

The relationship between substance abuse, health status and health behaviours of patients attending HIV clinics

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Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the authorship owner thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

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Abstract

HIV infection, substance abuse, and psychiatric disorders are major public health issues in South Africa. Psychiatric disorders and substance-use disorders together have a negative impact on the health outcomes of people living with HIV and AIDS (PLWHA), such as poor adherence to anti-retrovirals (ARVs), HIV disease progression, lower CD4 counts, vulnerability to opportunistic infections, high viral loads, possible drug resistance, and an earlier onset of death. The overall aim of this study was to investigate the relationship between substance abuse practices and the health status and health behaviour of patients attending HIV clinics in the Cape Metropole.

The study used a cross-sectional study design for collecting data on hazardous or harmful use of alcohol and problematic drug use, demographic information and health status among patients attending eight HIV clinics in the Cape Metropole. A sub-sample of patients were assessed on the following domains: depression, psychological distress, psychopathology, post-traumatic stress disorder (PTSD), risky sexual behaviour, adherence to ARVs, levels of resilience, levels of social support and patient's work, family and social functioning. Of the 608, 10% of consecutively selected patients completed an additional psychiatric diagnostic interview (Mini International Neuropsychiatric Interview).

The main findings to emerge from this study are:

1. Patients reporting hazardous or harmful use of alcohol and/or drug use are significantly more likely to be non-adherent to ARVs and have lower CD4 counts than their non-substance abusing counterparts

2. Hazardous or harmful use of alcohol has a direct influence on CD4 count resulting in lower CD4 counts and participants being less likely to be on ARVs.
3. Hazardous or harmful use of alcohol has a direct relationship in predicting tuberculosis (TB).
4. Hazardous or harmful users of alcohol and/or problematic drug users are more likely to report psychological distress (anxiety and depression), depression and low levels of family support than their non-using counterparts.
5. Participants who met the criteria for major depression are significantly more likely to be non-adherent to ARVs.
6. Gender, depression, psychological distress, and PTSD were found to be significant determinants of hazardous or harmful use of alcohol.
7. Psychological distress (anxiety and depression) is significant in directly predicting ARV non-adherence.
8. Male participants and those who stopped taking their ARVs were more likely to have lower CD4 counts than female participants and those who did not stop.
9. PTSD was found to predict psychological distress indicating that participants who experienced trauma were more likely to suffer from psychological distress (anxiety and depression) compared to those who did not experience any PTSD. Participants with lower levels of family support were more likely to suffer from psychological distress than those with high levels of family support.

Opsomming

MIV infeksie, dwelmmisbruik en geestesversteurings is groot gesondheidskwessies in Suid-Afrika. Geestesversteurings en dwelmmisbruik het gesamentlik 'n negatiewe uitwerking op die gesondheid van mense wat met MIV en VIGS saamleef (PLWHA), soos byvoorbeeld nie-nakoming in die gebruik van antiretrovirale (ARV's), MIV-siekteverloop, laer CD4-tellings, vatbaarheid vir opportunistiese infeksies, hoë virale ladings, moontlike weerstand teen medikasie en 'n verkorte leeftyd. Die oorkoepelende doel van hierdie studie was om die verhouding tussen dwelmmisbruik en die gesondheidstatus en -gedrag van pasiënte wat MIV klinieke in die Kaapse Metropol besoek, te bestudeer.

Die studie het 'n deursnee-ontwerp gebruik om data in te samel oor die nadelige en gevaarlike gebruik van alkohol en problematiese dwelmgebruik, demografiese inligting, en die gesondheidstatus onder pasiënte wat agt MIV klinieke in die Kaapse Metropol besoek het. 'n subgroep pasiënte geassesseer op die volgende gebiede: depressie, psigologiese angstersteuring, psigopatologie, posttraumatiese stresversteuring (PTSV), riskante seksuele gedrag, nakoming in die gebruik van ARV's, weerstandigheidsvlakke, vlakke van sosiale ondersteuning, asook pasiënte se werk, familie en sosiale funksionering. Van die 608 deelnemers is 10% van die pasiënte opeenvolgend geselekteer om 'n addisionele diagnostiese psigiatriese onderhoud te ondergaan (Mini International Neuropsychiatric Interview).

Die vernaamste bevindinge wat uit die studie gekom het, is:

1. Pasiënte wat nadelige en gevaarlike gebruik van alkohol en/of dwelms rapporteer is beduidend meer geneig om nie die gebruik van ARV's na te kom nie, en het laer CD4-tellings as hulle eweknieë wat nie dwelms misbruik nie.

2. Die nadelige en gevaarlike gebruik van alkohol het 'n direkte invloed op CD4-tellings wat lei tot laer CD4-tellings en dat pasiënte minder geneig is om op ARV's te wees.
3. Die nadelige en gevaarlike gebruik van alkohol hou direk verband met die voorspelbaarheid van tuberkulose (TB).
4. Nadelige en gevaarlike gebruikers van alkohol en/of problematiese dwelmgebruikers, is meer geneig om psigologiese angsversteurings (angs en depressie), depressie, en laer vlakke van familieondersteuning te rapporteer as hul niegebruiker-eweknieë.
5. Deelnemers wat aan die kriteria vir ernstige depressie voldoen, is aansienlik meer geneig tot nie-nakoming in die gebruik van ARV's.
6. Daar is gevind dat geslag, depressie, psigologiese ang en PTSV beduidende bydraende faktore is tot die nadelige en gevaarlike gebruik van alkohol.
7. Psigologiese angsversteurings (angs en depressie) is beduidend om direk die nie-nakoming van ARV's te voorspel.
8. Manlike deelnemers en diegene wat hul ARV's gestaak het, was meer geneig om laer CD4-tellings te hê as vroulike deelnemers en diegene wat nie die gebruik van medikasie gestaak het nie.
9. Daar is gevind dat PTSV psigologiese ang voorspel het wat aandui dat deelnemers wat trauma ondervind het, meer geneig was om aan psigologiese angsversteurings (angs en depressie) te ly in vergelyking met diegene wat geen PTSV ervaar het nie. Deelnemers met laer vlakke van familieondersteuning was meer geneig om aan psigologiese angsversteurings te ly as diegene met hoë vlakke van familiebystand.

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Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy/treatment
ARV	Antiretroviral
ASD	Acute Stress Disorder
AUDIT	Alcohol Use Disorders Identification Test
BDI	Beck Depression Inventory
CAGE	Cut down, Annoy, Guilty and Eye-opener Scale
CD-RISC	Connor-Davidson Resilience Scale
CES-D	Center for Epidemiologic Studies Depression Scale
CIDI	Composite International Diagnostic Interview
cART	combined antiretroviral treatment
CIS-R	Clinical Interview Schedule-Revised
DOTS	Daily Observed Treatment
DTS	Davidson Trauma Scale
DUDIT	Drug Use Disorders Identification Test
EtG	Ethyl Glucuronide
FAEE	Fatty Acid Ethyl Esters
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
IHDS	International HIV Dementia Scale
IES	Impact of Event Scale
LMICs	Low and Middle Income Countries
MEMS	Medication Event Monitoring System
MINI	Mini International Neuropsychiatric Instrument
MSM	Men who sex with men
MSPSS	Multidimensional Scale of Perceived Social Support
PHQ	Patient Health Questionnaire
PLWHA	People living with HIV and AIDS
PTSD	Post-Traumatic Stress Disorder
RCTs	Randomised Control Trials
SCID	Structured Clinical Interview for DSM-IV
SIV	Simian Immunodeficiency Virus
TB	Tuberculosis
SAQ	Substance Abuse Questionnaire
SDS	Sheehan Disability Scale
STAI	State-Trait Anxiety Inventory

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CHAPTER 1: INTRODUCTION

1.1 HIV and AIDS in South Africa

The human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) have become a global pandemic and a major health challenge, especially in sub-Saharan Africa. There are 33.3 million people living with HIV in the world today. South Africa has an estimated 5.6 million HIV-positive people and continues to be the country with the largest epidemic in the world (UNAIDS, 2010). The overall prevalence for HIV in South Africa is estimated at 10.6% (Department of Health, 2010).

The predominant mode of transmission of HIV in South Africa is via heterosexual intercourse followed by mother-to-child transmission. Men who have sex with men (MSM) seems to be a growing concern with regard to the transmission of HIV, while injection drug use is currently not a major source of HIV infection in South Africa (Shisana *et al.*, 2009). The most at-risk populations in South Africa for contracting HIV are African women aged 20-34 years, African men aged 25-49 years, men \geq 50 years, MSM, high-risk drinkers, people who use drugs for recreational purposes, and people with disabilities (Shisana *et al.*, 2009). In South Africa, women continue to be the most vulnerable group and have a higher infection rate than men. The prevalence of HIV among women aged 20-24 years is approximately 21% compared to the 7% of men in the same age range (UNAIDS, 2010).

According to the South African National HIV Prevalence, Incidence, Behaviour and Communication (SABSSM) Survey conducted in 2008, the prevalence of HIV has stabilised to around 11% compared to 11.4% in 2002 and 10.8% in 2005. However, the prevalence across all nine provinces ranges from 15.8% in KwaZulu-Natal and 15.4% in Mpumalanga to 3.8% in the Western Cape and 5.9% in the Northern Cape (Shisana *et al.*, 2009).

1.2 Substance abuse in South Africa

Substance abuse, like HIV, is a major health challenge facing the country. Since South Africa's first democratic elections in 1994 and the country's re-entry into the global economy, there has also been an increase in drug trafficking. Although alcohol continues to be the primary and most abused substance in South Africa, in recent years there has been an increase in the use of heroin, cocaine and amphetamine-type stimulants (Parry & Pithey, 2006). South Africa had the 2nd highest prevalence of past year substance abuse (5.8%) compared to the 14 other participating countries in the World Mental Health Survey and an 11.4% of lifetime prevalence of alcohol abuse (Stein *et al.*, 2008).

In the Western Cape particularly, there has been an increase in heroin and methamphetamine as primary drugs of abuse. Cannabis remains the most common illicit drug used with 61% of adolescents in treatment centres in the Western Cape reporting cannabis use. For the reporting period January –June 2011, 94% of all admissions in Western Cape treatment centres were for methamphetamine, alcohol, cannabis and heroin. Methamphetamine was reported in 35% as a primary

substance of abuse, cannabis was reported as common primary substance of abuse in 18% of admissions and Mandrax was reported in 15% and heroin in 13% of admissions in the Western Cape (SACENDU, 2011).

Recent findings from the SABSSM 2008 survey assessed the extent of alcohol use and problem drinking using the Alcohol Use Disorders Identification Test (AUDIT) among a random population sample of 15 828 South Africans. This study found that 41.5% of men (aged 15 years and older) and 17.1% of women (aged 15 years and older) reported current (past month) use of alcohol (i.e. 27.7% of the total sample). Overall 9.6% of South Africans engaged in past-month binge drinking (4 or more drinks for females and 5 or more drinks for males on one occasion) and 9% of the sample (men and women) was found to engage in hazardous or harmful use of alcohol as defined by the AUDIT. This study concluded that there was an increase in the prevalence of current, binge, and hazardous or harmful drinking from 2005 to 2008 in South Africa (Peltzer, Davids & Njuho, 2011). According to the SABSSM 2008 survey, past-month binge drinking and hazardous/ harmful drinking (AUDIT \geq 8) was the highest among men (16.3%) and women (15.1%) in the Western Cape compared to other provinces (Peltzer et al., 2011).

The estimated burden of disease attributable to alcohol consumption in South Africa in 2004 was 1.3 million years. This is the number of years that were lost because of alcohol-related deaths and people living with an alcohol-related disability. The proportion of alcohol-related deaths in South Africa that can be directly related to the

impact of alcohol on the progression of HIV infection was 10% for men and 28% for women (Parry, Rehm & Morojele, 2010).

1.3 Substance abuse and HIV

There is overwhelming evidence in the literature regarding the relationship between substance abuse and HIV status (Parry *et al.*, 2010; Mellins, Kang, Leu, Havens & Chesney, 2003). Most of this research has centred on substance abuse as a risk factor for contracting HIV. However, recent research has focused on the impact of alcohol consumption in people who have already contracted the virus. Hazardous or harmful use of alcohol in PLWHA is found to be associated with poor adherence to ARVs, re-infection, decreasing viral suppression, viral replication and earlier onset of death (Chander, Lau & Moore, 2006; Schneider, Neuman, Chersich & Parry, 2012). Alcohol also has an impact on the deterioration of the innate and acquired immune system (Parry *et al.*, 2010). A literature review by Hahn and Samet (2010) reported that there is a strong biological basis for alcohol affecting HIV disease progression such as the impact of alcohol on the immune system, its interactions with other drugs and nutritional deficiencies due to a high caloric intake from alcohol. Furthermore, they report that behavioral factors such as lower retention in HIV care, poor ART adherence and mental illness that are associated with alcohol consumption are also associated with HIV disease progression. This review concluded that there is no conclusive evidence to indicate that heavy alcohol consumption leads to HIV progression. Further research is needed to investigate the complex relationship between heavy alcohol consumption and HIV diseases progression (Hahn & Samet, 2010).

Many studies have found that there is a high rate of substance abuse among people who are HIV positive (Cook *et al.*, 2001; Mellins *et al.*, 2003; Palepu *et al.*, 2008). The types of substances abused range from alcohol to illicit drugs such as heroin, cocaine, marijuana, stimulants and other drugs. Especially stimulant use among PLWHA was found to predict faster HIV disease progression, decrease in CD4 counts and AIDS related mortality (Carrico, 2011). These studies point to the fact that substance abuse has a negative impact on the health of persons living with HIV, but that the relationship between the two – substance abuse and an HIV-positive status – is complex and dynamic. Substance abuse among PLWHA can lead to non-adherence to treatment, especially anti-retroviral therapy. Non-adherence to ARVs may lead to a reduction in CD4 count, vulnerability to opportunistic infections, possible drug resistance, HIV-disease progression and an earlier onset of death (Hendershot, Stoner, Pantalone & Simoni, 2009; Morojele, Pithey, Pule & Joubert, 2006).

1.4 Substance use, psychiatric disorders and HIV

Psychiatric disorders are found to be more common in PLWHA than in the general population (Collins, Holman, Freeman & Patel, 2006; Freeman, Nkomo, Kafaar & Kelly, 2008). Depression is reported to be the most common psychiatric disorder in PLWHA and is associated with lack of social support, poor coping skills and poor ARV adherence (Catz, Gore-Felton & McClure, 2002; Rodkjaer, Laursen, Balle & Sodemann, 2010; Mellins *et al.*, 2009). Dual diagnosis of a substance-use disorder and a psychiatric disorder is also common in PLWHA (DeLorenze, Satre, Quesenberry, Tsai & Weisner, 2010; Gaynes, Pence, Eron & Miller, 2008).

Both studies conducted internationally and in South Africa have reported on substance abuse and, psychiatric disorders independently along with focusing on the association between the two disorders in PLWHA (Mellins *et al.*, 2003; Rothlind *et al.*, 2005; Sullivan *et al.*, 2008; Wagner, Holloway, Ghosh-Dastidar, Kityo & Mugenyi, 2011; Farley *et al.*, 2010; Olley *et al.*, 2003; Myer *et al.*, 2008). These studies will be discussed in the ensuing chapters.

Despite this, there has been scant investigation of the relationship between substance abuse, HIV and psychological distress and its impact on the health outcomes of PLWHA in South Africa.

