require treatment for HIV CNS infection. Nevertheless, the fact that only one of these participants was receiving ART at the time of interview and that most of these participants had CD4 counts less than 200 cells/ml is a matter for concern. It may be that these participants were part of the group of participants waiting to start on HAART. It would however, be important to track patients with psychotic disorders in an HIV-treatment setting to ensure that they are not unnecessarily deprived of HAART due to their mental state or psychiatric diagnosis.

5.3 Risk and protective factors

5.3.1 Risk and protective factors for current depressive disorders

Statistically significant risk factors for current depressive disorder identified on multivariate analysis in this study were a lifetime history of a depressive disorder (OR: 4.0), experiencing moderate or severe levels of psychosocial stress (OR: 5.5) and experiencing feelings of isolation (OR: 3.05).

A history of depressive disorder is one of the most important risk factors for developing depressive disorders, so this was not an unexpected finding. When associations with other mental disorders were explored, although there was a significant risk overall, no specific association between current or lifetime substance use disorders and current depressive disorder was found. This is unusual, since the literature indicates an association between substance use disorders and depressive disorders. It is possible that the size of the sample was insufficient to show this relationship, or that more detailed exploration of this relationship that was not within the scope of this study might have shown such a relationship.

The fact that over 50% of lifetime depressive disorders (and 60% of major depressive disorders) occurred for the first time after diagnosis of HIV infection is of interest. These may possibly have been related to HIV infection or to general medical conditions. They could also have been related to the psychosocial stress of receiving a diagnosis of HIV infection. However, they could also have been unrelated.

Age could have been a possible confounding factor here. As mentioned earlier, the mean age of onset for major depressive disorder is about 40 years, and onset in 50% of all patients occurs between the ages of 20 and 50 years (Kaplan, et al., 1997). Therefore, some individuals who developed a major depressive episode after the diagnosis of HIV infection was made might have developed a major depressive episode without this particular stressor. Moreover, psychosocial stressors other than knowledge of HIV status could have played a role in the onset of these depressive disorders.

A closer analysis of the relationship between current depressive disorder and the time of onset of lifetime mental or depressive disorder revealed that a past history of a depressive disorder prior to diagnosis of HIV infection did not significantly increase the risk of having a current depressive disorder. A mental disorder with onset prior to HIV diagnosis was not statistically significantly associated with a current one. However, with onset after diagnosis of HIV, both mental disorders in general, and depressive disorders in particular, significantly increased the risk of a current depressive disorder. (Odds ratios: 7.180 and 6.166 respectively on univariate analysis). These odds ratios were higher than for lifetime diagnoses pre-HIV diagnosis. This suggests that while a strong association with past psychiatric disorder exists, there appears to be a greater risk once the diagnosis has been made. The reasons for this are not clear but it suggests that knowing oneôs status and/or having HIV infection increases the risk of depressive disorder.

The strong relationship between psychosocial stressors and depressive disorder is also in keeping with general findings in the literature on depressive disorders. This study showed an increasing risk of depressive disorder with increasing severity of stress, such that those experiencing moderate or severe levels of psychosocial stress resulted in a five-times greater risk of having a current depressive disorder than those with no additional or mild additional psychosocial stress.

As discussed in the results section, the question probing feelings of isolation was problematic in terms of the interpretation. However, there does appear to be a relationship between feelings of isolation and depressive disorder. Whether being, or feeling, isolated is a cause of depressive disorder or whether these feelings are a symptom of such a disorder is not clear. However, reporting these feelings resulted in a threefold increase in the risk of

having a depressive disorder, and this could be an important indicator of depressive disorder to be monitored in clinical practice.

The negative findings in this study, of the relationship between various demographic, clinical and psychosocial variables and the presence of depressive disorder, also require consideration. Clinical stage and CD4 count did not appear to influence the risk of developing a depressive disorder. This is contrary to findings of studies of depressive disorders in general, and to those of some studies of depressive disorder in HIV-infected individuals. Gender and age may have been confounding factors in this study. Seventy percent of the study population was female. Risk of depressive disorders is thought to be twice as high in females as it is in males in the general population, and it was expected that this would apply in this study. Females in this study also had significantly higher levels of lifetime depressive disorders. Therefore, expectation of higher rates of current depressive disorder in female participants would be usual.

However, no gender differences were found in the occurrence of current depressive disorders in this study. In fact, the occurrence of current depressive disorders was slightly greater in male participants overall. The male participants in the study were generally older than the females. In addition, males in the study were in later stages of HIV disease and had significantly lower CD4 counts than females. Males were also significantly more likely to have lifetime and current substance use disorders than females. Therefore it is possible that older age, clinical factors related to HIV infection and/or substance use may have explained the higher rates of depressive disorders in males than females in this study.

The lack of a significant relationship between clinical indicators and depressive disorder may also be due to the study design. Most of the studies exploring the relationship between depression and disease progression have been prospective cohort studies. The cross-sectional design of this study may have lacked the capacity to show such relationships at a single point in time.

It was hoped that factors that could protect HIV-infected individuals from depression would be identified in this study. The factors that were explored in the study included the impact of pre- and post-test counselling, the use of support groups, disclosure to others, the role of religious faith and the impact of antiretroviral treatment. Of these factors, being or having been in a support group was the only factor that was found to be protective of the presence of a current depressive disorder (OR=0.48; p=0.049) on multivariate analysis.

This study design was again probably not the most appropriate for exploring this area, and a closer examination of these factors in a prospective structured intervention study using qualitative research methods would probably be more useful.

It should not be concluded from these findings that counselling and other psycho-social interventions are not useful in this context. There is clear evidence from this study that the participants felt that these interventions were helpful in terms of enabling them to cope with their illness.

Certain critical protective factors, particularly other forms of social support, were not explored. Data were obtained on people with whom participants lived, but there was no exploration of those whom participants relied upon for support. During interviews it was

clear that many participants found relationships with particular family members or friends to be helpful, and it is possible that these relationships played a part in preventing depressive disorders. This would have been an important area to explore, and again is probably best studied over a longer period, using a combination of quantitative and qualitative research methods.

Given the reported high levels of stigma related to HIV-infection in South Africa, the investigator expected that levels of disclosure in the study population would be low. This was not the case. Most participants had disclosed their status to at least one other person outside the health services, and most felt that this was important in terms of helping them to cope with the diagnosis. On the other hand, most participants were careful to whom they disclosed their status, and only a small percentage of participants were completely open about their status.

This was a selected sample of HIV-infected individuals who were attending treatment sites. It is possible that levels of disclosure in community samples of HIV-infected individuals could be quite different. In particular individuals who are attending treatment sites with the intention of accessing antiretroviral treatment would be much more likely to disclose their status to at least one person. Many HAART treatment programmes require the patient to have a ñbuddyò/ person to support them in their treatment.

Several studies have found a decrease in depressive disorders with antiretroviral therapy. This was not found in this study, again largely because of the cross-sectional study design and the fact that most participants had only recently started HAART when the ART roll-out was initiated.

5.3.2 Risk and protective factors for current mental disorders

The results of the logistic regression analysis showed a statistically significant association ($p \leq 0.05$) between the following variables and the presence of a current mental disorder:

- Clinical stage 3 and 4 (OR = 2.16; p=0.025)
- Presence of any additional psychosocial stress (OR = 2.2: p=0.023
- Feeling that oneôs faith was marginally helpful or not at all helpful in coping with HIV status (OR= 2.3: p=0.044)
- The presence of a lifetime history of a depressive disorder (OR= 2.37: p=0.022)
- The presence of a lifetime history of a substance use disorder (OR= 4.3: p<0.0001)

Of note again is that a lifetime history of depressive disorder prior to the diagnosis of HIV infection was not found to be statistically significantly associated with a current mental disorder.

Whereas clinical stage and medical condition did not influence depressive disorders, these factors played a significant role in current mental disorders overall. Participants in clinical Stages 3 and 4 were twice as likely to have a current mental disorder as those in Stages 1 and 2.

It might also be expected that a low CD4 count would be associated with a current mental disorder. However, the only significant association between mean CD4 count and a current mental disorder was in participants who screened positive for possible HIV-associated dementia on the IHDS (cut-off score of 10 or less). Participants with a current substance use disorder had a lower mean CD4 count than those without, but this was not statistically significant.

The presence of psychosocial stressors was again found to be a significant risk factor (OR: 2.2), although this factor appears to have had a greater impact in relation to depressive disorders in particular.

While disclosure of HIV status was not found to be statistically significantly protective in terms of current depressive disorders in particular, it was found to be protective in terms of current mental disorders as a whole (OR=0.42; p=0.044). It is not clear why this should be so.

Religious belief and the use of religious faith as a coping mechanism was explored in this study and it was found that more than half of the participants described themselves as religious and almost two-thirds of these found their faith very helpful in coping with their HIV-status. Both having a religious faith and finding it helpful in coping were significantly protective against current mental disorder on univariate analysis. However, on multivariate analysis it appears that it is the **impact** that the participantsô faith has in terms of coping that is protective against current mental disorder.

It is not clear from this study how religious faith and the way people use it to cope, influences mental disorder. There is some evidence to show that prayer decreases depressive symptoms in HIV-infected individuals (Desai, Desai & Naik, 2004). Therefore, there may be a direct effect. However, in this study no association between religious faith and depressive disorder was identified. Therefore, the reduction in mental disorder as a result of religious faith may be due to its impact on mental disorders other than depression. A possibility may be that individuals who use their faith to cope use fewer maladaptive coping mechanisms, such as abusing substances.

Another factor which may partially express disease progression is time since diagnosis of HIV status. Although there was no statistically significant association between this factor and current mental disorder, there was a trend towards the period of 4 months to 3 years being a period of lower risk of mental disorder (p=0.05 to 0.09). This may suggest that the first few months after diagnosis are a period of high risk as a result of the psychosocial stress of receiving bad news, and that as individuals live for longer periods with the disease, their risk of disease progression increases, and with that there may be an increased risk of mental disorder. This study also found an increased risk of mental disorder in Clinical Stages 3 and 4. The finding by Lyketsos et al (1996a) of an increased risk in the 18 months prior to development of AIDS also suggests an increased risk later in the course of HIV-infection. This would be an interesting area to explore in a follow-up longitudinal cohort study in South Africa.

Another factor explored that was found to be marginally statistically significant on univariate analysis was the experience of discrimination, and in particular, the impact of this on the individual. Those who felt that discrimination made coping very difficult appeared to possibly be at increased risk of having a mental disorder (p=0.0989). However, this did not reach statistical significance on the multivariate analysis. It is again likely that this is a complex issue that would be better explored in a qualitative study, since the perception of discrimination may be a reflection of an individualôs mental state as much as a contributing factor to developing a mental disorder.

Antiretroviral therapy was also not found to decrease the risk of having a current mental disorder, probably again because of the short duration of time that most participants had been on treatment.

Of the postulated protective factors (pre- and post-counselling, support groups and other psychosocial support interventions), being in or having been in a support group showed a significant association with a decreased risk of current depressive disorder. Because of the study design it was only possible to explore these issues in a very superficial manner, however, this is an area that merits further study.

Another area of interest was the reduction in substance use disorders, from lifetime to current levels; previously mentioned as an important finding. Further research in terms of confirming and exploring the reasons for this could be useful.

5.4 Limitations of the study

This was a cross-sectional descriptive-analytic study of occurrence of depressive and anxiety disorders in an HIV-seropositive population. It was a selected sample, in that only people attending particular HIV-treatment sites were included in the study. Therefore, no conclusions can be drawn on the prevalence of depressive and anxiety disorders in HIV-seropositive individuals in the community who may not be accessing treatment. It is possible that individuals who attend HIV-treatment sites are more mentally healthy because they have the energy and motivation to access treatment. On the other hand, the opposite could be true and they might use HIV-treatment sites in help-seeking behaviour. From this study it is not possible to draw conclusions on this issue.

There were, moreover, no HIV-seronegative controls in this study, so it was not possible to make comparisons between HIV-seropositive and HIV-seronegative individuals at the sites. However, the comparison with general population prevalence studies does appear to indicate some increased risk of depressive and anxiety disorders in this study population.

As already mentioned, the exploration of risk and mitigating factors was not ideally done in a cross-sectional study. The questionnaire used to probe for risk and protective factors was, furthermore, problematic in terms of exploring complex interventions and experiences in a closed-ended questionnaire. A prospective cohort study, possibly also with randomised controlled interventions, would give a more accurate understanding of risk and mitigating factors for mental disorders, including depressive and anxiety disorders. It would be better able to track disease progression and determine the interaction between clinical indicators and mental disorders, including depressive and anxiety disorder. A more qualitative approach to the exploration of some of these factors would also add to understanding of their influence.

Another limitation to consider is the particular time when this study was done, which was just before and during the implementation of the public-sector roll-out of ART, when people with HIV infection may have been feeling generally more optimistic about their disease status. However, the period was too soon after the roll-out for the effects of ART on mental disorders to have manifested themselves.

5.5 Conclusions

Despite these limitations, while the estimates are more conservative than those of other similar studies in South Africa, the results of this study confirm previous research that depressive and anxiety disorders are common in HIV-infected individuals in South Africa. This study also shows that current mental disorders, in general, are common in individuals attending HIV-treatment sites. The high background prevalence of these disorders in the general population, the methodology of the study and the small sample size made it impossible to demonstrate a statistically significant difference between HIV-infected

individuals and non-HIV-infected individuals in similar populations. There is a need for this kind of study to be conducted on a larger scale, with matched HIV-seronegative controls. However, the results suggest that more attention needs to be paid to these disorders, particularly in the light of literature demonstrating the impact of mental disorders, especially depression and anxiety, on disease progression and adherence to antiretroviral medication.