This study aims to address this gap in research. More specifically the objectives of this study are:

1. To compare the AUDIT and DUDIT versus biomarkers as useful short screening tools for primary health care settings.
2. To determine the extent and severity of substance abuse as measured by scores on the AUDIT and Drug Use Disorders Identification Test (DUDIT) (i.e. cut off scores on either measure indicating hazardous or harmful use of alcohol and/or drugs and possible dependence among patients attending HIV clinics).
3. To document the general patterns (type, frequency, quantity) of substance use and abuse among patients attending HIV clinics.
4. To determine the relationship between substance abuse and the following: depression, psychological distress, psychopathology, PTSD, physical health

status, HIV disease progression, poor adherence to ARV's, perceived social support, risky sexual behaviour, resilience in dealing with personal challenges in their life and performance at work among patients attending HIV clinics.

1.5 Brief overview of chapters

- Chapter 2 reviews the local and international literature on the prevalence of hazardous and harmful use of alcohol and/or drugs (including substance use disorders) among PLWHA. This chapter also explores the literature on psychiatric disorders among PLWHA.
- Chapter 3 reviews the local and international literature on the link between hazardous or harmful use of alcohol and/or drugs and psychiatric disorders and their impact on ARV adherence and disease progression among PLWHA.
- Chapter 4 describes the methods used for the study.
- Chapter 5 provides data on the pilot study conducted to determine the validity of the AUDIT and DUDIT compared with biological markers as screening tools for primary health care settings. This Chapter has been published as a paper and will be presented as such.
- Chapter 6 discusses the results of the study :
 - Firstly, the prevalence of hazardous or harmful use of alcohol and/or drugs of patients attending HIV clinics will be discussed.
 - Secondly, a comparison of substance users and non-users on the following domains: depression, psychological distress, psychopathology, PTSD, physical health status, HIV disease progression, poor adherence to ARV's, perceived social support, risky

sexual behaviour, resilience and disability (work, social and family), will be presented. In addition, the predictors of hazardous or harmful use of alcohol and problematic drug use among HIV patients and the predictors of psychological distress (anxiety and depression) and ARV adherence among this population will be presented.

- Chapter 8 provides recommendations, policy issues and implications and future research needs.

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CHAPTER 2: LITERATURE REVIEW

Hazardous and harmful use of alcohol and drugs and psychiatric disorders among people living with HIV and AIDS

2.1 Introduction

Psychiatric and neuropsychiatric disorders are highly prevalent and more common in PLWHA than in the general population. For example, PLWHA are two and half times more likely to have a mental disorder than the general population (Sorsdahl, Mall, Stein & Joska, 2010; Collins *et al.*, 2006; Freeman *et al.*, 2008). Likewise substance abuse, co-occurring with psychiatric disorders, is common among PLWHA (Mellins *et al.*, 2009). Individuals with a diagnosis of a psychiatric disorder in combination with a substance-use disorder are known to have a co-morbid disorder, dual diagnosis or co-occurring disorder (Kaplan, Sadock & Grebb, 1994). Comorbidity of HIV, psychiatric illness and a substance-use disorder is known as 'triple diagnosis' (Desnoyers, 2006). The concepts of both dual and triple diagnosis will be covered in this literature review.

In addition to common psychiatric disorders, such as mood and anxiety disorders, studies have documented high rates of alcohol and drug abuse and dependence among PLWHAs (Chander, Himelhoch & Moore, 2006; Gaynes, Pence, Eron & Miller, 2008). In comparison to high-income countries, research on psychiatric disorders and substance abuse in South Africa is limited.

The complex interplay between HIV infection, substance abuse, and psychiatric disorders can present diagnostic and therapeutic challenges to clinicians.

Several studies have reported an association between being HIV positive, having a mental illness, abusing substances and non-adherence to ARVs, which independently and in combination can lead to poorer health outcomes (Farley *et al.*, 2010; Olley *et al.*, 2003; Rothlind *et al.*, 2005; Sullivan *et al.*, 2008; & Wagner *et al.*, 2011). PLWHA who use substances have a higher prevalence of medical and psychiatric disorders compared to PLWHA who do not use substances (Altice, Kamarulzaman, Soriano, Schechter & Friedland, 2010). Furthermore, the presence of a psychiatric disorder (depression, anxiety, PTSD and substance abuse) can significantly impact on the quality of life of the PLWHA through virological suppression, suicide attempts, and increased risky behaviours (Colibazzi, Hsu & Gilmer, 2006; Chander *et al.*, 2006; Nel & Kagee, 2011).

In high-income countries, there have been many studies conducted on the mental health needs and psychopathology of PLWHA, while in LMICs there is a paucity of research documenting psychopathology in PLWHA (Kaharuza *et al.*, 2006). This review (in this chapter as well as in the following chapter) will examine studies of major psychiatric disorders as well as co-occurring disorders (or dual diagnosis) in PLWHA, both in high and LMICs. A review of the impact, which psychiatric disorders have on ARV adherence and on the health status of PLWHA, will also be done. As a result of extensive research on the link between mental health and HIV in high-income countries, there has been an integration of mental health services into HIV services in some settings for many years (Green & Smith, 2004). Such integration is

seen as being beneficial for dually and triply diagnosed patients (Parry, Blank & Pithey, 2007). However, in LMIC, integration of HIV and mental health services remains a challenge. This chapter will provide substantial evidence of the existence of dual and triple diagnosis in PLWHA in LMICs, and hence, the need for an integration of mental health and HIV services to improve health outcomes in PLWHA.

2.2 Psychopathology and HIV/AIDS in high-income countries

2.2.1 Major Depression

Depression continues to be the most common psychiatric diagnosis in PLWHA. In particular, numerous studies in high-income countries have reported the high prevalence of depression in PLWHA, with rates ranging from 43.5% to 81% followed by co-occurring disorders (psychiatric disorder and substance-use disorder), in the order of 12.1% to 38% (Berger-Greenstein *et al.*, 2007; Mijch *et al.*, 2006; Tegger *et al.*, 2008; Whetten *et al.*, 2005; DeLorenze *et al.*, 2010).

One such study of 205 PLWHA at a university hospital in Denmark, reported that 38% of patients had symptoms of depression and 26% had major depression, as assessed by the Beck Depression Inventory (BDI). Patients with a risk of major depression were nearly six times more likely to miss at least one dose of highly active antiretroviral therapy (HAART). Furthermore, this study found that depression was under-diagnosed in PLWHA. In addition, depression was associated with stress, loneliness, financial problems, poor adherence and unsafe sex (Rodkjaer *et al.*, 2010).

Other studies have also reported that a dual diagnosis of depression and substance abuse in PLWHA is associated with non-adherence to ARVs. For example, in a convenience sample of 273 patients in Louisiana, USA, 49.8% of them reported depression. In a bivariate analysis, depression was associated with non-adherence, while in multivariate analysis, problem drinking was associated with non-adherence. Non-adherence with ARVs was reported in 34.4% of participants (Mohamed *et al.*, 2004). The prevalence of depression was almost similar to the above-mentioned study in a sample of 1 138 PLWHA in the USA with a dual diagnosis of a psychiatric and substance abuse disorder, of whom 52% had a diagnosis of depression as assessed on the structured Clinical Interview for DSM IV (SCID). Non-adherence was significantly associated with increased psychological distress and this was independent of substance abuse. Non-adherence to ARVs was reported in 45% of participants (Mellins *et al.*, 2009). In a retrospective observational cohort study over 12 years (1996-2007), out of 9 751 PLWHA in a private medical care programme in California (USA), 81% were diagnosed with major depression and 12.1% had a dual diagnosis of substance-use disorder and a psychiatric disorder. Patients with a dual diagnosis had a higher mortality risk compared to patients with neither diagnosis (DeLorenze *et al.*, 2010).

However, not all PLWHA with a diagnosis of a psychiatric disorder, including depression, are non-adherent to ARVs. In an Australian sample of 525 PLWHA, 40% were diagnosed with major depression and were found to have a high adherence to their ARVs. The increased use of health care services in this population is

presumably associated with adherence to ARVS (Mijch *et al.*, 2006). This is consistent with a study of 85 HIV-positive participants attending two urban medical centres in the USA which found that 72.9% met the criteria for a major depressive disorder as assessed by the SCID. Most of the participants were African-American and unemployed. This study reported that PLWHA who had depression adhered to ARVs more than those who reported fewer symptoms of depression. The authors suggest that there could be a few reasons for this. Firstly, depressed individuals are probably more concerned about their health and longevity and are more likely to adhere to their medication. Secondly, it could be that these individuals were inaccurate in reporting adherence because of the interference of depressive symptoms with memory recall, or because of social desirability or other needs. Thirdly, it could be on account of their engagement with health care, as the greater the distress experienced, the more likely they would be to seek help from treatment providers who may also monitor their medication (Berger-Greenstein *et al.*, 2007).

The prevalence of psychiatric disorders in HIV-positive women continues to remain high. Using discharge data from a nationwide inpatient sample of HIV-positive women in the USA from 1994-2004, 13 037 with HIV/AIDS were hospitalized with a psychiatric diagnosis in 1994, and 22 606 were hospitalized in 2004. HIV-positive women with a psychiatric diagnosis had a higher prevalence of alcohol/other substance abuse than uninfected women hospitalized with a psychiatric diagnosis (Bansil, Jamieson, Posner & Kourtis, 2009). African-American HIV-positive women from low socio-economic backgrounds are vulnerable to psychiatric disorders and were more prone to non-adherence of ARV medication. In a study of 100 HIV-positive women, mostly of African-American origin and from low socio-economic

backgrounds, 56% reported symptoms of depression on the CES-D. Their depression was significantly associated with avoidant coping strategies, less social support, poor problem-solving skills and more life stressors (Catz *et al.*, 2002). In a longitudinal study of 128 HIV-positive women, of whom 58% were African-American attending a public clinic in the USA, 50% met the criteria for a psychiatric disorder at baseline. Non-adherence was associated with negative life events, parenting stress, non-disclosure of status, substance abuse and the presence of a psychiatric disorder (Mellins *et al.*, 2003).

These data suggest that psychiatric disorders, especially depression, are highly prevalent in PLWHA. Co-occurring disorders are common and need to be considered by health care providers when a PLWHA presents with a single psychiatric disorder as this has important implications regarding treatment and care for HIV-positive people (Gaynes *et al.*, 2008). These studies are summarised in Table 2.1.

2.2.2 Anxiety disorders

Anxiety disorders, like depression have a negative impact on the health status of PLWHA. Very few studies have investigated anxiety disorders in PLWHA. A retrospective observational cohort study over 12 years (1996-2007) in 9 751 HIV-positive people in a private medical care programme in California, USA, found 17.1% diagnosed with panic disorder (DeLorenze *et al.*, 2010). Another study on a sample of 100 HIV-positive women in Louisiana, USA, reported symptoms of anxiety, as assessed by the State-Trait Anxiety Inventory (STAI), to be high (mean = 43.0, SD =

14.0). Most of these women had a low income and were African-Americans. Their anxiety was significantly associated with medical and psychosocial factors, shorter time since diagnosis, elevated stress levels, less social support and poor problem-solving skills (Catz *et al.*, 2002). A study on HIV-positive and negative women in the USA, found that the HIV-positive women had significantly higher anxiety scores (mean = 8.8, SD = 8.9) than those who were HIV-negative (mean = 3.6, SD = 5.5) (Morrison *et al.*, 2002).

Studies have found that PLWHA are rarely diagnosed with anxiety disorders alone and are more likely to have co-occurring disorders. In a study of 152 consecutively sampled HIV-positive patients at an academic medical centre in the Southeastern United States, 21% of patients reported past year and 17% past month symptoms of anxiety on the SCID. Of the participants with anxiety disorder, 54% had a mood disorder and 36% met the criteria for mood, anxiety and substance-use disorder. Being young and having HIV medical-related symptoms were associated with these co-occurring disorders (Gaynes *et al.*, 2008). In a study of a community-based convenience sample of 1 138 PLWHA from several states in the USA with a dual diagnosis of psychiatric and substance abuse disorder, 24% of them reported an anxiety disorder including PTSD (Mellins *et al.*, 2009). The authors concluded that mental health and substance abuse were associated with ARV non-adherence in 45% of this population. These studies are summarised in Table 2.1.

2.2.3 Post-traumatic stress disorder

Several studies have examined PTSD in PLWHA in higher-income countries. In a study of 210 HIV-positive patients attending primary healthcare services in Northern California, USA, 34% reported PTSD and 43% reported acute stress disorder (ASD). More women reported ASD than men (Israelski *et al.*, 2007). This is consistent with the findings of a study by Beckerman and Auerbach (2011) that more women living with HIV report PTSD symptoms than men. Women also tended to report more emotional distress experienced from a traumatic event in the past, while men reported to feel more distant or cut off.

A study on 110 PLWHA in a Mid-western city, USA, examining the impact of PTSD on disease markers and ARV adherence, found PTSD symptoms, as assessed by the Impact of Event Scale (IES), to be highly prevalent in this population. Participant scores ranged from 0-75 (mean 32.4 ± 18.9). PTSD symptoms were significantly related to poor adherence (taking medication off schedule, missing medications and medical appointments). This study also found that PTSD symptoms were associated with lower cortisol levels and higher CD4 counts, indicating that this relationship is complex and multifaceted (Delahanty, Bogart & Figler, 2004). In contrast, a study on 164 PLWHA in Massachusetts, found that PTSD was not associated with poor adherence but that depression was. In this study, participants were assessed at five time points for PTSD and depression and they screened positive for PTSD and depression at 20% and 22% of these visits, respectively. Of the participants who screened positive for PTSD at the initial visit, 56% screened positive for PTSD at all other visits. Those with PTSD were at a higher risk of developing depression and vice versa (Vranceanu *et al.*, 2008). These studies are summarised in Table 2.1.

2.2.4 Substance-use disorders

Studies in high income countries report rates of alcohol abuse/dependence in PLWHA in the range of 32% to 69.4% and rates of drug abuse/dependence as high as 95.3% (Berger-Greenstein *et al.*, 2007; Tegger *et al.*, 2008; Whetten *et al.*, 2005).

The prevalence of substance abuse is high in PLWHA and is associated with non-adherence to ARVs, disease progression and overall poorer health outcomes in this population. Studies reporting on problems regarding substance abuse also report that there often is a co-occurring disorder in PLWHA who abuse substances (Mohammed *et al.*, 2004; Sullivan *et al.*, 2008; & Rothlind *et al.*, 2005). In a convenience sample of 273 HIV-positive patients from a rural town in Louisiana, USA, 12.8% reported binge drinking, 12.8% reported problem drinking on the CAGE (Cut down, Annoy, Guilty and Eye-opener) index and 16.5% reported illicit drug use in the past month. Problem drinking (OR [95% CI]: 3.91 [1.69, 9.06]) was significantly associated with poor adherence. Problem drinking was also associated with illicit drug use and binge drinking. Of the participants, 34.4% were non-adherent to HAART (Mohammed *et al.*, 2004). In a study of 85 PLWHA, attending two urban medical centres in the USA and abusing substances, 69.4% were diagnosed with alcohol abuse or dependence, 95.3% were diagnosed with drug abuse or dependence, and 62.4% were diagnosed with alcohol and drug abuse or dependence. Of the participants, 66% met the criteria for cocaine abuse/dependence, 35% for heroin abuse/dependence, 4.7% for cannabis abuse/dependence, and 3.5% for sedative abuse/dependence. Co-occurring disorders were reported in 66% of participants, while 21% had a triple diagnosis.