Other mental disorders found in this study, besides depressive and anxiety disorders, also constitute a significant burden. In particular, mental disorders resulting from general medical illness and substance abuse are common. These need appropriate treatment (sometimes including antiretroviral treatment). Substance use disorders in themselves are also common, and are a significant factor to consider in the treatment of HIV disease, as they also impact on disease progression and adherence and may result in untoward side-effects and drug-substance interactions.

Risk factors that were identified for the development of depressive disorders are: a lifetime history of a depressive disorder, particularly after diagnosis of HIV infection is made, increased levels of psychosocial stress and feelings of isolation in the individual. Being or having been in a support group was protective against the development of a current depressive disorder.

Regarding mental disorders in general, being in clinical stages 3 or 4, a lifetime history of depressive or substance use disorder and experiencing feelings of discrimination increased the risk of having a current mental disorder. Finding oneôs faith helpful in terms of coping

with the diagnosis and disclosing oneôs status were found to be significant protective factors against having a current mental disorder.

CHAPTER 6

RECOMMENDATIONS

6.1 Introduction

The research conducted in this project shows the extent of depressive and anxiety disorders as well as other mental disorders in HIV-infected individuals attending treatment sites in Gauteng and a rural area in Mpumalanga. The results show that there are significant mental health problems that need attention in this population. They also show that a number of factors could either increase or decrease the risk of individuals with HIV infection developing co-morbid mental disorders. The burden of mental disease and the likely contributors to such disease have implications for health services in South Africa.

The aim of this research was primarily to study depressive and anxiety disorders. Other disorders that were found in the research to be significant problems were substance use disorder and organic mental disorders. These too have implications for health services.

6.2 Implications

As outlined in Chapter 2, depressive and anxiety disorders cause considerable suffering, increase the risk of suicidal behaviour and may impact on HIV disease progression and adherence to antiretroviral treatment. As a result, there are considerable implications associated with the high levels of these disorders in this population (one in five participants in this study). It is important to increase awareness of these conditions in health workers and service users, and to develop ways of identifying and managing these disorders as early as possible.

Substance abuse is a common and serious problem in South Africa. The findings of this research indicate that the occurrence of substance use disorders decreased in the study participants (lifetime rates compared to current rates), suggesting that knowing their HIV status may have made participants more aware of the need to reduce intake of alcohol and recreational drugs. Whether this outcome was simply a result of this awareness, due to unpleasant drug-substance interactions, or a result of psycho-education and support to individuals who attend these HIV-treatment sites, is unclear. Caution should be exercised in generalising these findings to other sites, and this area should be explored further.

While considerable organic mental disorder was found in this study, it is important to remember the context of the study; that it covered November 2004 to November 2005. During this period the public-sector antiretroviral roll-out was implemented. Many of the participants who were not on antiretroviral treatment at the time of interview will have begun antiretroviral treatment since then. This is likely to have had an impact on the occurrence of organic mental disorders in this population. There is concern, however, in mental health services (Phakathi, 2007) about the difficulty in accessing ART for people who present with neuropsychiatric conditions resulting from HIV CNS infection, particularly since this treatment has been shown to be effective in treating these conditions.

6.3 Recommendations

1. **Findings from this research should be disseminated to public sector health service managers, mental healthcare professionals, HIV-physicians, other health workers, HIV-infected individuals and their families.**

Providing information to health services and to those affected by the HIV epidemic, on the relationships between HIV infection and mental disorders, in particular depression and

anxiety, would be an important first step in developing responses to the problems highlighted in this study. Both health workers and individuals accessing services could act on this information. This might result in further learning and development of locally appropriate interventions. It has been shown, particularly in the field of HIV, that self-help or consumer-driven initiatives can be successful (Treatment Action Campaign, 2007; Stephen Lewis Foundation, 2007). Some mental health not-for-profit organisations are also well-positioned to provide support (The South African Depression and Anxiety Group, 2007).

2. Management of mental disorders, including depressive and anxiety disorders, in HIV-infected individuals should be improved: health systems issues.

It has been suggested that the best way of providing comprehensive care for people with HIV-infection is for HIV-treatment sites to provide mental healthcare together with the physical healthcare needed for the condition (Green, et al., 2004; The Nucleus Consulting Group, 2005). This should include management of substance use disorders. An example of such a service in Denver, Colorado is described by Kobayashi and Standridge (2000) in their chapter on comprehensive HIV care, in Cournos and Forsteinôs book: ñWhat Mental Health Practitioners Need to Know about HIV and AIDSò. They argue that members of an HIV-treatment team should include HIV-physicians, psychiatrists, HIV- and mental health-trained nursing staff, pharmacists, lay counselors, social workers, psychologists and specialists in other areas of physical care. In such a setting, there would be cross-pollination of knowledge and skills. Support for staff should also be provided, considering the nature of the work involved in caring for people with serious conditions and the considerable psychosocial ramifications.

While the above model may work in well-resourced settings, it is a pipe-dream for the countries most affected by the HIV/AIDS epidemic. These countries have very poor healthcare resources and mental healthcare, in particular, is generally very limited (WHO, 2001). South Africa is a middle-income country, with wide disparities between rich and poor. The majority of people with HIV infection are poor and their only access to healthcare (including mental healthcare) is through public sector health services and not-for-profit healthcare organisations.

At present HIV-treatment and ART roll-out sites are somewhat ñspecialisedò but the aim is to make this service accessible throughout the primary healthcare system. Mental health services are also largely ñspecialisedò but South African mental health policy is to integrate these services to make them accessible throughout the primary healthcare system and to deliver mental health services in the community/ district health service as far as possible.

The issue of mental healthcare for people with HIV infection highlights the existing difficulties in implementing mental health policy in South Africa. Mental health service provision is inadequate and inequitably distributed across the country (Lund & Flisher, 2006). While many people make use of traditional healers for both physical and mental healthcare, and this could be considered an additional resource, the roles and functions of such practitioners are not clearly defined. It is unlikely that the traditional healthcare system would ever be able to fill the gap in mental health service provision. Mental health professionals currently working in the public sector would argue that they do not have the capacity to expand into HIV-treatment services. On the other hand it can be argued that, since the prevalence of HIV infection is so high and many infected people will come for

treatment, this is an opportunity for more people to access mental health services and for these services to be integrated into general health services (Thom, 2007).

The question remains as to how comprehensive HIV care (including mental healthcare) can best be provided in developing countries such as South Africa. Freeman, Patel and Collins (2005) addressed this issue in their article ñIntegrating mental health in global initiatives for HIV/AIDSò. They described the World Health Organisationôs initiative to integrate mental healthcare into HIV care through its ñ3 by 5ò programme. While this initiative was not wholly successful, various training materials developed in this process could be used in South Africa. These include clinical training materials as well as suggestions for organisational restructuring.

Freeman et al.ôs primary recommendation was based on the fact there are insufficient trained mental health service providers in developing countries to offer additional mental health services in HIV/AIDS treatment programmes. Therefore, primary care providers (including lay counsellors) in HIV treatment settings should be trained to provide as much primary mental healthcare as possible. They did caution, however, against overloading these front-line workers. The need to support primary care workers once they have been trained and to provide easily accessible referral sources was also highlighted.

The disparities in resources and organisation between South African provinces need to be recognised in developing models of HIV care that include mental healthcare. In provinces with poor mental health resources (such as Mpumalanga) it is likely that the best approach to delivering comprehensive HIV care would be through strengthening the knowledge and skills of primary care practitioners. Existing training material could be used to achieve this.

As emphasised above, experience with training of primary care practitioners has shown that it is very difficult to implement training without adequate support and supervision. Mpumalanga currently has one psychiatrist employed in the public sector, who is based at Witbank Hospital. The community mental health service is provided by primary healthcare nurses, trained mental health nurses and generalist doctors who do outreach from general hospitals. It is important that mental health professionals in these settings also be trained in the field of HIV psychiatry. Increased support and encouragement should, moreover, be given for primary care doctors to obtain the Diploma in Mental Health. In addition, provinces with very poor resources could consider the use of telemedicine, regular in-service training, collaboration with NGOs and visiting experts to support primary care practitioners in their work.

Provinces with more resources may be able to adapt existing systems of mental healthcare and physical healthcare resulting in restructuring along the lines suggested in the South African mental health policy. For example; Gauteng is fortunate to have a secondary level community mental health service in the district health service but it is currently inappropriately utilised. A small number of highly trained mental health professionals spend most of their time managing people with chronic serious mental illness in the community, many of whom are stable most of the time and could be managed at primary care level. As a result of this and other obstacles, development of a comprehensive mental health service has not occurred.

A recent development in the district health service in Gauteng which could make a significant difference in improving primary healthcare services is the decision to establish Family Medicine as a discipline in the district health service (Gauteng Provincial

Government, Department of health, 2007). It is likely that this will improve the quality of care provided in the district health service, by improvements in staffing levels, increased training and ensuring that standards of care are adequate in training sites that are to be accredited by professional councils.

The family medicine approach is well-suited to deliver comprehensive health services, including primary mental healthcare. Through training of family medicine practitioners, much of the service load currently inappropriately carried by the secondary level service could be devolved to primary care services. This would free the specialist professionals in the secondary level service to do what they are supposed to do: to be a referral resource for primary care practitioners, provide training and supervision to primary care practitioners and continue to develop comprehensive mental health services in the community.

Family medicine practitioners are likely to be managing the ART programme in the district health service. They need to be convinced of the importance of identifying and treating mental disorders in HIV-infected individuals whom they treat. This research and further local research can be used to do this. Training of these practitioners in management of mental disorders in conjunction with HAART is important. Mental health professionals and family medicine practitioners should work together to ensure that mental healthcare services are accessible through this programme, and eventually throughout the primary healthcare service.

At secondary and tertiary hospitals physicians and mental healthcare professionals need to come together to determine how best to ensure that both HIV-treatment and mental healthcare treatment are available to all at these levels of care. Again, this is likely to

involve training of HIV-practitioners in mental healthcare as well as training of mental healthcare practitioners in HIV-care. Good communication and good working relationships are probably more important in the successful provision of these services than merely having both services at the same site.

Even without additional staffing and/or training in HIV mental healthcare, an essential organisational strategy is to expand psychosocial services at HIV-treatment sites across all levels of care. The current services at these sites, in particular support groups, have been shown to be helpful. Most of these services are provided by non-professionals (lay counsellors) with limited knowledge of healthcare, particularly, mental healthcare. It is necessary to increase awareness of mental health issues in these individuals and to assist them in identifying individuals who may be at risk of depressive or anxiety disorders. However, providing these counsellors with support, supervision and easily accessible referral resources is then also necessary.

Besides lay counsellors, mental healthcare professionals such as social workers and psychologists can play a crucial role in the provision of psychosocial support. A good network of social services is critical, as this study has shown the extent of social disadvantage in individuals at public sector HIV-treatment sites. Both social workers and psychologists can play an important role in training and supervising lay counsellors and being the primary referral resource for these counsellors (Clacherty & Kistner, no date).

One key issue in HIV care is the provision of psycho-social support to ensure adherence. Here it is even more important to identify those individuals who are at risk of depressive or anxiety disorders, since there is strong evidence that these disorders impact on adherence.

Numerous organisations have already developed programmes to assist in this aspect of adherence work (Saloner, 2005). This needs to be expanded to become a routine part of management at ART treatment sites.

Much funding is being channelled into AIDS care and a strong argument can be made in favour of using some of this on mental healthcare in HIV-treatment settings. Even if this were to be done on a short-term basis and attempting to attract mental health professionals currently working outside the public sector, it would be an effective way of providing training in the mental healthcare aspects of managing HIV disease to staff who are primarily involved in the physical care of such patients.

In order to improve mental healthcare to people living with HIV/AIDS, all involved in their care need to improve their awareness, knowledge and skills. Mental health professionals also need to improve their knowledge of HIV psychiatry. Currently the Department of Psychiatry at the University of Toronto is involved in a grant-funded project to determine the learning needs of African psychiatrists in HIV psychiatry (Maggi and Halman, 2006). The South African Society of Psychiatrists has an HIV psychiatry special interest group, which can facilitate the improvement in mental healthcare for people living with HIV/AIDS in South Africa through the dissemination of research findings, advocacy, the development of management guidelines and input into training (South African Society of Psychiatrists, 2006).

3. HIV practitioners should be assisted to identify depressive and anxiety disorders.

A range of screening instruments are available that can be used by HIV practitioners to identify patients with possible depressive and anxiety disorders. These include the SRQ

(Cherian, Peltzer and Peltzer, 1998), the CES-D (Cheng, Chan & Fung, 2006) and the Modified MINI Screen(Sheehan, Lecrubier & Hairnet-Sheehan, 1998). Some have been used in South African research studies and validated as satisfactory screening tools for these disorders in our population (Brandt, Dawes & Bray, 2006). Further work may need to be done to ensure that these are the most appropriate tools to use in our country (Parry, 1996). Enquiry on past psychiatric history is not included in most of these instruments and should be included in any screening for mental disorder. The immediate period after diagnosis of HIV status should be considered a period of elevated risk of developing a depressive or anxiety disorder, but those in the later stages of HIV disease are also likely to be at risk.