This study concluded that PLWHA, who have a substance-use disorder, are likely to have a co-occurring psychiatric disorder too (Berger-Greenstein *et al.*, 2007). This is consistent with a study of 1 362 PLWHAs attending an infectious disease clinic in North Carolina, USA, in which 32% participants reported substance use problems and 23% reported problems both with substance use and mental illness. Being of a younger age, male and having a higher viral load were associated with substance abuse in this study (Whetten *et al.*, 2005).

An even higher prevalence of mood disorders (63%) was found in 152 PLWHA, who reported substance-use problems at an academic medical centre in the Southeastern United States. Of the participants who reported a substance abuse problem, 22% reported past year and 11% reported past month substance-use disorders (Gaynes *et al.*, 2008). In a prospective study of 400 PLWHAs living in Boston, USA, current alcohol dependence was associated with having depressive symptoms. Of the participants, 64% reported current illicit drug use, 10% reported alcohol dependence, 31% were heavy drinkers and 11% were moderate drinkers. Alcohol use was measured using the Composite International Diagnostic Interview (CIDI). Depression was assessed using the CES-D and the mean score was 22 (SD = 12.9, range = 0.56). This study concluded that mental disorders and substance use are not only intricately linked with physical health problems but there is also a significant relationship between mental disorders and substance-use disorders (Sullivan *et al.*, 2008). A higher rate of non-adherence (45%) was found in a community-based convenience sample of 1 138 PLWHA in the USA, with a dual diagnosis of a psychiatric and substance-abuse disorder. The recent use (past 30 days) of crack or cannabis was significantly associated with poor ARV adherence. Of

the participants, 40% met the criteria for alcohol and drug abuse/dependence, with 46% reporting only drug use and 24% only alcohol use. Forty-nine percent of participants reported lifetime injecting drug use (heroin or heroin and cocaine mixed). Eighty-one percent reported using drugs (42% used cannabis, 35% used cocaine, 36% used crack), and 64% reported using alcohol during the past 30 days (Mellins *et al.*, 2009). In a study of 1 774 PLWHA attending a clinic at the University of Washington, USA, 45% of participants had a substance-use disorder and 38% met the criteria for a mental illness and a substance-use disorder. Almost one third of the patients were found to have an alcohol-use disorder, 18% used cocaine, 17% used amphetamines, 12% used opiates and 2% used other drugs. Participants who used opiates or amphetamines had a longer time to HAART initiation than those without a substance-use disorder and those with a co-occurring disorder (substance use and mental illness) took the longest time to initiate HAART (Tegger *et al.*, 2008).

Heavy alcohol use in PLWHA has also been associated with impairments in neuropsychological functioning. A cross-sectional study of 268 adults living in San Francisco found that heavy drinking and HIV infection resulted in significant impairments in cognitive (e.g., working memory), motor and visuomotor functioning of PLWHA. Heavy drinking and impairment in executive functioning can lead to poor anti-retroviral therapy (ART) adherence as memory is adversely affected which could lead to forgetting to take medication (Rothlind, *et al.*, 2005). Heavy drinking and high scores were associated with poor ARV adherence in this population.

From these studies on substance abuse in PLWHA, it is clear that substance abuse and other psychiatric disorders co-exist and need to be treated in an integrated manner. It is important to understand the complex relationship between substance abuse and other psychiatric disorders, as this has implications for the packages of treatment and care that should be provided to PLWHA (Sullivan *et al.*, 2008). These studies are summarised in Table 2.1.

2.2.5 Suicide risk

There are a few studies of suicidality in PLWHA in high-income countries. A study of lifetime suicidal ideation and attempts among 1 560 PLWHA at six US academic medical centres found that 26% and 13% of participants reported lifetime suicidal ideation and lifetime suicide attempts, respectively, and they had higher depression scores on the BDI (Badiee *et al.*, 2012). In a cross-section sample of 2 932 PLWHA in France, 22% of participants reported a suicide attempt at least once in their lifetime. This suicide rate was fairly evenly split among men (19.5%) and women (26.7%), although a slightly higher proportion in women. This is much higher than in the general population of France, where 6% of men and 9% of women have attempted suicide. Factors associated with suicide attempts were younger age, lower level of education, unemployment financial problems, homosexuality, injection drug use, binge drinking, discrimination regarding seropositive status, bodily changes due to HIV, and no support from family and friends (Preau *et al.*, 2008). Similar factors were associated with suicidal thoughts in PLWHA from rural communities in eight states in the USA. Of these, 38% had reported suicidal thoughts during the previous week. However, suicidal thoughts were not associated with drug and alcohol use in

this sample (Heckman *et al.*, 2002). The above-mentioned studies report on suicidality and risk factors that may be associated with suicidality in PLWHA. In considering the higher rates of suicidality in PLWHA, it is important to focus on prevention measures that can be implemented to assist are vulnerable to suicide attempts (Preau *et al.*, 2008). These studies are summarised in Table 2.1.

Table 2.1: Psychopathology and HIV in higher-income countries

Authors	Study setting	Population characteristics	Study design	Main findings
Badiee <i>et al.</i> , 2012	Academic medical centres, USA	1560 PLWHA	Cross-sectional study Stellenbosch University http://scholar.sun.ac.za Measures: Depression (CIDI & BDI)	26% reported lifetime suicide ideation, 13% reported lifetime suicide attempts.
Bansil <i>et al.</i> , 2009	Hospital inpatient database, USA	13037 HIV+ women	Used hospital discharge data	Significant association of alcohol/substance abuse with psychiatric disorders
Beckerman <i>et al.</i> , 2011	Community centres, New York, USA	184 PLWHA	Cross-sectional study Measures: Life Stressor Checklist, PTSD (PTSD Checklist Scale)	Women reported higher levels of PTSD symptoms than men.
Berger-Greenstein <i>et al.</i> , 2007	Hospital & Medical Centre, USA	85 PLWHA	Measures: Psychiatric disorders (SCID), Depression (BDI), Adherence (Self-report)	72.9% met criteria for major depressive disorder, 69.4% met criteria for alcohol abuse, 95.3% met criteria for drug abuse, 42.4% met criteria for suicide ideation.
Catz <i>et al.</i> , 2002	HIV clinic, USA	100 HIV+ women	Cross-sectional study Measures: Depression (CES-D), Anxiety (Trait Anxiety Inventory, Coping (Ways of Coping Questionnaire), CD4 count (medical records)	Anxiety & depressive symptoms were associated with higher stress, few coping mechanisms and perceiving less social support.

Delahanty <i>et al.</i> , 2004	Mid-western State HIV service organisations, USA	101 PLWHA	Cross-sectional study, survey Measures: Health status (self-report), Adherence (self-report), PTSD (Impact of Event Scale)	PTSD was associated with poor adherence,
DeLorenze <i>et al.</i> , 2010	Private medical care, USA	9751 PLWHA	Retrospective observational study Measures: Psychiatric disorders (ICD-9), Substance abuse/dependence (ICD-9)	25.4% met a psychiatric diagnosis, 25.5% met a substance-use disorder, 12.1% had psychiatric and substance-use diagnosis. The highest risk of death was among dual diagnosed participants.
Gaynes <i>et al.</i> , 2008	Academic medical centre, USA	153 PLWHA	Cross-sectional study Psychiatric disorders (SCID)	Mood disorders (32% past years & 21% past month), anxiety (21% past year & 17% past month), substance-use disorder (22% past year & 11% past month), 40% with past month disorders met criteria for multiple diagnosis.
Heckman <i>et al.</i> , 2002	8 States (rural communities, HIV service organisations), USA	201 PLWHA	Cross-sectional study, Self-administered surveys Measures: Suicide (BDI), Depression, SCL-90-R), Life stressor (HIV-Related Life Stressor Burden Scale), Coping (Ways of Coping Checklist), Substance use (self-report)	38% reported suicide ideation. Suicide thought associated with depressive symptoms, more stress due to HIV stigma, poor coping skills, suicide thoughts not predicted by substance use
Israelski <i>et al.</i> , 2007	HIV care services, USA	210 PLWHA	Cross-sectional study Measures: Depression (BDI), PTSD (PTSD checklist), Acute Stress (Stanford Acute Stress Reaction Questionnaire)	38% met criteria for depression, 34% for PTSD, 43% for ASD and 38% screened positive for two or more disorders

Mohamed <i>et al.</i> , 2004	HIV clinics, USA	273 PLWHA	Cross-sectional study Measures: Alcohol (CAGE), Adherence (self-report)	Problem drinking was associated with poor adherence.
Mellins <i>et al.</i> , 2003	HIV clinic, USA	128 HIV+ women	Longitudinal study Measures: ARV Adherence (self-report), Psychiatric disorder (CDQ), Substance abuse (CDQ) Stellenbosch University http://scholar.sun.ac.za	50% met criteria for current psychiatric disorder, 25% for substance-use disorder, 9% met criteria for both psychiatric and substance-use disorder. 23% reported non-adherence to ARVs at all three interviews.
Mellins <i>et al.</i> , 2009	Multi-sites, USA	1138 PLWHA	Data from a larger multisite intervention study	Non-adherence was associated with alcohol and drug use and psychological distress.
Mijch <i>et al.</i> , 2006	Hospital, Australia	2981 PLWHA	Retrospective study. Measures: Hospital records	17.6% diagnosed with Mental Health Disorder (MHD). HIV exposure, CD4 count and ARV therapy was not affected by MHD.
Morrison <i>et al.</i> , 2002	Florida, USA	93 HIV+ women 63 HIV- women	Cross-sectional study. Measures: Depression & Anxiety (SCID) & Hamilton Depression Scale	Depression was four times higher in HIV+ women than HIV- women. HIV+ women reported higher symptoms of anxiety than HIV- women.
Preau <i>et al.</i> , 2008	Hospitals, France	2932 PLWHA	Cross-sectional study Measures: face-to-face questionnaire assessing suicide attempts, social support, substance use	22% had attempted suicide, 24% reported binge drinking in the past 12 months. Binge drinking was associated with suicide attempts.
Rodkjaer <i>et al.</i> , 2010	University hospital, Denmark	205 PLWHA	Cross-sectional study Measures: Depression (BDI)	Depression is under-diagnosed in PLWHA; depression was associated with poor adherence.
Rothlind <i>et al.</i> , 2005	San Francisco,	268 PLWHA	Cross-sectional study Measures: Psychiatric disorders	Heavy alcohol use and executive functioning was associated with poor adherence

	USA		(SCID), Alcohol (Life time drinking history interview), Depression (BDI)	
Springer <i>et al.</i> , 2012	USA & outside countries	82 studies	Systematic review	Lower ARV adherence amongst depression PLWHA
Sullivan <i>et al.</i> , 2008	Boston, USA	400 PLWHA	Used data from a prospective study Measures: Depression (CES-D), Alcohol (CIDI), Adherence (self-report)	Alcohol dependence & heavy alcohol use were significantly associated with higher CES-D scores
Tegger <i>et al.</i> , 2008	University of Washington, USA	1774 PLWHA	Longitudinal observational Study Measures: Data from hospital records	63% had a mental illness, 45% had a substance-use disorder, 38% had both. Patients with depression and/or anxiety were less likely to initiate HAART.
Vranceanu <i>et al.</i> , 2008	Medical centre & Community health centre, Boston, USA	164 PLWHA	Randomised crossover trial Measures: Depression & PTSD (brief self-report), Adherence (MEMS)	Participants screened positive for PTSD at 20% of visits and depression at 22% of visits. Depression and PTSD was associated with poor adherence.
Whetten <i>et al.</i> , 2005	HIV clinics, USA	1362 PLWHA	Cross-sectional study Measures: Mental health screening (CIDI), alcohol use (AUDIT)	60% reported mental illness, 32% reported substance abuse, 23% reported substance abuse & mental illness

2.3 Psychopathology and HIV/AIDS in low- and- middle- income countries

2.3.1 Major depression

Compared with research in the northern hemisphere, there have been relatively few studies in sub-Saharan Africa, especially in South Africa, examining the relationship between psychiatric disorders or psychological distress and HIV disease in PLWHA.

A systematic review of the prevalence of psychiatric disorders in PLWHA living in lower- and middle-income countries (LMICs) documented rates of depression in this population ranging from 0% to 63.3%. The review concluded that there was a higher prevalence of depression in PLWHA than in non-infected people (Collins *et al.*, 2006). This is consistent with a systematic review on the mental health needs of PLWHA in India that reported depressive disorders, anxiety, adjustment disorders, suicidal ideation and attempts and alcohol dependence were all highly prevalent among PLWHA (Das & Leibowitz, 2011). Studies conducted in sub-Saharan Africa have reported rates of depression in PLWHA ranging from 13% to 54% (Wagner *et al.*, 2011; Kaharuza *et al.*, 2006; Nakasujja *et al.*, 2010; Do *et al.*, 2010). A longitudinal prospective cohort study conducted in two HIV clinics in Kampala and Kakira in Uganda of 602 patients, for example, reported a rate of depression of 13%, as assessed on the Patient Health Questionnaire (PHQ). Depression in this population was associated with physical health, economic stability, social support and sexual health behaviour (Wagner *et al.*, 2011). A much lower rate of depression (7.6%) was found in a Nigerian study of 167 HIV patients attending a hospital in Sokoto. Being divorced and not having a tertiary education were associated with

depression and anxiety in this population (Yunusa *et al.*, 2011). In both studies, psycho-social factors seem to be an important determinant in PLWHA experiencing depression.

These rates are lower in comparison to other studies conducted in other sub-Saharan countries reporting prevalence of depression of over 30% and as high as 64%. Kaharuza *et al.* (2006), in their study of 1 017 PLWHA in Uganda, found the prevalence of depressive symptoms to be very high, with 47% reporting depressive symptoms on the CES-D. Depression was associated with lower CD4 counts, being female, older than 50 years and having no income. The finding of this study is consistent with that by Nakasujja *et al.* (2010) in Uganda, which documented a rate of 54% of depressive symptoms on the CES-D in PLWHA in comparison with a 28% rate of depressive symptoms at baseline among HIV-negative individuals. In addition, 68.8% PLWHA endorsed cognitive impairment compared to 16% of uninfected individuals. The prevalence of both conditions (depression and cognitive impairment) in PLWHA was 39.2%. After initiating HAART both the depressive symptoms and cognitive impairments improved at follow-up. Despite the variation in the rates for depression, the common factors seemed to be psycho-social stressors (being single or divorced, female, poor health, financial stress, lack of social support and having a diagnosis of HIV) in studies that reported high and low rates of depression. However, a possible explanation for this variation in depression rates could be because of the different measures used by different studies to determine the diagnosis of depression.

Studies in South Africa report prevalence of psychiatric disorders among PLWHA ranging from 14% to 56%. The most common psychiatric disorders identified among PLWHA, locally, were depression and other mood disorders, ranging from 11.1% to 80%. One such study was conducted by Freeman *et al.* (2008) across five provinces to investigate the prevalence of mental disorders in PLWHA using the CIDI. Findings revealed 43.7% with a mental disorder, 11.1% with major depression, and 29.9% with mild depression. These findings indicate that PLWHA are two and a half times more susceptible to a mental disorder than the general population. There was a strong association between depression and disease progression (as defined by the WHO stages for HIV disease based on clinical symptoms) with 39.8% and 37.2% of PLWHA experiencing symptoms of a mental disorder in stage 1 and stage 2, respectively. Another 49.7% had a psychiatric diagnosis in stage 3 and 68.8% were diagnosed with a disorder in stage 4 of the illness. Persons being unemployed was significantly associated with a mental disorder. In a sample of 85 HIV-positive patients attending three clinics in the Stellenbosch Municipality in the Western Cape, 24.7% reported mild to moderate depression, 20% moderate to severe depression, while 17.6% reported severe depression on the BDI. Patients taking ARVs reported significantly less severe symptoms of depression than patients not on ARVs. This finding could be because patients on ARVs were more hopeful of their future due to being on ARVs (Kagee & Martin, 2010).