4. **The treatment of HIV-infected individuals with depressive and anxiety disorders should be improved.**

Treatment for depressive disorders in HIV-infected individuals

Because patients on HAART take large amounts of medication, clinicians are often reluctant to add yet another medication to treat a depressive disorder, especially those with the potential to interact with HAART medications. However, there is strong evidence that depressive disorders in HIV-infected individuals can be effectively treated, with both pharmacological and psychotherapeutic interventions (Olatunji, Mimiaga & OõCleirigh, 2006). The SSRIõs are the treatment of choice as first-line agents; in particular, citalopram, which has a different metabolic pathway from the antiretroviralsõ, and does not have active metabolites. Mirtazepine, Buproprion and Venlafaxine have also been found to be effective with minimal side-effects (Stolar, et al., 2005), but these medications are not readily available in the public sector. Fluoxetine, with its long half-life, active metabolites, and metabolism by the cytochrome p450 system, may accumulate and result in a serotonin syndrome (De Silva, Le Flore & Marston, 2001). Amitryptaline is commonly used in South

Africa as a treatment for painful peripheral neuropathy in doses of 25 mg nocte but this may be insufficient to treat severe depressive disorders. Tricyclic antidepressants are effective agents (Markowitz, Kocsis & Fishman, 1998), and Amitryptaline is readily available and inexpensive in South Africa, but should be used with caution, owing to the high risk of drug-drug interactions resulting in toxicity. Nortryptaline and desipramine are preferred tricyclic drugs because of their low anti-cholinergic burden and lack of active metabolites (Kaplan & Sadock, 1998:524-580). Methylphenidate and testosterone have also been used in the treatment of depressive disorders in HIV, particularly when there are severe difficulties with energy levels and hypogonadism (Wagner, Rabkin & Rabkin, 1996; Martin, et al., 2002). Research on newer pharmacological treatments is ongoing, both in depression *per se*, and in depression in HIV-infected individuals (Ho & Douglas, 2004).

There is good evidence that psychotherapy interventions are effective in treating depressive disorders, particularly those of mild to moderate severity. Interpersonal psychotherapy and cognitive behavioural therapy have both been found to be effective in randomised controlled trials (Kelly, et al., 1993b; Markowitz, Klerman & Clougherty, 1995).

Treatment of anxiety disorders in HIV-infected individuals

The management of anxiety disorders in HIV-infected individuals should follow the principles of management in the general population and in other medically ill populations (Martin, et al., 2002:139). A primary focus should be exploration of psychosocial stressors and psychotherapeutic interventions. Medication should be considered secondarily if these interventions are insufficient or ineffective, or if the disorder is severe and acute, causing significant distress or impairment. Benzodiazepines and other tranquillising medication

should be used for short periods only to assist the individual over the crisis period, and with due regard for drug-drug interactions with anti-retroviral medication and for the presence of comorbid substance use disorders, which are common. Should the need for longer term medication arise, the treatment of choice is SSRIs. These have been shown to be effective and safe for the treatment of chronic anxiety disorders in HIV-infected individuals.

From this study it is suggested that the use of support groups should be encouraged, and while the study was not able to show statistically significant effects of counselling, the study does confirm that participants find these interventions useful in coping. Identifying individuals who feel isolated, and encouraging those with strong religious faith to use it as a coping mechanism can also be important interventions.

5. Interventions that can assist HIV-infected individuals to reduce substance use disorders should be developed.

As stated before, this study did not clearly identify the cause of the reduction in substance use disorder from lifetime to current levels. This requires further exploration. It is clear from the literature that substance use disorders may share common neurobiological pathways with HIV CNS infection (Hauser, El-Hage & Stiene-Martin, 2007), that they may accelerate disease progression (Kapadia, Vlahov & Donahoe, 2005), and that they impact on adherence (Tucker, et al., 2003). Screening for substance use disorders is critical in HIV-infected individuals. The two most commonly used screening tools for alcohol abuse, the CAGE and the AUDIT, have both been used in South African studies (Danson & Peden, 1999, Betancourt & Herrera, 2006). Motivational interviewing is a skill that can be learnt by primary care workers, and probably by lay counsellors as well (Beckham,

2007). Counselling to reduce substance abuse is a critical component of adherence counselling and support (Saloner, 2005). Individuals with co-morbid substance use disorders, mental disorders, and HIV infection (particularly those on HAART) may require specialised care, and should be referred to mental health services if interventions at the HIV-treatment site are insufficient to manage the patient.

6. Appropriate treatment guidelines for the management of organic mental disorders related to HIV infection should be developed and widely distributed within health services, to HIV practitioners and mental health practitioners.

This study, using the International HIV Dementia Scale, revealed that almost 19% of the participants screened positive for possible HIV-associated dementia. International evidence shows that antiretroviral medication is effective in preventing further progression of HIV associated dementia and, possibly, even in reversing some of the damage due to HIV CNS infection (Sacktor, Nakasujja & Skolasky, 2006). In developed countries, treatment with ART is now initiated at higher CD4 counts than the current South African or World Health Organisation recommendations suggest, and HIV-associated dementia is seen less commonly as a presenting clinical feature of HIV disease (Halman, 2007; personal communication). As South Africa reviews the outcomes of anti-retroviral treatment, it is possible that local ART treatment guidelines may also change.

The national treatment policy for HIV infection is to initiate Highly Active Antiretroviral Treatment at a CD4 count of </= 200 cells/mm3 or in the presence of an AIDS-defining condition. HIV-associated dementia is such a condition, and HAART should be initiated in patients with HIV-associated dementia, irrespective of CD4 count (National Department of Health, 2004:2). As discussed in Chapter 5 (Section 5.2.3), in 2007 the National

Department of Health reviewed treatment practices in relation to HIV-associated dementia and requested the Mental Health and Substance Abuse Directorate to develop treatment guidelines with an estimation of the likely numbers of people who require treatment and the costs involved. A draft document with suggested assessment tools and treatment guidelines was developed (National Department of Health, 2007). It remains for this draft document to be finalised and implemented as a national guideline with the appropriate monitoring, evaluation and revision as necessary.

Among the major impediments to initiating antiretroviral treatment in individuals with cognitive impairment is their capacity to consent to treatment and to adhere to it. While these issues may raise ethical and logistic dilemmas, these are not sufficient to deprive individuals with cognitive impairment related to HIV infection, the right to treatment for their condition. Legislation (South Africa, 2003) and guidelines are in place that can inform clinicians in terms of managing these patients.

An essential aspect of treating HIV-infected individuals with cognitive impairment is the provision of support to ensure adequate adherence. This may involve ensuring that each such patient has a ñbuddyò to monitor their treatment or even, in some cases providing residential care during the period of initiation of therapy until the individual has recovered sufficiently to manage their own medication. An interesting model in this regard evolved from AIDS hospice care in Toronto (Casey House Hospice, 2007), where this hospice now provides care to HIV-infected individuals with neuropsychiatric complications (and often comorbid mood and substance use disorders). Patients who need this kind of assistance are admitted to the hospice and provided with both antiretroviral and psychiatric treatment. Usually, after 6 months the individuals are able to be discharged back to their homes and

they are followed up in the community by HIV-trained nurses. It is possible that this kind of model could be adapted in South Africa, using existing resources and expanding them as they are demonstrated to be successful.

6.4 Suggestions for further research

1. **Ongoing epidemiological studies of mental disorders in the community and in primary care settings are needed.**

The lack of accurate information on the burden of mental disorders in South Africa makes it very difficult to plan services. There is likely to be always a shortage of mental healthcare resources. Therefore, basing prioritisation of service needs and services on accurate information is critical. This will also help to focus resources and reduce fruitless expenditure which can ill be afforded.

2. **Community-based studies of mental disorder in HIV-infected individuals should be conducted.**

Very little information is available on the burden of mental disorder in HIV-infected individuals in community settings in South Africa. These would include people who are not accessing treatment, and in this setting the extent of mental disorder may well differ from that in treatment sites. While the 2005 HIV Household Survey (Shisana, et al., 2005) by the HSRC included some screening questions for mental disorder and found significant levels of symptoms, a need exists for more comprehensive assessment of the number of people requiring intervention. Controlled prevalence studies with HIV-seronegative controls are needed to compare, more accurately, the prevalence in those who are infected with HIV with the prevalence of mental disorders in general.

3. **Follow-up and intervention studies are needed to assess the impact of identifying and treating mental disorders related to HIV infection.**

In order to best utilise scarce resources, local interventions studies are needed to identify cost-effective and time-limited interventions that can make a difference to peopleôs lives and to the extent of distress, morbidity and mortality that results from untreated depression and anxiety.

4. **Prospective cohort studies of HIV-infected individuals are needed to identify more clearly, risk and protective factors for mental disorders in this group.**

While multivariate analysis of various factors in this study, did identify possible risk and mitigating factors, a cross-sectional study design is not the best method for identifying such factors, while prospective cohort studies and qualitative exploratory studies could add to our understanding of which factors are significant.

5. **Prospective cohort studies are needed to assess the impact of HAART on mental disorders in HIV-infected individuals.**

Most individuals who were on HAART in this study had recently commenced treatment. International studies show that, while there is substantial improvement in mental health status generally in individuals who take HAART, HIV-infected individuals continue to suffer a high burden of mental disorder. It is important to document the situation in South Africa and to suggest the type of ongoing interventions that may help to support such individuals.

6. **The impact of knowledge of HIV-status, psychosocial interventions in HIV-positive individuals and HAART on substance use behaviour should be explored.**

Since substance use disorders play a significant role in risky behaviour, disease progression and adherence, this is an important area to explore. Intervention models are in place, but need to be evaluated for effectiveness.

7. **Health systems research to develop appropriate models of comprehensive service delivery to HIV-infected individuals is needed.**

Research from developed countries suggests that integrated services provide the best model for comprehensive service delivery to HIV-infected individuals. It is also suggested that access to mental healthcare through general healthcare services is the most effective model in general. It was on the basis of this premise that the WHO mental health programme and the ñ3 by 5ò programme developed mental health training packages to be included in training packages for health workers treating people with HIV infection (Freeman, et al., 2005). These training packages need to be used and evaluated in terms of their effectiveness in achieving comprehensive care. Any attempts to develop or change models of mental health service delivery to HIV-infected individuals should be evaluated, so that the best recommendations for such service delivery can be made.

8. **Research is needed into factors that increase resilience and coping in HIV-infected individuals.**

While much of the emphasis of this and other research is on risk factors for mental disorders in HIV-infected individuals, little work has been done on identifying protective factors, particularly in South Africa. From that which has been done, it is suggested that this is a very important area on which focus is needed, particularly in relation to the efficient utilisation of scarce resources.

Appendix 1:

Postulated risk or mitigating factors: odds ratios and tests of statistical significance of the possible influencing variables for current mental disorder and current depressive disorder

** statistically significant effect (p<0.05)

* marginally statistically significant effect (p<0.10)

	Current mental disorder			Current depressive disorder		
Variable	**Odds ratio**	**95% Confidence interval**	**P value**	**Odds ratio**	**95% confidence interval**	**P value**
Site			**0.3543**			**0.9727**
PHRU	0.579	0.272 to 1.231	0.1553	1.282	0.475 to 3.458	0.6236
Tintswalo Hospital	0.905	0.342 to 2.391	0.8398	0.898	0.230 to 3.508	0.8765
Nthabiseng HIV clinic CHB Hospital	0.905	0.399 to 2.050	0.8102	1.167	0.388 to 3.506	0.7837
Nthabiseng ARV clinic CHB Hospital	0.521	0.221 to 1.228	0.1360	1.167	0.388 to 3.506	0.7837
Weilerôs Farm	1.00			1.00		
Gender			**0.2787**			**0.7605**
Male	0.749	0.444 to 1.264	0.2787	0.901	0.459 to 1.766	0.7605
Female	1.00			1.00		
Age			**0.9520**			**0.1491**
Mean age CMD Yes CDD Yes	1.001	0.973 to 1.029	0.9520	0.973	0.938 to 1.010	0.1500
Mean age CMD No CDD No	1.00			1.00		
Age group			**0.6959**			**0.4961**
18 to 24	0.618	0.188 to 2.030	0.4276	1.869	0.533 to 6.555	0.3288
25 to 39	1.012	0.598 to 1.713	0.9645	1.419	0.709 to 2.842	0.3231
40 +	1.00					
Relationship status			**0.4705**			**0.9413**
Single	0.833	0.507 to 1.368	0.4705	0.977	0.526 to 1.816	0.9413
In a relationship	1.00			1.00		
Level of Education			**0.3857**			**0.1222**
No/some primary education	0.972	0.465 to 2.030	0.3118	0.717	0.280 to 1.832	0.4865
Completed primary education	1.410	0.490 to 4.051	0.6474	2.352	0.733 to 7.543	0.1504
Some secondary education	1.532	0.740 to 3.173	0.2448	1.283	0.526 to 3.130	0.5845
Completed secondary education	1.00			1.00		
Employment			**0.7523**			**0.1187**
Unemployed	0.774	0.350 to 1.710	0.5263	0.458	0.187 to 1.121	0.0873*
Part-time employment	0.909	0.366 to 2.260	0.8375	0.795	0.289 to 2.188	0.6572
Full-time employment	1.00					