An earlier study conducted among a convenience sample of 149 HIV-positive patients receiving medical care at an Infectious Diseases Clinic in Cape Town, found

a high prevalence of mood disturbance in the sample. The most common psychiatric disorders, as assessed on the Mini International Neuropsychiatric Instrument (MINI), were major depression (34.9%) and dysthymic disorder (21.5%) (Olley *et al.*, 2003). In a prospective study of 65 patients at the same clinic who were newly diagnosed with HIV, 56% of the patients reported at least one psychiatric disorder at baseline, and 48% reported at least one psychiatric disorder at 6 months follow-up. The most prevalent disorder was depression (34.8% at baseline and 26% at follow-up). A greater number of negative life events, declining CD4 counts and disability in (work/family/social functioning) were significantly associated with depression on follow-up (Olley *et al.*, 2006). Similarly, in a later cross-sectional study evaluating the impact of HIV among 105 Coloured (from mixed ancestry) and black women who were newly recently diagnosed with HIV (< 1 year) over a six-month period at Tygerberg Hospital in Cape Town, 56.2% and 51% of them were diagnosed with at least one psychiatric disorder at baseline and at follow-up. While 38.1% met the criteria for major depression at baseline, 21.6% were diagnosed with major depression at follow-up (Olley, 2006). The findings suggest that among Coloured and black African women living with HIV, negative life events are a contributory factor to the recurrence of major depression. These studies are summarised in Table 2.2.

2.3.2 Anxiety disorders

There are few studies reporting on anxiety disorders in PLWHA in low- and middle-income countries. In a study in India, 36% of PLWHA (n=51) who were assessed for mental disorders within 4-6 weeks after learning about their positive status, reported

symptoms of anxiety (Chandra, Ravi, Desai & Subbakrishna, 1998). In a cross-sectional study in rural Tanzania, 15.5% of PLWHA (n=220) attending an outpatient clinic were identified with depression or mixed anxiety and depression, as assessed by the Clinical Interview Schedule-Revised (CIS-R). Phobias and panic disorders were reported in 3.2% and 1.4% of patients, respectively (Marwick & Kaaya, 2010). Similarly, in a cross-sectional study of 167 HIV patients attending a hospital in Sokoto, Nigeria, the prevalence of anxiety disorder was found to be 8.8% (Yunusa *et al.*, 2011). While in another study in Nigeria on 88 PLWHA, there was about a four-fold higher rate (34%) of some form of anxiety disorder reported on the MINI. This prevalence was much higher than that in the HIV-negative control group (Adewuya *et al.*, 2007).

Few studies have been conducted in South Africa. One such study, reported high levels of anxiety and depression (52.9%) in a sample of 85 HIV-positive patients attending three clinics in the Stellenbosch Municipality in the Western Cape (Kagee & Martin, 2010). In a study of 456 PLWHA attending primary health care clinics in South Africa, 13.1% of participants met the criteria for at least one anxiety disorder. The most prevalent anxiety disorders were; PTSD (5.1%), agoraphobia (4.8%), and generalised anxiety disorder (4.6%) (Fincham, Smit, Carey, Stein & Seedat, 2008). These studies are summarised in Table 2.2.

2.3.3 Post-traumatic stress disorder

Very few studies have focused on PTSD in PLWHA in LMICs. Stigma is an important factor consequent to trauma and the development of PTSD. A study of 190 PLWHA

in Nigeria found that 27.4% of participants reported PTSD resulting from HIV-stigma. Some of the predictive factors that are associated with PTSD resulting because of HIV-stigma in this sample were past trauma, exposure to multiple events, low self-esteem, poor social support and the presence of psychopathology. Findings of this study suggest that PTSD may develop after an intensely stigmatizing situation or an event related to HIV-positive status, although the development of PTSD in these contexts is controversial (Adewuya *et al.*, 2009). Similarly, a South African study conducted at an outpatient Infectious Diseases Clinic at Tygerberg Hospital, which examined prevalence and correlates of PTSD among 149 newly HIV-diagnosed patients, found that 14.8% met criteria for PTSD. Of the patients diagnosed with PTSD, 29% had a major depressive disorder compared to 7% of non-PTSD patients; 54% PTSD patients reported suicidal ideation compared to 11% non-PTSD patients, while 40% PTSD patients had social anxiety disorder versus 11% non-PTSD patients. Patients with PTSD also reported significantly more work impairment and use of alcohol as a means of coping than non-PTSD patients (Olley, Zeier, Seedat & Stein, 2005). In a study of 85 newly diagnosed HIV-positive patients attending clinics in the Boland area of the Western Cape, Martin and Kagee (2011) found that 54.1% of the participants met the criteria for lifetime PTSD and 40% met the criteria for HIV-related PTSD.

Other studies in South Africa have had comparable results. For example, a Cape Town study on 65 newly diagnosed HIV patients a rate of 14.8% PTSD at baseline and 20% at follow-up was found (Olley *et al.*, 2003; Olley *et al.*, 2006). This is consistent with the findings of 105 Coloured and black newly HIV-diagnosed women (< 1 year) at an out-patient infectious disease clinic at Tygerberg Hospital where the

rate of PTSD increased from 19% at baseline to 29.4% at 6 month follow-up (Olley, 2006). This increase in PTSD at follow-up is explained by the authors as a possible delay in the onset of PTSD or that patients could have been exposed to further trauma between baseline and follow-up. A lower rate of PTSD of 5% was reported in a study of 465 HIV-positive patients enrolled for HIV treatment at primary health care services in Cape Town (Myer *et al.*, 2008). This discrepancy between the rates of PTSD could be reason of different methodologies and measures being used to assess PTSD (from screening instruments to clinically validated instruments such as the MINI) or because of the difference in the study population (Myer *et al.*, 2008). These studies are summarised in Table 2.2.

2.3.4 Substance-use disorders

Only a few studies on the prevalence of alcohol and drugs in LMICs have been reported. In sub-Saharan Africa, the prevalence of alcohol abuse/dependence among PLWHA has been found to range from 8.8% to 24.3% (Farley *et al.*, 2010; Yunusa, Obembe, Ibrahim & Njoku, 2011; Sebit *et al.*, 2003). A study in western Kenya reported hazardous drinking to be as high as 54% in patients with and without HIV attending public clinics (Shaffer, Njeri, Justice, Odero & Tierney, 2004).

One recent study was conducted in Nigeria among 399 patients attending an HIV-speciality clinic at the University of Abuja Teaching Hospital. The number of patients who were on ART was 222, with 177 who were ART naïve. The AUDIT and CES-D were used to screen ART experienced and ART naïve patients for hazardous alcohol use and depressive symptoms. Among ART naïve patients, 12% scored ≥ 8 on the AUDIT, and 7% of ART naïve and ART experienced patients scored ≥ 10 on the

AUDIT. Overall, 24% of the men participating in the study scored ≥ 8 on the AUDIT indicating hazardous or harmful use of alcohol. Of these participants, 13% scored ≥ 16 on the CES-D and 6% scored ≥ 21 on the CES-D indicative of symptoms of depression and associated with poorer ART adherence. The findings of this study demonstrate the need for integration of mental health services as part of comprehensive HIV treatment (Farley *et al.*, 2010).

Similarly, in a previously described cross-sectional study of 167 HIV patients attending a hospital in Sokoto, Nigeria, half of the patients reported psychoactive substance use (tobacco, coffee, kola nuts and solvents) while 8.8% reported harmful use of alcohol. More men than women were found to use substances. Substance use was associated with having a tertiary education and being divorced (Yunusa *et al.*, 2011). Similar results were found in a cross-sectional prospective study of 300 PLWHA attending an outpatient clinic in Botswana where 9.9% of participants reported current use of alcohol (daily to three times a week), 7.3% and 2.6% reported moderate and heavy alcohol use, respectively. This study also found that depression, alcohol use, and not disclosing one's status to a partner were predictors of poor ARV adherence (Do *et al.*, 2010). In a study of HIV-positive and negative people conducted in Zimbabwe, 24.3% of PLWHA reported alcohol use/misuse compared to 16.5% who were HIV negative (Sebit *et al.*, 2003).

South African studies among PLWHA have focused more on alcohol abuse/dependence than on drug abuse/dependence and reported rates of alcohol abuse/dependence in PLWHA range from 7% to 12.4% (Olley *et al.*, 2003; Myer *et*

al., 2008). From published studies, the prevalence of alcohol abuse/dependence among PLWHA seems to be higher in men than in women. In a convenience sample of 149 HIV-positive patients receiving medical care at an Infectious Diseases Clinic in Cape Town, 10.1% met criteria for alcohol dependence. In this sample, the proportion of men who reported alcohol dependence was significantly higher than women (22.7% vs. 4.7%, respectively) (Olley *et al.*, 2003). Similarly, in a study by Freeman, Nokomo, Kafaar and Kelly (2007) across five provinces in South Africa, 12.9% were diagnosed with an alcohol abuse disorder on the CIDI. Men had more alcohol-related problems than the women. In a study conducted on PLWHA at a general state hospital in Durban 23% of men and 18% of women were found to have substance abuse, which was mostly alcohol-related. Those reporting substance abuse had a history of substance abuse that preceded their HIV diagnosis (Schlebusch & Vawda, 2010). In a study of 465 HIV-positive patients enrolled for HIV treatment and primary health care services in Cape Town, 7% reported alcohol dependence/abuse as assessed on the AUDIT (Myer *et al.*, 2008).

Substance abuse is highly prevalent in PLWHA as is other psychiatric disorders. Health care providers should be aware of co-occurring disorders with a substance-use disorder as treatment aimed at substance abuse may not prove effective if a co-occurring psychiatric disorder is not timeously identified and treated (Gaynes *et al.*, 2008). These studies are summarised in Table 2.2.

2.3.5 Suicide risks

There is a paucity of research in LMICs on PLWHA. However, a few published studies from South Africa and India have been reported. One such study, conducted at a general state hospital in Durban on a cohort of 112 HIV-positive patients, the risk for HIV-related suicide risk was found to be between 13.3% and 18.87% (Schlebusch & Vawda, 2010). Similarly, in a study of 65 patients attending a clinic in Cape Town, the rate of suicidality at baseline and follow-up was 6.2% and 9.2%, respectively (Olley *et al.*, 2006). In a study of newly diagnosed (4-6 weeks) HIV-positive people living in India, 14% endorsed serious suicide intent (Chandra *et al.*, 1998). These studies are summarised in Table 2.2.

Table 2.2: Psychopathology and HIV/ AIDS in low-income countries

Authors	Study setting	Population characteristics	Study design	Main Findings
Adewuya <i>et al.</i> , 2007	Western Nigeria, sub-Saharan Africa	190 PLWHA	Cross-sectional study Measures: General health questionnaire, Rosenberg Self-Esteem Questionnaire, MINI	HIV-stigma-related PTSD was reported in 27.4% of PLWHA.
Brandt, 2009	Africa	PLWHA	Literature review (23 studies)	Most studies found PLWHA had a psychiatric disorder, depression being the most common disorder.
Do <i>et al.</i> , 2010	Gaborone, Botswana	300 PLWHA	Cross-sectional prospective survey Measure: 87-question study survey	9.9% reported active alcohol use, 7.3% reported moderate alcohol use, 2.6% reported heavy alcohol use, 21.2% reported being severely depressed.
Chandra <i>et al.</i> , 1998	India	51 PLWHA	Cross-sectional study	40% reported depression, 36% reported anxiety & 14% reported suicide intent.
Collins <i>et al.</i> , 2006	Developing countries	PLWHA	Literature review (39 studies)	Depression ranged from 0 to 63.3%, psychosocial factors were significantly associated with health outcomes.
Farley <i>et al.</i> , 2010	HIV clinic, Nigeria	222 ART experienced 177 ART naïve	Cross-sectional study Measures: Depression (CES-D), Alcohol (AUDIT)	Higher CES-D scores were associated with poor adherence.

Fincham <i>et al.</i> , 2008	HIV clinics, Western Cape, South Africa	456 PLWHA	Cross-sectional study Measures: Depression (CES-D), Psychiatric disorders (MINI),	13.1% met criteria for at least one anxiety disorder, 5.1% met criteria for PTSD, 4.8% met criteria for agoraphobia, 4.6% met criteria for generalized anxiety disorder.
Freeman <i>et al.</i> , 2008	5 Provinces, South Africa	900 PLWHA	Cross-sectional study Measures: Mental disorders (CIDI),	43.7% had a diagnosable mental disorder, depression was most common disorder (11% major & 29.9% with mild disorder), and 12.4% met criteria for alcohol abuse disorder.
Kagee & Martin, 2010	HIV clinics, Stellenbosch, Western Cape, South Africa	85 PLWHA	Convenience sampling Measures: Hopkins Symptoms Checklist and the BDI	52.9% scored in the elevated range on the HCL, 24.7% reported mild to moderate range of depression, 20% reported moderate to severe depression and 17.6% reported severe depression on the BDI.
Kaharuza <i>et al.</i> , 2006	AIDS support organizations, Uganda	1017 PLWHA	Cross-sectional study Depression (CES-D), CD4 count(blood samples)	Depression was associated with low CD4 counts.
Marwick & Kaaya, 2010).	HIV/AIDS care centre, Tanzania, sub-Saharan Africa	220 PLWHA	Cross-sectional study. Measures: Psychiatric disorders (Clinical Interview Schedule)	15.5% met criteria for depression or mixed anxiety and depression and 4.5% suffered other anxiety disorders.
Meyer <i>et al.</i> , 2008	Primary care HIV centres	465 PLWHA	Cross-sectional study. Measures: Psychiatric disorders (MINI), Depression (CES-D), PTSD (HTQ),	14% reported depression, 5% reported PTSD and 7% reported alcohol dependence/abuse.

			Alcohol use (AUDIT)	
Nakasujja <i>et al.</i> , 2010	HIV clinic, Uganda	102 PLWHA 25 HIV-	Comparative study Measures: Depression (CES-D), Cognitive impairment (IHDS),	Depressive symptoms & cognitive impairment was higher among HIV+ at baseline compared to HIV- people.
Olley, Zeier, Seedat & Stein, 2005).	Tygerberg Hospital, Cape Town, South Africa	149 PLWHA	Cross-sectional study. Measures: Psychiatric diagnosis (MINI), Carver Brief Cope Scale, Sheehan Disability Scale	14.8% met criteria for PTSD, depression and suicidality were associated with PTSD.
Olley, 2006	HIV clinic, Cape Town, South Africa	105 HIV+ women	Cross-sectional study Measures: Psychiatric diagnosis (MINI), Coping styles(COPE), Disability (SDS), Stressful life events(clinician administered checklist), Risky sexual behaviour (20 item checklist)	56.2% met criteria for a psychiatric disorder at baseline. Major depression (38.1%) and dysthymic disorder (22.9%) were most common, 11.4% were at risk of suicide, 19% met criteria for PTSD, 6.7% met criteria for generalized anxiety disorder.
(Olley <i>et al.</i> , 2003	Tygerberg Hospital, Cape Town, South Africa	149 PLWHA	Cross-sectional study Measures: MINI, Carver Brief Cope Scale, Sheehan Disability Scale	34.9% reported depression, 21.5% dysthymic disorder, 14.8% PTSD, and 10.1% reported alcohol dependence.
Olley <i>et al.</i> , 2006	HIV clinic, Cape Town, South Africa	65 PLWHA	Prospective study	56% met criteria for psychiatric disorder at baseline and 48% at follow-up. Depression and PTSD most common disorders at baseline and follow-up.
Schlebusch & Vawda, 2010	State hospital, Durban, South Africa	112 PLWHA	Measures: Hospital records & semi-structured questionnaire	80% met criteria for a psychiatric disorder, 23% males & 18% females met criteria for substance abuse.