Appendix 1: Postulated risk or mitigating factors for current mental disorder and current depressive disorder

Household situation			**0.8216**			**0.5501**
Not enough for basics	1.040	0.466 to 2.319	0.9245	0.613	0.241 to 1.558	0.3038
Basics only	1.202	0.549 to 2.630	0.6456	0.794	0.326 to 1.937	0.6125
Most of important things	1.00					
Clinical stage			**0.0514****			**0.6210**
Stage 1	1.00			1.00		
Stage 2	1.303	0.713 to 2.382	0.3896	1.147	0.546 to 2.408	0.7170
Stage 3	2.074	1.088 to 3.955**	0.0268**	1.619	0.743 to 3.528	0.2251
Stage 4	3.110	1.065 to 9.082**	0.0379**	0.848	0.176 to 4.091	0.8375
CD4 count			**0.9672**			**0.1636**
Mean CD4 Yes	1.000	0.999 to 1.001	0.9671	1.001	1.000 to 1.002	0.1668
Mean CD4 No	1.00			1.00		
CD4 range			**0.7165**			**0.3231**
>500 cells/ml	1.204	0.533 to 2.722	0.6552	2.071	0.823 to 5.210	0.1219
350-499 cells/ml	1.101	0.459 to 2.643	0.8292	1.709	0.620 to 4.711	0.3005
201-349 cells/ml	0.708	0.366 to 1.370	0.3054	0.949	0.413 to 2.184	0.9025
<200 cells/ml	1.00			1.00		
Presence of a medical condition			**0.0171****			**0.7601**
Yes	1.815	1.109 to 2.970	0.0177**	1.100	0.597 to 2.028	0.7602
No	1.00			1.00		
Time since diagnosis			**0.1329**			**0.3727**
<4 months	0.993	0.454 to 2.171	0.9862	0.466	0.158 to 1.373	0.1658
4 months to 1 year	0.573	0.296 to 1.110	0.0986*	0.574	0.258 to 1.276	0.1730
1 to 3 years	0.531	0.277 to 1.019	0.0571*	0.606	0.280 to 1.311	0.2033
> 3 years	1.00			1.00		
Duration of attendance (in months)			**0.7720**			**0.4399**
Mean CMD Yes CDD Yes	1.003	0.984 to 1.021	0.7713	1.008	0.987 TO 1.030	0.4401
Mean CMD No CDD No	1.00			1.00		
ART			**0.7211**			**0.2108**
On ART	1.110	0.627 to 1.965	0.7211	1.536	0.782 to 3.015	0.2127
Not on ART	1.00			1.00		
Impact of ART on coping			**0.1220**			**P=0.1375**
Pretest counselling			**0.4449**			**0.6166**
Yes	0.806	0.463 to 1.402	0.4454	1.207	0.584 to 2.496	0.6120
No						

Appendix 1: Postulated risk or mitigating factors for current mental disorder and current depressive disorder

Effect of pretest counselling			**0.2303**			**0.3575**
Not helpful	1.533	0.572 to 4.110	0.3961	1.495	0.462 to 4.837	0.5018
Marginally helpful	2.021	0.834 to 4.899	0.1192	2.453	0.925 to 6.503	0.0712*
Helpful	1.00			1.00		
Posttest counselling			**0.2150**			**0.6795**
Yes	0.730	0.444 to 1.201	0.2157	0.877	0.472 to 1.633	0.6796
No				1.00		
Both pre- and post-test counselling			**0.2504**			**0.9078**
Yes	0.691	0.368 to 1.300	0.2504	1.050	0.460 to 2.397	0.9078
No	1.00			1.00		
Post-test counselling number of sessions			**0.8244**			**0.6693**
Once	0.611	0.163 to 2.289	0.4649	0.526	0.124 to 2.231	0.3834
2 to 3	0.789	0.210 to 2.964	0.7258	0.466	0.107 to 2.032	0.3092
4 to 10	0.625	0.126 to 3.087	0.5641	0.314	0.043 to 2.265	0.2504
> 10	1.00			1.00		
Effect of post-test counselling			**0.4914**			**0.4238**
Not helpful	1.619	0.371 to 7.065	0.5217	1.971	0.375 to 10.368	0.4231
Marginally helpful	1.660	0.644 to 4.283	0.2944	1.848	0.617 to 5.535	0.2727
Helpful	1.00			1.00		
Support group			**0.5119**			**0.1540**
Yes	0.846	0.514 to 1.394	0.5121	0.628	0.329 to 1.196	0.1565
No	1.00			1.00		
Effect of support group			**0.4729**	Cant do		**0.3738**
Not helpful	1.127	0.272 to 4.678	0.8692	<0.001	<0.001 to >999.999	0.9732
Marginally helpful	1.973	0.626 to 6.214	0.2459	1.000	0.202 to 4.955	1.000
Helpful	1.00					
Still in support group			**0.5189**			**0.6497**
Yes	0.774	0.355 to 1.688	0.5189	1.284	0.436 to 3.786	0.6503
No	1.00					
Duration of attendance at support group			**0.6236**			**0.6158**
< 6 months	0.752	0.317 to 1.785	0.5188	0.458	0.142 to 1.483	0.1926
7 to12 months	0.566	0.170 to 1.881	0.3527	0.699	0.161 to 3.035	0.6329
> 12 months	1.00					
Number of times attended support group			**0.8188**			**0.3581**
Once	1.055	0.444 to 2.508	0.9039	0.495	0.144 to 1.703	0.2644
2 to 10	0.743	0.253 to 2.186	0.5896	0.409	0.083 to 2.020	0.2724

Appendix 1: Postulated risk or mitigating factors for current mental disorder and current depressive disorder

>10	1.00					
Disclosure			**0.1744***			**0.6648**
Yes	0.593	0.278 to 1.268	0.1799	0.811	0.314 to 2.093	0.6652
No	1.00					
Open re status			**0.4227**			**0.7907**
Yes	0.749	0.369 to 1.521	0.4239	0.889	0.373 to 2.119	0.7908
No	1.00					
Belonging to activist organisation			**0.2719**			**0.6537**
Yes	0.495	0.138 to 1.778	0.2808	0.709	0.156 to 3.219	0.6556
No	1.00					
Discrimination			**0.4449**			**0.1006**
Yes	1.241	0.713 to 2.159	0.4454	1.723	0.895 to 3.316	0.1032
No	1.00					
Impact of discrimination			**0.0773***			**0.2779**
Made coping very difficult	3.500	0.791 to 15.495	0.0989*	3.542	0.674 to 18.623	0.1354
Affected coping a lot	2.167	0.628 to 7.474	0.2210	1.971	0.454 to 8.551	0.3648
Affected coping a little	0.300	0.030 to 2.966	0.3031	0.567	0.052 to 6.211	0.6422
Has not affected ability to cope	1.00					
Feelings of isolation			**0.2746**			**0.0192****
Closer to others	1.108	0.653 to 1.881	0.7038	1.400	0.699 to 2.804	0.3430
Isolated	1.828	0.865 to 3.863	0.1140	3.289**	1.390 to 7.781	0.0067**
No change	1.00					
Religious belief			**0.0302****			**0.3220**
Not religious	2.193	1.123 to 4.281**	0.0215**	0.936	0.380 to 2.303	0.8853
Just a little religious	1.739	0.875 to 3.459	0.1145	0.959	0.389 to 2.363	0.9280
Somewhat religious	2.388	1.096 to 5.201**	0.0285**	2.145*	0.896 to 5.135	0.0867*
Very religious	1.00					
Effect of faith on coping			**0.0469****			**0.7048**
Not helpful	2.406	1.278 to 4.531**	0.0065**	0.996	0.431 to 2.303	0.9924
Marginally helpful	2.197	1.026 to 4.702**	0.0426**	1.465	0.588 to 3.648	0.4125
Helpful	1.00					
AIDS deaths			**0.6945**			**0.2355**
Yes	0.907	0.556 to 1.479	0.6945	1.444	0.785 to 2.655	0.2370
No	1.00					
Effect of AIDS deaths			**0.1953***			**0.1004**
Severe impact	0.707	0.210 to 2.375	0.5750	0.152	0.018 to 1.269	0.0819*

Appendix 1: Postulated risk or mitigating factors for current mental disorder and current depressive disorder

Moderate impact	0.246	0.063 to 0.951**	0.0421**	0.361	0.092 to 1.420	0.1449
Mild impact	0.622	0.272 to 1.425	0.2618	0.438	0.169 to 1.132	0.0883*
No impact	1.00					
Number of AIDS deaths	1.094	0.833 to 1.438	**0.5196**	**1.321**	**0.958 to 1.820**	**0.0870***
Losses in past year			**0.8769**			**0.5611**
Yes	1.047	0.588 to 1.865	0.8764	**1.230**	**0.612 to 2.472**	0.5615
No	1.00					
Impact of losses			**0.9986**			**0.5856**
Severe impact	0.918	0.181 to 4.655	0.9181	0.704	0.064 to 7.743	0.7740
Moderate impact	1.071	0.264 to 4.341	0.9230	1.583	0.274 to 9.166	0.6080
Mild impact	1.000	0.281 to 3.556	1.0000	2.375	0.511 to 11.047	0.2701
No impact	1.00					
No of losses in past year	0.895	0.570 to 1.406	**0.6315**	**1.086**	**0.638 to 1.849**	**0.7601**
Total number of bereavements	1.044	0.837 to 1.301	**0.7048**	**1.235**	**0.952 to 1.602**	**0.1109**
Levels of psychosocial stress			**0.0157****			**0.0004****
Severe additional stress	3.909	1.518 to 10.069**	0.0047**	7.809**	2.569 to 23.733	0.0003**
Moderate additional stress	2.259	0.825 to 6.188	0.1130	5.124**	1.580 to 16.620	0.0065**
Mild additional stress	2.235	1.205 to 4.148**	0.0108**	2.191	0.911 to 5.272	0.0800*
No additional stress	1.00					
Lifetime mental disorder			**<0.0001****			**0.0005****
Yes	11.587	6.470 to 20.752**	<0.0001**	2.937**	1.570 to 5.495	0.0008**
No	1.0			1.0		
Lifetime mental disorder pre-HIV diagnosis			**<0.0001****			**<0.0001****
Mental disorder onset post-HIV diagnosis	14.603**	6.348 to 33.594**	<0.0001**	7.180**	3.171 to 16.261**	<0.0001**
Mental disorder onset pre-HIV diagnosis	10.582**	5.665 to 19.767**	<0.0001**	1.801	0.866 to 3.746	0.2598
No mental disorder	1.0			1.0		
Lifetime depressive disorder			**0.0289****			**<0.0001****
Yes	2.014	1.066 to 3.804**	0.0309**	4.903**	2.452 to 9.806	<0.0001**
No	1.00			1.00		
Lifetime depressive disorder pre-HIV diagnosis						<.0001**
Depressive disorder onset post-HIV diagnosis				6.166**	2.615 to 14.538**	<.0001**
Depressive disorder onset pre-HIV diagnosis				3.357**	1.269 to 8.879**	0.0147**
No mental disorder						
Substance use disorder – current	**n/a**	**n/a**	**N/a**			**0.7011**
Yes				1.222	0.438 to 3.411	0.7015
No				1.00		

Appendix 1: Postulated risk or mitigating factors for current mental disorder and current depressive disorder

Substance use disorder – lifetime			**<0.0001****			**0.8238**
Yes	4.558	2.492 to 8.338**	<0.0001**	1.090	0.509 to 2.336	0.8238
No						

Appendix 2: International HIV Dementia Scale

Memory-Registration – Give four words to recall (dog, hat, bean, red) (in Luganda, kopo,engatto,doodo,myufo)ï 1 second to say each. Then ask the patient all four words after you have said them. Repeat words if the patient does not recall them all immediately. Tell the patient you will ask for recall of the words again a bit later.

1. Motor Speed: Have the patient tap the first two fingers of the non-dominant hand as widely and as quickly as possible.

4 = ≥ 15 in 5 seconds
3 = 11-14 in 5 seconds
2 = 7-10 in 5 seconds
1 = 3-6 in 5 seconds
0 = 0-2 in 5 seconds

2. Psychomotor Speed: Have the patient perform the following movements with the non-dominant hand as quickly as possible:
1) Clench hand in fist on flat surface. 2) Put hand flat on surface with palm down. 3) Put hand perpendicular to flat surface on the side of the 5th digit. Demonstrate and have patient perform twice for practice.

4 = 4 sequences in 10 seconds
3 = 3 sequences in 10 seconds
2 = 2 sequences in 10 seconds
1 = 1 sequence in 10 seconds
0 = unable to perform

3. Memory-Recall: Ask the patient to recall the four words. For words not recalled, prompt with a semantic clue as follows:
animal (dog); piece of clothing (hat); vegetable (bean); color (red).

Give 1 point for each word spontaneously recalled.
Give 0.5 points for each correct answer after prompting
Maximum ï 4 points.

Total International HIV Dementia Scale Score
This is the sum of the scores on items 1-3. The maximum possible score is 12 points. A patient with a score of ≤10 should
be evaluated further for possible dementia.

(Sacktor et al. Neurology 2003 60;1:A186-187)

Appendix 3:
HUMAN RESEARCH ETHICS COMMITTEE CLEARANCE CERTIFICATE

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