Sebit <i>et al.</i> , 2003	Epworth, Harare, Zimbabwe, sub- Saharan Africa	115 HIV+ 79 HIV-	Cross-sectional study. Measures: AUDIT & MINI Mental State Test	24.3% of PLWHA reported alcohol use/misuse, common psychiatric symptoms were depressed mood sadness & suicide thoughts.
Wagner <i>et al.</i> , 2011	HIV clinics, Uganda	602 PLWHA	Cross-sectional study Measures: Depression (Patient Health Questionnaire-9), CD4 count (medical records)	Better physical health was predictive of greater self-efficacy but not depression.
Yunusa <i>et al.</i> , 2011	University Teaching Hospital, Nigeria, sub- Saharan Africa	167 PLWHA	Cross-sectional study Measures: Hospital Anxiety and Depression Scale	More males used substances than females. Presence of psychiatric illness and substance use had implications for clinic attendance.

2.4 Conclusion

From the review of the literature, it is clear that HIV is associated with significant psychiatric morbidity, with substance abuse, psychological distress and psychiatric disorders often co-occurring in PLWHA in high- and low-income countries. The prevalence of psychiatric disorders, especially depression and substance abuse, is high. So, too, is the experience of traumatic and stressful events. HIV-infected individuals who abuse substances and/or who suffer from mental disorders are more susceptible to poorer health outcomes, HIV-treatment failure, and at a greater risk of non-adherence to ARVs (Pence, 2009). Since there is a high prevalence of substance abuse and depression in PLWHA, it is crucial that these co-morbid diagnoses be addressed and managed comprehensively during treatment to ensure their optimal health outcomes (Sullivan, *et al.*, 2008).

The treatment of HIV infection, substance-use disorders and psychiatric disorders in PLWHA needs a multifaceted, comprehensive and multidisciplinary management approach to achieve optimal health outcomes for all three conditions. Successful treatment is also dependent on screening, diagnosis and appropriate referral. Furthermore, healthcare professionals need to be aware of the overlap between symptoms of depression and symptoms of HIV (Kagee & Martin, 2010).

Treatment for triple diagnosis and adherence to HIV treatment can be effective if a range of interventions, such as counselling, contingency management, supervised therapy (e.g., directly observed therapy), offered pharmacotherapy, and an integrated service-delivery platform is in place (Parry *et al.*, 2007).

Substance-use disorders and psychiatric disorders can be treated pharmacologically and behaviourally which may improve HIV-related outcomes (Chander *et al.*, 2006; Colibazzi *et al.*, 2006). In addition, patients diagnosed with a past or existing substance-use disorder need to be monitored on an on-going basis for substance use and for relapse prevention (Colibazzi *et al.*, 2006). Research has indicated that screening for psychiatric and substance-use problems at the beginning and during the course of HIV treatment, and providing appropriate treatment for patients presenting with a triple diagnosis, may reduce the risk of death and extend life in this population (DeLorenze *et al.*, 2010).

Identifying risk and protective factors in PLWHA with co-morbid disorders can be helpful in developing integrated public health interventions for these people (Freeman *et al.*, 2007). One study found that being in a support group was significantly associated with a mental disorder and that most PLWHA found support groups helpful. PLWHA found comfort in their religion and belonging to organizations with other PLWHA and these could be seen as protective factors. In contrast, isolation, discrimination and death of someone close as a result of AIDS are risk factors that can make PLWHA vulnerable to a mental disorder (Freeman *et al.*, 2007). Aside from individual or personal factors that contribute to mental disorders in PLWHA, poverty can be a consequence of mental disorders (Freeman *et al.*, 2008). The possibility that poverty and HIV together worsen the health conditions of PLWHA and hence increase the likelihood of mental disorders compared with other poor people or those PLWHA who are not poor (Freeman *et al.*, 2008). Governments, non-governmental organizations, service planners and policy makers need to understand the individual and structural barriers that make PLWHA vulnerable to

psychological distress, psychiatric disorders and substance-use disorders, and ensure that relevant and integrated intervention and treatment programmes and services are provided. In addition, family and partner support, and adaptive coping mechanisms may help PLWHA deal with depression, take care of themselves and improve mental well-being (Collins *et al.*, 2006).

PLWHA may be prone to psychological distress at different times during the course of illness, such as during the time of testing, the different stages of the illness, at the beginning of ARV treatment or in the terminal phase. Therefore, it is important that mental health care is provided throughout the course of HIV treatment (Das & Leibowitz, 2011). In PLWHA, stigma on various levels (HIV-positive status, substance use and psychiatric conditions) needs to be taken into account in treatment (Adewuya *et al.*, 2009; Sorsdahl *et al.*, 2010; Wingood *et al.*, 2008). Stigma needs to be addressed on an individual level as well as on a societal level and should include public education and awareness programmes, community level interventions addressing intolerance of HIV-related stigma, and legislation prohibiting HIV discrimination (Wingood *et al.*, 2008).

The studies presented in this overview suggest that psychiatric disorders (depression, anxiety, PTSD, substance use/dependence and suicidality), as well the co-occurrence of these disorders, are highly prevalent in PLWHA from high and LMICs. There is wide variation in prevalence of common psychiatric disorders and this could be attributed to many factors, such as the use of different measurement instruments and different methodologies used to assess psychiatric disorders. Some

studies used brief screening instruments, while other studies have used clinical diagnostic instruments. Some were self-administered, while others were administered by trained clinical personnel. In addition, the study populations have also ranged from clinic to hospital to community-based samples, and the former may have more access to treatment services and hence may be in better mental health compared to community samples that may not be accessing regular health-care services. Methodologically similar studies and use of common, standardized instruments are needed to allow for the comparability of studies and the development of scientifically sound evidence that can be used for policy, programme design and implementation (Collins *et al.*, 2010, Meyers *et al.*, 2008; Brandt, 2009).

Furthermore, studies have reported mixed findings on the association between a psychiatric disorder and ARV adherence with some studies reporting high adherence in PLWHA with a psychiatric diagnosis and others reporting non-adherence. Future research could focus on predictive factors that lead to high adherence in PLWHA with a psychiatric diagnosis as this could help in treating PLWHA with a psychiatric diagnosis and non-adherence to ARVs. Further research tracking the complex interplay between HIV-disease progression and psychiatric disorders are needed (Myer *et al.*, 2008). For example, other studies indicate that levels of depression vary in relation to the stage of HIV and to the physical condition of PLWHA (Wagner *et al.*, 2011; Kaharuza *et al.*, 2006). In addition, it would be important to study health care provider's attitudes towards PLWHA who present with a psychiatric disorder and/or with substance-abuse-related problems and to assess whether this influences the care, treatment and initiation of ARVs in PLWHA.

As most studies reported in this review were cross-sectional studies, more longitudinal studies are needed to understand the causal pathways between psychiatric disorders, substance abuse/dependence, co-occurring disorders and their impact on ARV adherence, disease progression and overall health status in PLWHA. Currently few studies have investigated lifetime psychiatric disorders in PLWHA and findings vary from people suffering from psychiatric disorders (depression, PTSD, anxiety) before being diagnosed and these symptoms being exacerbated after a diagnosis of HIV (Martin & Kagee, 2011; Olley, 2006; Mello, Segurado, & Malbergier, 2010). Specifically, future studies need to focus on why these associations may exist and whether people with psychiatric disorders and substance use disorders are at a higher risk of becoming infected with HIV or HIV infected people are at a higher risk of developing psychiatric disorders and substance use disorders.

More research also needs to be conducted on co-occurring disorders in PLWHA from LMICs. Most of the studies conducted in LMICs have focused on alcohol-related problems, and more fine-grained investigation of the impact of different drugs of abuse on health outcomes is needed. Furthermore, most of the PLWHA in sub-Saharan Africa are women and very few studies have specifically focused on mental health and service needs infected women may have (Brandt *et al.*, 2009).

Most studies have focused on the epidemiology of psychiatric disorders, substance-related disorders, co-occurring disorders and their impact on ARV adherence. This information can be used to inform preventative and other intervention strategies for

optimal health outcomes in PLWHA. In addition, implementation of psychosocial interventions for dual and triple diagnosis should be urgently considered as gaps still exist in the acknowledgment of psychosocial factors as important determinants in the lives of PLWHA (Brandt, 2009; Collins *et al.*, 2010).

Finally, as noted from this literature review, most of the research on HIV, psychiatric disorders and substance abuse has been conducted in high income countries. Future research in South Africa should focus on psychiatric disorders and substance abuse in the HIV infected population as research in this area is sparse.

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CHAPTER 3: LITERATURE REVIEW

Hazardous or harmful use of alcohol and/or drugs, psychiatric disorders, ARV adherence and disease progression

3.1 Introduction

Since the availability of ARVs, HIV and AIDS are no longer viewed as a death sentence but rather as a chronic condition that can be managed and treated. ARVs have prolonged life expectancy and have improved the quality of life of PLWHA. For ARVs to be effective and to prolong life, patients must adhere to these medications life-long.

3.1.1 ARVs in South Africa

South Africa has the largest ARV programme in the world, with over 1 million people having been on treatment at the end of 2010. The current criterion for initiating ARVs in South Africa is a CD4 count of < 350 cells/mm³ (Department of Health, 2010). According to the National Antiretroviral Treatment Guidelines of the Department of Health in South Africa, 95% adherence to ARVs is ideal for viral suppression and patients taking less than 95% of their medications are at risk of developing viral resistance (Department of Health, 2010). In South Africa currently the following regimens are available; nucleoside reverse-transcriptase inhibitors (NRTI's), nonnucleoside reverse-transcriptase inhibitor (NNRTI) and protease inhibitor's (PI's) (Department of Health, 2010). Research has indicated that $> 95\%$ adherence is required for viral suppression in patients who are receiving unboosted protease inhibitor regimens and nucleoside analogues. With the more potent ARVs

such as nonnucleoside reverse-transcriptase inhibitor (NNRTI) regimens viral suppression can be achieved at moderate levels of adherence (54%-100%) (Bangsberg, 2006). This is important especially in the case where health care providers are likely to withhold therapy if patients did not achieve 95% adherence (Wong et al, 2004).

3.1.2 Measuring ARV adherence

To ensure and monitor ARV adherence several measures have been developed. These measures range from objective measures such Medication Event Monitoring System (MEMS) cap data whereby a pill bottle cap containing a microchip is placed on the bottle and each bottle opening is recorded, to subjective measures such as the self-report questionnaires asking patients to recall whether they missed taking a dose or stopped taking ARVs (Golin *et al.*, 2002). There are several self-report measures such as the Adult AIDS Clinical Trials Group (AACTG) adherence Instrument, the 30-day Visual Analogue Scale (VAS), the Morisky ARV adherence scale (Chesney *et al.*, 2000; Wang et al., 2008; Morisky, Ang, Krousel-Wood & Ward, 2008). These scales measure adherence ranging from 1 day to a 30-day period. Other forms of assessing for adherence is doing a pill count to see if patients missed taking their ARVs.

3.1.4 Challenges to adherence

Measuring ARV adherence is crucial as non-adherence to ARVs has also been associated with low CD4 counts and HIV-disease progression (Paterson *et al.*, 2000). Disease progression in PLWHA is defined as having high viral loads, low CD4

counts, opportunistic infections and mortality (Hahn & Samet, 2010). PLWHA face several challenges in obtaining optimal adherence. Substance abuse and psychiatric disorders are one among the many challenges facing PLWHA in maintaining ARV adherence. Increasingly, literature has shown that substance abuse is highly prevalent among PLWHA and is associated with poor adherence to HIV medication, reduction in CD4 count, HIV-disease progression, re-infection, vulnerability to opportunistic infections, and poor viral suppression (Lucas, Cheever, Chaisson & Moore, 2001; Parsons, Rosof & Mustanski, 2008; Farley, *et al.*, 2010; Morojele, *et al.*, 2006; Hendershot *et al.*, 2009).

In addition to substance abuse, studies have reported a high prevalence of psychiatric disorders ranging from 14% to 56% among PLWHA in sub-Saharan Africa (Olley *et al.*, 2003; Myer *et al.*, 2008; Olley *et al.*, 2006; Olley, 2006; Schlebusch & Vawda, 2010; Wagner *et al.*, 2011; Kaharuza *et al.*, 2006; Nakasujja *et al.*, 2010; Bussmann *et al.*, 2010). Psychiatric disorders, especially depression, have been associated with poor ARV adherence and higher risk of mortality (Rodkjaer *et al.*, 2010; Mohamed *et al.*, 2004; DeLorenze *et al.*, 2010). Furthermore, depression was found to be higher in heavy drinkers than in moderate drinkers compared to non-drinkers. There was also a significant association between depression and HIV-disease progression (i.e. CD4+ T-cell decline) (Ghebremichael *et al.*, 2009).

A literature review of the association of depression and mortality in PLWHA documented that depression has an impact on disease progression, mortality and

morbidity. Studies that were reviewed indicated depression may have a negative impact on the immune system and was associated with significant alterations in immune functioning (e.g. lower CD8+ T lymphocytes, lower CD4 counts, increase in viral load and natural killer cell activity) in PLWHA. In addition to depressive symptoms and stressful life events, social support has also been found to be associated with progression of HIV infection. The review concluded that there is growing evidence to suggest that depression alters the functioning of killer lymphocytes in HIV disease and that natural killer cells and CD8+ lymphocytes are responsible for anti-HIV effects and the production of HIV-suppressive factors (Creuss *et al.*, 2003).

Independently, both conditions contribute to poor health outcomes. However, together both conditions can cause considerable harm that can lead to an increase in morbidity and mortality (Azar, Springer, Meyer & Altice, 2010). The following review will focus on the impact of alcohol, drugs and psychiatric disorders on ARV adherence and disease progression.

3.2 Alcohol

Hazardous or harmful use of alcohol is common among PLWHA and is associated with poor adherence to ARVs, decreased viral suppression, viral replication and earlier on set of death (Chander, *et al.*, 2006; Schneider, *et al.*, 2012). In a meta-analysis of the association between it alcohol use and ARV adherence, it was found that those who used alcohol were 50%-60% as likely (OR = 0.548, 95% CI: 0.490 to 0.612) to be adherent compared with those who abstained (or drank relatively less).

This meta-analysis of the alcohol-adherence association concluded that there is a significant and reliable association of alcohol use and ARV non-adherence (Hendershot et al., 2009). In a Pennsylvanian sample of 212 patients attending an outpatient HIV clinic, researchers found that problem drinking was associated with decreased adherence to medication. In particular, patients with heavy and hazardous drinking patterns were more likely than others to have problems with adherence to medication. In this sample, problem drinkers were more likely to report a missed dose (17% vs 12%, $p = 0.38$) and significantly more likely to take medication off schedule (45% vs 26%, $p = 0.02$) compared to persons without problem drinking. Taking medication off schedule was significantly associated with heavy drinking (OR, 4.70; 95%CI, 1.49 to 14.84; $p < 0.05$), and hazardous drinking (OR, 2.64; 95%CI, 1.07 to 6.53; $p < 0.05$) but not with binge drinking (Cook, *et al.*, 2001). Heavy drinking in this study was defined as more than 12 drinks consumed by women and more than 16 drinks consumed by men, per week during the past month. Binge drinking was reported if women had at least 5 drinks and men at least 6 drinks one occasion at least monthly and hazardous drinking was defined as a score >8 on the AUDIT.

Similarly, in a New York City sample of 272 PLWHA, who were problem alcohol users (scoring ≥ 8 on the AUDIT) and on HAART at the time, participants were reported to have almost nine times higher odds of non-adherence ($< 95\%$) to HIV medication on the days they drank. The odds increased by 20% with each additional drink (Parsons *et al.*, 2008).

A cross-sectional study in South India on 198 HIV-infected men and women was conducted to assess variables associated with HAART non-adherence. The researchers found that 16.7% of participants reported drinking during the previous month, with 67.7% of this group reporting using alcohol once a week or more. Only half of the participants had an adherence level of greater than 95%. Those participants that reported alcohol use were over five times more likely to be non-adherent compared to participants who did not use alcohol (Venkatesh *et al.*, 2010). Other barriers to non-adherence in this population were high levels of distress, lower levels of general health perceptions and patients being on HAART for more than 24 months. These studies are summarised in Table 3.1.

3.3 Alcohol and drugs

Several studies have documented that PLWHA, who drink alcohol, are also likely to abuse drugs. For example, a longitudinal study to assess the combined and independent effects of alcohol and drug use on ARV adherence (self-report) and viral suppression was done in a cohort of 1 711 HIV-positive patients living in Baltimore. Findings revealed that moderate (any alcohol use at least less than hazardous levels) and hazardous (>7 drinks per week or >3 drinks per occasion for women and >14 drinks per week or >4 drinks per occasion for men) use of alcohol was associated with decreased adherence to ARVs (≥ 2 missed doses in the two weeks preceding this study) compared to non-alcohol users. Hazardous drinkers reported lower adherence (AOR, 0.46; 95% CI: 0.34 to 0.63) than moderate drinkers (AOR, 0.78; 95% CI 0.64 to 0.95) and active drug users were reported to be 45% less adherent than non-drug users. Hazardous drinkers and active drug users were

25% and 38% less likely to suppress their viral load than non-drinkers and non-drug users, respectively compared to those who do not use alcohol and drugs. Hazardous use of alcohol and drug use together were associated with the lowest odds of ARV use (AOR, 0.40; 95% CI: 0.29 to 0.57), adherence (AOR, 0.32; 95% CI: 0.21 to 0.51) and viral suppression (AOR, 0.50; 95% CI: 0.32 to 0.77) in PLWHA (Chander *et al.*, 2006). This study is important in that it emphasizes that the combined use of alcohol and drugs had greater negative effects on HIV outcomes than the independent use of alcohol or drugs.

Consistent with the findings of this study, in a retrospective study of 1 030 HIV-positive women attending the John Hopkins HIV clinic in the USA, women who were heavy drinkers were three times more likely to be active drug users and to have hepatitis C than non-drinkers. Of these women, 17% reported heavy alcohol consumption (≥ 4 drinks per occasion or daily drinking of >1 per day), 29% reported occasional consumption (light or occasional use) and 13% reported past alcohol use and 42.3% were active drug users (heroin or cocaine). Heavy drinking was independently associated with earlier death in these women and active drug use was associated with increased mortality risk. The delayed initiation of combined antiretroviral treatment (cART) was associated with active drug use (Neblett *et al.*, 2011).

Aside from alcohol consumption leading to poor adherence, heavy alcohol consumption has also been associated with lower CD4 counts in PLWHA. In a longitudinal study on 595 PLWHA with past or current alcohol problems, researchers

documented that participants with heavy alcohol consumption (>14 drinks per week or ≥ 5 drinks on a single occasion for men and >7 drinks per week or ≥ 4 drinks on a single occasion for women) and not on ARVs had lower CD4 counts (average 48.6 cells/ul) than those who abstained from alcohol. However, there was no significant association between heavy alcohol consumption and viral load for these patients (Samet *et al.*, 2007). This study concluded that alcohol consumption has a direct effect on HIV-disease progression. However, in a cross-sectional study of 319 PLWHA attending the Washington University HIV clinic in the USA, no significant association between amount of alcohol consumed and ARV adherence was found, though at-risk drinkers ($\geq 4/5$ drinks per week) were reported to have viral loads > 400 copies/ml compared to those who drank $\leq 4/5$ drinks per week. At-risk drinkers were found to have the lowest median CD4 counts. This study defined at-risk drinking as women exceeding four drinks and men exceeding five drinks per week (Shacham, Agbebi, Stamm & Overton, 2011). The study concluded that alcohol consumption is associated with viral load suppression.

In another study to assess the impact of alcohol consumption on survival of PLWHA, a simulated cohort of HIV-positive people with different levels of alcohol consumption was used. People were classified as non-drinkers (no alcohol consumption), hazardous drinkers and non-hazardous drinkers (consuming less than five drinks on a drinking day). Non-hazardous drinkers decreased their survival rate by more than a year if they drank once per week or more and by 3.3 years if they drank daily. Hazardous drinkers decreased their survival rate by more than three years if they drank once per week or more and by 6.4 years if they drank daily (Braithwaite *et al.*,

2007). This study concluded that alcohol can be a regulating risk factor in the survival of PLWHA.

The use of alcohol can impact on the disease progression and mortality of PLWHA through several pathways. Firstly, through immunosuppression, thereby increasing HIV mortality, secondly, through increasing the toxicity of ARVs on the liver (hepatotoxicity), and thirdly, increasing the risk of liver damage that is unrelated to HIV or ARVs and thereby increasing the risk of mortality (Braithwaite & Bryant, 2010). Animal studies have also demonstrated the harmful effects of alcohol consumption in simian immunodeficiency virus (SIV)-infected monkeys, where alcohol intake was associated with nutritional deficiencies because of the high caloric intake from alcohol, the decrease absorption of nutrients, and poor metabolism of nutrients. Moreover, at the at-terminal stage, SIV+ animals with alcohol intake had significantly lower body weight and body mass index, than SIV+ animals without alcohol intake. This study concluded that nutritional deficiency as a result of alcohol consumption might lead to rapid HIV-disease progression (Molina, Lang, McNurlan, Bagby & Nelson, 2008). Furthermore, in their review, Molina *et al.* (2010) reported that alcohol abuse impacts on different aspects of the immune system and weakens the natural course and outcome of bacterial and viral infections, thereby increasing the risk of infections. Their review also found that alcohol abuse affects the gastrointestinal and respiratory tract immune barriers and compromises the main parts of the innate and adaptive immune systems.

Only a few studies in sub-Saharan Africa have investigated the relationship between alcohol abuse and ARV adherence. One such study is a cross-sectional survey on 2 920 patients receiving HAART from eight treatment centres in Benin, Côte d' Ivoire and Mali in sub-Saharan Africa. Current alcohol use (OR 1.4; 95% CI 1.1-2.0) and hazardous drinking (OR 4.7; 95% CI 2.6-8.6) were associated with non-adherence to HAART (Jaquet *et al.*, 2010). This study concluded that alcohol use and hazardous drinking (≥ 8 on the AUDIT) is associated with non-adherence (<95% adherence during the past 4 days) to HAART among patients from West Africa. Recommendations are that health-care providers should be informed and educated about the harmful effects of alcohol use and this should be a priority area in the treatment of patients attending clinics for HIV treatment.

In a South African study of 168 patients attending a local clinic for ARV medication in rural setting in the Eastern Cape, 37.5% of the patients were found to be non-adherent, with more men (41.8%) being non-compliant than women (34.5%). Poor adherence in men was associated with being single (48.9%), having a tertiary education (60%), regular use of alcohol (47.1%) and being unemployed (56.1%). Poor adherence in women was associated with being single (36.5%) and the use of alcohol (60.7%). Patients reported that the use of alcohol contributed towards them forgetting to take their medication (Bhat *et al.*, 2010).

Findings in a cross-sectional sample of 439 HIV-positive patients from all nine provinces in South Africa who completed a survey assessing barriers to ARV adherence revealed that participants in the low adherence (< 70% ARV adherence)

level and danger zone (< 70%-90%) level had difficulty adhering to medication when they were depressed (18.8% and 25.1%, respectively). Of the low adherence group, 18.8% and of the danger zone group, 22.2% had difficulty adhering to medication when they had consumed too much alcohol (Van Dyk, 2010). In a review of studies examining the relationship between substance abuse and adherence, Parry *et al.* (2007) reported that poor utilization and sub-optimal adherence was more common among persons with a triple diagnosis (HIV positive, substance abuse and a psychiatric disorder) than among those without. These studies are summarised in Table 3.1.

3.4 Illicit drugs

In addition to hazardous or harmful consumption of alcohol impacting on ARV adherence and disease progression, numerous studies have reported illicit drug use to be equally harmful in PLWHA. In a cohort of 764 HIV-1 infected patients attending an outpatient clinic in Baltimore, USA, 44% of active drug users were found to be underutilizing HAART, compared to 22% of former drug users and 18% of non-drug users. Of the participants on ARVs, 34% of active drug users, 17% of former drug users, and 24% of those who never used drugs reported non-adherence. At baseline CD4 count in active drug users was 65 cells/mm³, in non-users 116 cells/mm³, and in former users 122 cells/mm³. This study concluded that active drug use was significantly associated with poor adherence and suboptimal virologic and immunologic responses to antiretroviral therapy (Lucas *et al.*, 2001).

In a study to investigate factors associated with non-adherence in an initially adherent sample of 96 French PLWHA that were infected through injecting drug use, 22.9% reported non-adherence at 14.7 months follow-up. Non-adherence to ARVs was found to be associated with continued active drug use. In addition, factors such as depression and lack of a stable relationship also contributed to non-adherence in this population that was adherent to ARVs at initiation (Carrieri *et al.*, 2003). Similar levels of poor adherence was reported in a longitudinal study of 1 711 PLWHA in Baltimore, where active drug users reported 45% less adherence to ARVs (≥ 2 missed doses in the past two weeks) and were 38% less likely to have suppressed viral loads compared to non-drug users (Chander *et al.*, 2006).

Studies have, however, shown that drug abuse may not be a reliable predictor of non-compliance to HAART. In a study of 214 patients attending outpatient clinics in Italy, 28% reported current drug use (cannabis, heroin, cocaine, ecstasy, acid, psychoactive drugs and other) and alcohol use (> 6 U/day). Drug users had lower levels of compliance (48.3%) compared to non-users (29.8%). Low compliance was defined as patients missing a dose, interrupting the entire combination, changing the time combination, wrong combinations and wrong count of pills in the past two months. However, patients in the group that reported using heroin and cocaine achieved higher compliance levels than patients who did not use any substances (50% and 46% vs. 42.3%). Possible reasons for compliance in this group of substance users could be that compliance was self-reported and patients were selectively enrolled among those who were thought to be compliant (Martini *et al.*, 2004).

Similarly in a study of 1 161 PLWHA in the USA who were injecting drug users, 636 were taking ARVs and 75% reported good adherence ($\geq 90\%$). Good adherence was associated with being a high-school graduate, not believing that ARVs increase the metabolism of methadone, having a positive attitude towards ARVs, not sharing or lending needles, greater self-efficacy and fewer depressive symptoms. Poor adherence, on the other hand, was associated with sharing of needles, negative beliefs about methadone-ARV interaction, negative attitude towards ARVs, poor self-efficacy, and depressive symptoms (Arnsten *et al.*, 2007). This study emphasises that drug taking alone is not responsible for poor adherence but psychosocial factors also contribute towards poor adherence and need to be considered in interventions targeted towards enhancing ARV adherence. This is consistent with the review conducted by Gonzalez, Barinas and O’Cleirigh (2011), which reports that within the context of substance abuse, structural and individual factors need to be factored when counselling on ARV adherence.

Data taken from a larger study that was conducted in the USA, Puerto Rico and South Africa to investigate the relationship between substance abuse and HIV symptoms, reported significant correlations between marijuana use, tobacco use, being male, number of years living with HIV, and the symptom burden of HIV. Of the participants, 45.8% reported tobacco use and 14.3% reported marijuana use, while 12.6% reported illicit drug use and 8.5% alcohol use. Although tobacco was the most prevalent substance used, this was significantly associated with fewer HIV symptoms. Fatigue and confusion/distress were significantly associated with alcohol use, illicit drug use, marijuana and tobacco use. PLWHA who reported amphetamine use, injecting drug use, heavy alcohol use, tobacco and marijuana use also reported

high levels of HIV-symptom burden. Participants reported that fatigue and depression high in symptom intensity and this was significantly associated with substance abuse (Brion *et al.*, 2011). This is consistent with a systematic review conducted by Malta, Strathdee, Magnanini and Bastos (2008) to assess adherence to HAART in PLWHA using drugs as well as identifying factors that are associated with non-adherence. The findings of this study indicate that there is an association between active substance use, depression and poor social support and moderate adherence to HAART. In contrast, a recent literature review conducted by Gonzalez, *et al.*(2011) on the impact of substance use and adherence to HIV medication, substance abuse was found to be a significant barrier to ARV adherence. Their review documented that besides alcohol, heroin, cocaine and methamphetamines were also related to poor ARV adherence. However, the review indicated inconsistent findings on marijuana use: some studies found that marijuana could be a facilitator in ARV adherence, while other studies found that it could hinder ARV adherence.

Studies have reported that PLWHA have used marijuana for therapeutic purposes other than for recreational purposes. One such study conducted on 408 PLWHA, 59.8% of participants indicated some use of marijuana within the previous six months. Of these, 55.7% reported recreational use only, while 44.3% indicated they used marijuana for therapeutic and recreational purposes. PLWHA who used marijuana for therapeutic purposes were significantly more likely to have tried other alternate therapies, experienced HIV/AIDS-related symptoms in the previous twelve months, and had higher CD4 counts than those who used marijuana for recreational purposes only (Fogarty *et al.*, 2007). Similarly, in a longitudinal study on 2 628

women (HIV negative and positive) living in the USA, they were reported to have used marijuana for medical purposes. Seventy two percent reported lifetime use of marijuana at baseline, with 28% never having used marijuana. Of the HIV-positive women using marijuana, a lower incidence of weekly marijuana use was associated with undetectable viral load, while a higher incidence of weekly marijuana use was associated with AIDS wasting syndrome. However, CD4 count was not associated with the rate of weekly marijuana use. The authors suggest that women with wasting syndrome might have increased their intake of marijuana to alleviate the symptoms of the wasting syndrome and may have used this as alternative medicine (Kuo *et al.*, 2004).

In a study of 67 PLWHA who were using ARVs and divided into two groups (smoking or oral use of cannabinoid) and not using cannabinoids, it was found that short-term (21 days) use of cannabis did not make a difference in the viral load of either group. Neither CD4 nor CD8 counts were affected by the use of cannabis in both these groups (Abrams *et al.*, 2003).

Studies have been done which show that stimulants, particularly cocaine and methamphetamine, can contribute towards non-adherence to ARVs. For example, in a cross-sectional sample of 653 PLWHA attending two outpatient clinics in San Francisco, 39% of men who had sex with men, 33% of heterosexual men, and 11% of women reported methamphetamine use in the previous 12 months. Participants using methamphetamine in the previous 12 months were less likely to be on ARVs (57.5% vs 70%, $p < 0.02$; PR = 0.7, 95% CI:0.6-0.9) compared to non-users-

(Marquez, Mitchell, Hare, John & Klausner, 2009). Furthermore, in a longitudinal study on 150 PLWHA in Los Angeles, USA, ARV adherence was assessed over a 6-month period using an electronic monitoring device. In this study, the drug-positive group reported 63% adherence rate compared to the drug-negative group which reported 79% adherence. Good adherence was defined as participants taking at least 90% of their prescribed medication and poor adherence was taking less than 90% of their medication over a 6 month period. Stimulant users' (cocaine & methamphetamine) adherence rate was significantly lower than other drug users and non-drug users. Further group analysis indicated that cocaine and methamphetamine users reported an adherence rate of 54.5% and only cocaine users reported 68.1% adherence. Overall, drug users were four times more likely to be non-adherent than non-drug users and stimulant users were seven times more likely to be non-adherent than non-drug users. This study concluded that stimulants are particularly disruptive to ARV adherence and that methamphetamine causes a greater disruption to lifestyle than cocaine (Hinkin *et al.*, 2007). In addition, in a study on 1 196 HIV-positive black women in the USA, 26% reported being crack users (OR=0.37, 95%, CI=0.24-0.56) and users of other drugs (OR=0.47, 95%, CI=0.36-0.68) and were less likely than non-users to take their ART medication as prescribed (Sharpe, Lee, Nakashima, Elam-Evans & Fleming, 2004). Stimulant use is particularly disruptive to ARV adherence because of the effect it has on sleeping and eating patterns as well as the environmental instability caused by the use of it (Reback, Larkins & Shoptaw, 2003). These studies are summarised in Table 3.1.

3.5 Psychiatric disorders

Psychosocial factors and psychiatric disorders have also been associated with non-adherence and poorer health outcomes in PLWHA. In a prospective, observational cohort study in Boston, USA, 266 PLWHA with alcohol problems were assessed every six months from 2001-2005 for ARV adherence. Eighteen percent reported discontinuation, while 5.8% had stopped ARVs during this reporting period. Of these participants, 45% used cocaine, 20% used heroin, 29% reported heavy alcohol use on the CIDI, and 40% reported depressive symptoms on the CES-D. Depressive symptoms were significantly associated (AOR=1.66; CI: 1.04, 2.65) with discontinuing ARVs, but not cocaine, heroin or heavy alcohol use. In this population of PLWHA, with alcohol problems, participants with depressive symptoms were twice as likely to discontinue ARVs six months later than those who reported no depressive symptoms (Kim *et al.*, 2007). This study suggests that ARVs should not be withheld because of alcohol and/or drug use, which may lead to poor adherence. However, an assessment of depression should also be taken into consideration to enhance ARV adherence. Similarly, in a study of 168 PLWHA who were using HAART at the time, depressive symptoms were negatively associated with ARV adherence and found to mediate the relationship between current smoking and 7-day ARV adherence. Depressive symptoms were also significant in affecting 3-month adherence, while controlling for smoking. This study concluded that poor adherence in current smokers may attribute to having more depressive symptoms (Webb *et al.*, 2009). The findings of this study are consistent with the review by Gonzalez *et al.* (2011), which documented that in addition to substance abuse, psychological distress was a significant predictor of non-adherence and decreased viral suppression.

Furthermore, in a cross-sectional study of 71 PLWHA attending two outpatient clinics in France, patients of younger age, patients on repeated drug holidays (RR, 4.4; 95% CI 2.0-9.5; $p = 0.0001$), patients with depression (RR, 2.1; 95% CI, 0.9-3.9; $p = 0.13$) and with previous non-adherence behaviours (RR, 1.7; 95%CI, 1.1-2.5; $p = 0.034$) receiving ARVs were significantly more likely to have virologic failure compared to older, non-depressed and adherent patients on ARVs (Parienti *et al.*, 2004). Furthermore, in a cross-sectional survey of 887 PLWHA attending HIV clinics in Denmark and Copenhagen, 31% of participants reported that they often felt depressed or overwhelmed that was associated with risk of treatment and virologic failure. Other psychosocial factors associated with increased risk for virologic failure were not being happy to be in treatment, missing doses of ARVs, and not sure whether treatment is beneficial (Barfod *et al.*, 2005).

In PLWHA, mood state has been found to be a significant factor in determining ARV adherence. In a community sample of 122 HIV-positive MSM or transgendered individuals in the USA, who were on ARVs at the time and who reported using methamphetamine in the previous 30 days, 53% reported using methamphetamine weekly and 63% binge use of methamphetamine. Thirty-three percent reported using crack/cocaine weekly and another 33% binge use of crack/cocaine. Negative affect was associated with weekly methamphetamine use, and HIV-specific traumatic stress was associated with weekly cocaine/crack use. Higher positive affect was associated with decreased injecting drug use in the previous month and the increased likelihood of perfect ARV adherence (100% adherent) in the previous

month. This study concludes that affect regulation is a key determinant of substance abuse and has an impact on ARV adherence (Carrico, Johnson, Colfax & Moskowitz, 2010). These studies are summarised in Table 3.1.

3.6 Co-occurring disorders

Co-occurring disorders (psychiatric disorders and substance-use disorders) are common in PLWHA and have been associated with poor adherence and virological suppression and possible treatment failure (Chander *et al.*, 2006; Whetten *et al.*, 2005). For example, in a study of 152 HIV-positive patients at an academic medical centre in the Southeastern, United States, co-occurring disorders were common in this population. Of patients diagnosed with a mood disorder in the previous month, 53% also had an anxiety or substance-use disorder. Of those with anxiety disorder, 62% were also diagnosed with mood or substance-use disorder, and of patients with a substance disorder, 63% had a diagnosis of a mood or anxiety disorder too (Gaynes *et al.*, 2008). Similarly, in a study at the University of Washington's medical centre on 1774 HIV-positive patients receiving primary care, 38% reported mental illness and substance-use disorder, and more than half 50% reported depression or anxiety (Tegger *et al.*, 2008). In this study, the authors reported that patients with depression and/or anxiety were less likely to initiate HAART than patients without depression and/or anxiety. However after being treated with medication for depression/anxiety, these patients were equally likely to initiate HAART than those without a mental illness.

In a cross-sectional prospective survey conducted on 300 patients attending an outpatient adult infectious clinic in Gaborone, Botswana, findings show that alcohol use, depression and non-disclosure were predictors of poor adherence to ART (Do, *et al.*, 2010). Furthermore, in a study of 1 362 PLWHA attending an infectious disease clinic in North Carolina, United States, 23% of the participants were reported to have co-occurring symptoms of mental illness and substance abuse. This study concluded that patients with mental illness, substance abuse and patients with mental illness and substance abuse were more likely to have HIV-RNA levels greater than 500 (Whetten *et al.*, 2005).

Higher mortality risks were also found in participants diagnosed with both a substance substance-use disorder and a psychiatric disorder in comparison to participants with neither diagnosis. In a study conducted over 12 years (1996-2007) on 9 751 HIV-positive people in a private medical care programme in California, USA, 25.4% of participants met the criteria for a psychiatric diagnosis, 25.5% met diagnosis for substance-use disorder, and 12.1% met the criteria for both these disorders. Findings of this study reported the highest risk for death among patients with a dual diagnosis or co-occurring disorder (psychiatric and substance-use disorder) without treatment compared to patients with neither disorder (DeLorenze *et al.*, 2010). These studies are summarised in Table 3.1.

3.7 Conclusion

The relationship between alcohol and drug use and its role in HIV-medication adherence is complex and could be confounded by many factors, such as the

quantity and frequency of alcohol and drug use, personality traits, psychiatric symptoms, cognitive or attitudinal factors, situational factors, socio-economic factors and other structural barriers (Kagee & Delpont, 2010, Coetzee, Kagee & Vermeulen, 2011; Gonzalez *et al.*, 2011). When treating people living with HIV, health-care providers should understand and be aware of the complex interplay existing among HIV, substance abuse, mental health and other barriers to ARV adherence. This awareness is crucial for the appropriate treatment of people living with HIV who abuse substances which leads to non-adherence to ARVs.

Sometimes patients choose not to take ARVs when drinking alcohol because they are concerned about the toxic effects alcohol has on ARVs (Braithwaite & Bryant, 2010). The belief of alcohol being toxic when taking ARVs can prevent PLWHA from taking their medication. For example, in a sample of 145 PLWHA in Atlanta, USA, 40% were current drinkers and 1 in 4 indicated that they stopped taking their HIV medication because they thought that mixing this with alcohol is toxic (Kalichman *et al.*, 2009). Similarly, in a study of 333 PLWHA who were taking ARVs and drinking, 52% were non-adherent and reported that they stopped taking their ARVs when they were drinking (Kalichman *et al.*, 2012). The researchers emphasize that health workers and patients should be educated that there are no known adverse effects when taking their HIV medication and drinking alcohol. Patients who drink should be advised to continue taking their medication and misperceptions and false beliefs about mixing alcohol and HIV medication being toxic needs to be dispelled (Kalichman *et al.*, 2009). A systematic review and meta-analysis by the same authors (Malta *et al.*, 2008; Malta, Magnanini, Strathdee & Bastos, 2008) support the notion that PLWHA who use drugs can achieve good adherence to HAART.

However, adequate psychosocial support, which addresses comorbidities and proper management of their drug use and HIV treatment, should be provided.

Screening, brief intervention and appropriate referral for treatment may help improve ARV adherence and viral suppression in PLWHA. Screening should be conducted for alcohol, drugs and psychiatric disorders. On-going counselling and support should be provided for PLWHA who have stopped abusing substances to prevent relapse and ensure continued adherence to ARVs (Carrieri *et al.*, 2003).

While considerable research has been conducted on alcohol and its impact on HIV-disease progression, further research needs to be conducted on the impact illicit drug use has on HIV-disease progression. Further investigation needs to be carried out on the pharmacokinetics of ARVs and substance abuse (Brion *et al.*, 2011). In addition, smoking has been shown to have an impact on ARV adherence and the health of PLWHA, yet very few studies have focused on this area. Recommendations have been made that future research should focus on longitudinal studies that investigate the association between smoking and ARV adherence and the effects of mediating variables (Webb *et al.*, 2009).

There are several methods of measuring ARV adherence, ranging from subjective methods such as self-reports to more objective methods such as electronic monitoring. Most studies focused on patients' self-report measures which could be biased and suggest a social desirability effect. Study findings have revealed that patients' self-reporting on ARV adherence tend to overestimate adherence when

compared to objective measures, such as electronic monitoring (Wagner & Rabkin, 2000). Therefore, a more standardised and objective method of assessing ARVs should be considered that will provide a more accurate measurement of ARV adherence in future.

Most studies were cross-sectional and hence the directionality of any association between substance abuse, psychiatric disorders, ARV adherence and disease progression cannot be established. Therefore, in general more longitudinal studies are needed to investigate the temporal order of these relationships.

Table 3.1: Substance abuse, ARV adherence and disease progression

Study authors	Study setting	Population characteristics	Substance	Poor adherence	Lower CD4 count	Decreased viral suppression	Other health outcomes
Abrams <i>et al.</i> , 2003	San Francisco, USA	67 PLWHA	Marijuana	Not significant	Not significant	Not studied	Not studied
Arnsten <i>et al.</i> , 2007	USA	1161 PLWHA (injecting drug users)	Injecting drug use	√	Not studied	Not studied	Not studied
Brion <i>et al.</i> , 2011	Africa, Puerto Rico & USA	775 PLWHA	Alcohol & Drugs	Not studied	Not studied	Not studied	Fatigue, confusion, distress, depression
Bhat <i>et al.</i> , 2010	Eastern Cape, South Africa	168 PLWHA (on ARVs)	Alcohol	√	Not studied	Not studied	Not studied
Do <i>et al.</i> , 2010	Gaborone, Botswana	300 PLWHA	Alcohol	√	Not studied	Not studied	Not studied
Braithwaite <i>et al.</i> , 2007	Yale University, USA	2702 computer simulated PLWHA	Alcohol	Not studied	Not studied	Not studied	Decreased survival
Carrieri <i>et al.</i> , 2003	France	96 PLWHA	Injecting drug users	√	Not studied	Not studied	Not studied
Chander <i>et al.</i> , 2006	Baltimore, USA	1711 PLWHA (on ARVs & ARV eligible)	Alcohol & Drugs	√	Not studied	√	Not studied

Cook <i>et al.</i> , 2001	Pennsylvania, USA	212 PLWHA	Alcohol	√	Not studied	Not studied	Not studied
Farley <i>et al.</i> , 2010	Nigeria, sub-Saharan Africa	222 ART experienced 177 ART naive	Alcohol	√	Not studied	Not studied	Not studied
Fogarty <i>et al.</i> , 2007	Victoria & New South Wales, Australia	408 PLWHA	Marijuana	Not significant	Not studied	Not studied	Not studied
Hinkin <i>et al.</i> , 2007	Los Angeles, USA	150 PLWHA (drug users)	Drugs	√	Not studied	Not studied	Not studied
Jaquet <i>et al.</i> , 2010	Benin, Cote d'Ivoire & Mali, West Africa	2920 PLWHA (on HAART)	Alcohol	√	Not studied	Not studied	Not studied
Kuo <i>et al.</i> , 2004	6 States, USA	2059 HIV+ women 569 HIV-women	Marijuana	Not significant	Not significant	Not significant	AIDS wasting syndrome
Lucas <i>et al.</i> , 2001	Baltimore, USA	764 PLWHA	Drugs	√	√	√	Not studied
Marquez <i>et al.</i> , 2009	San Francisco, USA	653 PLWHA	Methamphetamine	√	Not studied	Not studied	Not studied
Neblett <i>et al.</i> , 2011	John Hopkins HIV clinic, USA	1030 HIV+ women	Alcohol & Drugs	Not studied	Not studied	Not studied	Hepatitis C Increased mortality risk
Parsons <i>et al.</i> , 2008	New York, USA	272 PLWHA (on ARVs & have an	Alcohol	√	Not studied	Not studied	Not studied

alcohol problem)							
Samet <i>et al.</i> , 2007	Boston, USA	595 PLWHA (with alcohol problems)	Alcohol	Not studied	√	No significant association	Not studied
Shacham <i>et al.</i> , 2011	Washington University, USA	391 PLWHA	Alcohol	No significant association	√	√	Not studied
Sharpe <i>et al.</i> , 2004	USA	1196 HIV+ women	Crack/Cocaine	√	Not studied	Not studied	Not studied
Van Dyk, 2010	All 9 Provinces, South Africa	439 PLWHA	Alcohol	√	Not studied	Not studied	Not studied
Venkatesh <i>et al.</i> , 2010	Chennai, India	198 PLWHA (on HAART)	Alcohol	√	Not studied	Not studied	Not studied

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CHAPTER 4: METHODOLOGY

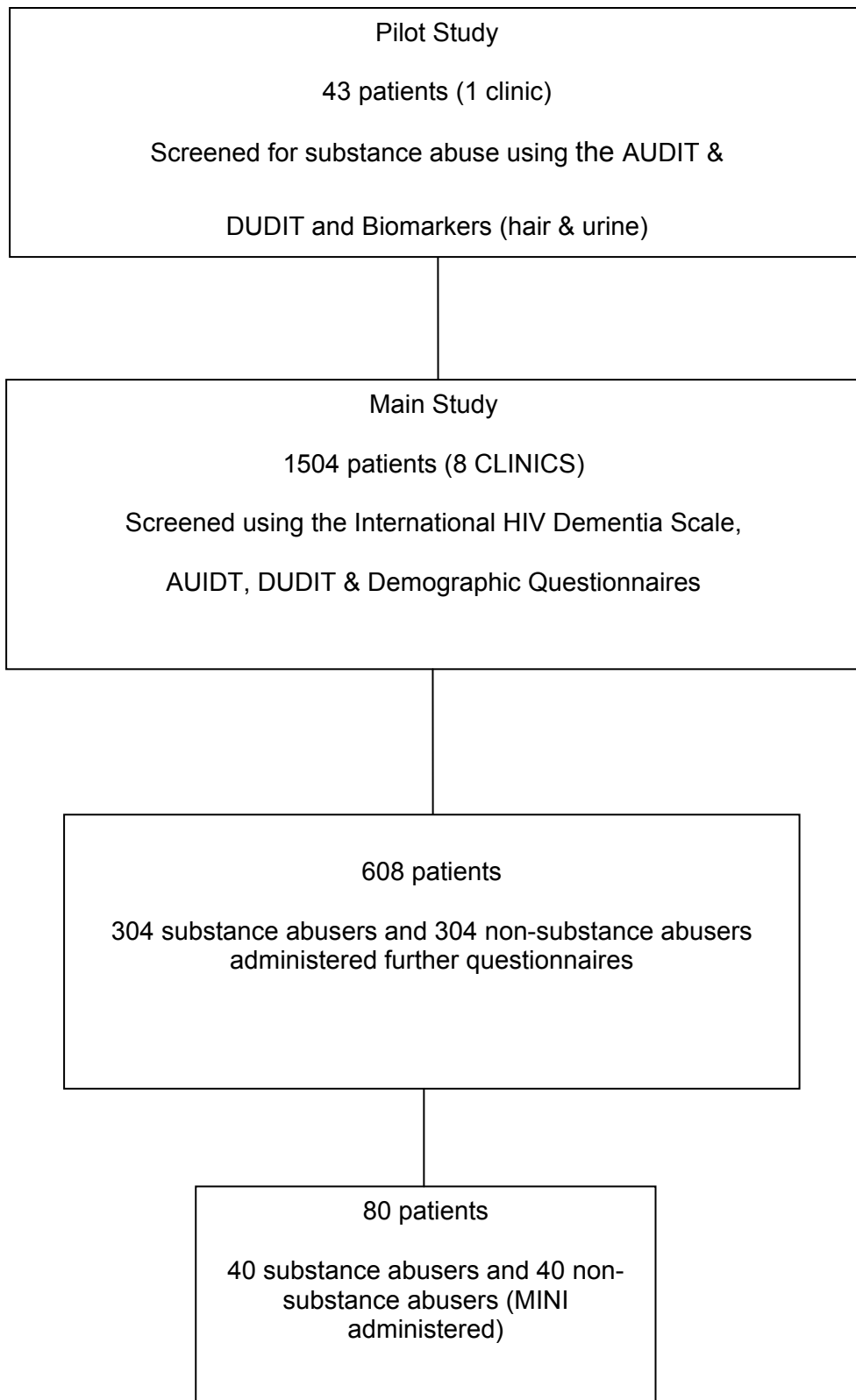
4.1 Overview of study design

A pilot study was conducted to assess the feasibility of the study protocol and prepare for the main study. The pilot study was conducted at the Wallacedene Community Health Clinic in Kraaifontein, Cape Town.

The main study used a cross-sectional study design for collecting data on substance use and abuse among patients (n=1 504) attending HIV clinics. A sub-sample of 608 patients, 304 who screened positive for substance abuse (i.e. patients who scored above the cut-points on the AUDIT and/or DUDIT) and 304 who did not abuse substances (i.e. patients who scored below the cut-points on the AUDIT and/or DUDIT) were invited to further participate in the study. Of the consecutively selected patients (n=608), 10% completed an additional psychiatric diagnostic interview (MINI) for assessing the feasibility of using the MINI in future research.

Data were collected between May and July 2011 from the following 8 clinics in the Cape Metropole; Wallacedene Community Health Clinic (CHC), Mitchell's Plain CHC, Heideveld CHC, Mfuleni CHC, Matthew Goniwe CHC, Izama Zabantu CHC, Crossroads CHC, and Dr Ivan Toms CHC.

Figure 4.1: Diagrammatic presentation of the study



4.2 Study design

Research setting

Fifteen clinics were selected in order of their geographic locations within the Cape Metropole and their representativity of the population in South Africa. This list of 15 clinics was submitted to the Provincial Department of Health, which subsequently approved eight of these. These eight HIV Community Health Care clinics in the Cape Metropole were: Mitchell's Plain CHC, Heideveld CHC, Crossroads CHC, Mfuleni CHC, Inzama Zabantu CHC, Mathew Goniwe CHC, Wallacedene CHC, and Dr Ivan Toms CHC. The Heideveld and Mitchell's Plain CHC serve mainly the Coloured population, while Mfuleni, Inzama Zabantu CHC, Crossroads CHC, Mathew Goniwe CHC, Wallacedene CHC and Dr Ivan Toms CHC serve the majority of the black population. The terms 'white', 'black', and 'coloured', originate from the apartheid era. They refer to demographic markers and do not signify inherent characteristics. These terms refer to people of European, African and mixed ancestry (African, European and/or Asian), respectively and were chosen for their historical significance. Their continued use in South Africa is important for monitoring improvements in health and socio-economic disparities, identifying vulnerable sections of the population, and planning effective prevention and intervention programmes.

Stakeholder participation

The stakeholders for this project were the; Provincial Department of Health, Cape Town City Health and clinic managers. The project was discussed with the various stakeholders regarding its feasibility, of the project, it's relevance to the public health

sector, and for logistical purposes. Clinic managers and staff were contacted and further informed about the study before the research was undertaken at their facilities. Patients were also told about the study by the clinic staff and the researchers.

Study participants

- Inclusion criteria: The sample comprised male and female adult patients (18 years and older) attending HIV clinics in the Cape Metropole. This included patients currently on ARVs as well as ARV naïve patients. All patients were fluent in any one of the three languages: English, Afrikaans or isiXhosa.
- Exclusion criteria: Patients who were under the age of 18 years and those that screened positive for cognitive impairment on the International HIV Dementia Scale (IHDS).

Reimbursement for participation

- Participants in the study were given a grocery voucher of R50 (approximately \$7.70) as reimbursement for their time.

Consent process

Prior to proceeding with screening and/or interviews, study participants were asked to sign a consent form with information about the study and processes to be followed. Participants were notified that all information given was strictly confidential and they would only be identified by a participant number. The consent form also

stated that there would be no negative consequences if they refused to participate or wanted to drop out of the study at any time. The consent forms were administered in isiXhosa, Afrikaans and English. Participants were given a copy of the consent form to take home. The fieldworkers administering the questionnaires were responsible for obtaining consent from them.

There were two fieldworkers at each clinic. Fieldworkers were proficient in English and Afrikaans or isiXhosa. The training of fieldworkers was conducted by the principal investigator. The fieldworkers were trained on primary ethical considerations (informed consent, protection of anonymity, confidentiality, protection of data from harmful access or use). The fieldworkers were also trained in interviewing skills and how to administer the various instruments to be used in the study. The fieldworkers were paid for each interview conducted. Ethical approval to conduct this research was provided by the Health Research Ethics Committee of the University of Stellenbosch.

4.3 Study procedures

Pilot study

As mentioned, the pilot study was conducted at the Wallacedene Community Health Clinic in Kraaifontein, Cape Town. Meetings were held with the clinic manager and nursing staff to discuss study procedures and study-related logistics. The pilot study was conducted without experiencing any major problems. The study afforded the researchers a good opportunity to understand the practical and logistical functioning of clinics along with providing greater insight on procedural aspects for the main

study. In view of lack of encouraging validation data from the pilot study, it was decided to reduce the number of questionnaires, in the interest of reducing respondent burden, and to drop biomarkers for alcohol and drug use. The pilot study is discussed in detail in the next chapter.

Screening of HIV-positive patients for substance abuse

For the screening a sample of 1504 patients (aged 18 years and older) was selected from eight HIV clinics in the Cape Metropole. Patients attending these HIV clinics were informed of the study by their attending clinician (nurse, doctor, HIV counsellor). If patients showed an interest in participating in the study, they were screened for cognitive impairment using the International HIV Dementia Scale and permission was sought for further participation if they showed no cognitive impairment. These patients were then screened for substance abuse (i.e. score above the recommended cut-off point for hazardous or harmful use of alcohol on the AUDIT and for drugs on the DUDIT). The AUDIT and DUDIT took approximately ten minutes to administer in total. A demographic and health status questionnaire was also administered to obtain descriptive socio-demographic and health-related data and to match subjects for the 2nd component.

Investigation of the relationship between substance abuse and health status and health behaviours of substance abusing and non-abusing patients attending HIV clinics

Of the 1 504 patients (188 patients per clinic) initially screened and interviewed, a sub-sample of 303 patients who screened positive for substance abuse (i.e., patients

who scored above the cut-off on the AUDIT and/or DUDIT) and 304 who did not abuse substances (i.e., patients who scored below the cut-off on the AUDIT and/or DUDIT) were invited to further participate in the study. One patient had to be dropped from the study for not meeting the inclusion criteria, hence a sub-sample of 607 patients. The sample selected to participate further, comprised the first 38 patients at each of the eight clinics who were substance abusers and the first 38 patients who were not substance abusers. This sample of 607 patients were interviewed using a structured interview schedule which took approximately 60 minutes to complete. This assessment included a battery of instruments that measured the following domains: depression, psychological distress, psychopathology, PTSD, risky sexual behaviour, adherence to ARV's, levels of resilience, levels of social support and patient's work, family and social functioning. Eighty patients were non-randomly selected to complete the MINI. This was done more to facilitate the assessing of the MINI for future research rather than for epidemiological purposes.

Sampling, including sample size and statistical power

This study comprised a three-stage sampling process. The first stage consisted of selecting eight HIV clinics that were geographically representative of the population of HIV-positive patients attending HIV clinics in the Cape Metropole. The second stage of sampling consisted of a cross-sectional sample of 1 504 patients from these eight clinics. The third stage consisted of 608 substance abusers and non-abusers. The average patient population serviced by these eight clinics is approximately one thousand (1 000) patients per month.

A statistician at the Medical Research Council was consulted regarding the sampling size. The power calculation indicated that a sample size of 1 504 participants was needed. The following assumptions were used in conducting the power analysis:

- The prevalence of HIV in the Western Cape in South Africa is 11% and in the Western Cape 3.8% (South African National HIV Survey, 2008).
- Approximately 21% of people living with HIV are substance abusers in South Africa (Olley, 2005) and 48% of patients attending HIV clinics meet the criteria for at least one major psychiatric disorder (Olley *et al.*, 2003).
- 40% of HIV positive males are substance abusers compared to 10% of HIV positive females who are substance abusers
- Two thirds of females are HIV positive and one third males are HIV positive.

A significance level of 0.025 and power of 90% were specified. This yielded an optimal sample size of 216 substance abusers. To enable sub-analyses of data, and in agreement with the statistician, we appropriately included 300 substance abusers and 300 non-substance abusers at the eight clinics. This required 188 patients to be recruited per clinic (i.e. a total of 1 504 patients).

The power analysis was based on the following hypotheses:

- Patients attending HIV clinics in Cape Town have a higher prevalence of hazardous and harmful use of alcohol and/or drug use than the general national population of South Africa

- Hazardous and harmful use of alcohol and/or drug use in patients attending HIV clinics may be associated with poor physical health, HIV disease progression and a decline in CD4 counts
- Hazardous and harmful use of alcohol and/or drug use in patients attending HIV clinics may be associated with increased psychological distress, poor adherence to ARVs, poor social support, risky sexual behaviour compared to their non-substance abusing counterparts.
- Males are more likely to be hazardous and harmful user of alcohol/andor drugs than females.

4.4 Research instruments

All questionnaires were translated into Afrikaans and isiXhosa and then back translated. The instruments were administered in English, Afrikaans and isiXhosa depending on participant preference. These instruments have not been validated in South Africa among the different language and ethnic groups in any comprehensive way. However, several studies done in South Africa have used some of the instruments in all three languages (Olley *et al.*, 2006; Olley, 2006; Olley *et al.*, 2005; Myer *et al.*, 2008).

Research Instruments

- ***Socio-demographic variables***

A brief demographic questionnaire was used to collect information about age, race, sex, occupation, marital status, highest level of education, employment status, and family income.

- **Clinical and health characteristics**

Data such as, date of diagnosis, date of commencement of ARVs, date of diagnosis of tuberculosis (TB) and other opportunistic infections (candidiasis, herpes simplex virus, cytomegalovirus, pneumocystis pneumonia & seborrheic dermatitis) were taken directly from patients clinical records. .

- ***The International HIV Dementia Scale***

The IHDS was used to screen patients for cognitive impairment. The IHDS has three sub-tests; timed finger tapping, timed alternating hand sequence test and recalling four items after two minutes. The maximum score is 12 and a score of < 10 is indicative of further assessment for dementia (Sacktor *et al.*, 2005). In studies conducted in developed and developing countries, the IHDS has been reported to be a useful screening test and has been validated as a sensitive and useful tool in measuring HIV dementia (Sacktor *et al.*, 2005; Berghuis, Uldall & Lalonde, 1999). In a South African study, the IHDS showed a sensitivity of 45% and specificity of 79% at a cutoff score of 10 when compared to a battery of neuropsychological test [the Mental Alternate Test (MAT), the Mental control Test (MCT), the Hopkins verbal Learning Test (HVLT), the Brief Visuospatial Memory Test(BVMT), Finger Tapping (FT), the Grooved Pegboard Test (GPT),Trail Making Test part A(TMTA), Color Trails Test 1 (CT1), Digit Symbol-Coding (DSC), Stroop Colour-Word Test(SCW) and the Winconsin Card-Sorting Test (WCST)] (Joska *et al.*, 2011).

- ***The Alcohol Use Disorders Identification Test***

The AUDIT was developed by the World Health Organisation and is used to screen people for hazardous and harmful patterns of alcohol use and alcohol dependence. A total score of eight or more on the AUDIT indicates hazardous and harmful alcohol use as well as possible alcohol dependence (Babor, Higgins-Biddle, Saunders & Monteiro, 2001). The AUDIT is a 10-item self-rating questionnaire and has been validated for use in primary health-care settings and community settings. While some studies have reported a lower cut-off score for females (Aalto, 2009; Pradhan et al., 2012). Other studies have indicated that scores of greater than 8 has a good capacity to indicate, risky, hazardous/harmful and dependence/abuse drinkers in both males and females (Moussas et al., 2009; Kaarne, Aalto, Kuokkanen, & Seppa; 2010; Saunders, Aasland, Babor, de La Fuente & Grant, 1993). As there are conflicting views on precise cut-off points for males and females and to distinguish hazardous and harmful drinkers from dependent drinkers, Babor et al. 2001 suggest that a cut-off of 8 is likely to identify a large number of hazardous and harmful drinkers. The South African National HIV Prevalence, Incidence, Behaviour and Communication Survey of 2008 also used a cut-off score for both men and women (HSRC, 2009). It was thus decided to use a cut-off score of 8 for both men and women in this study. The Cronbach alpha for the AUDIT was 0.81 for this sample.

- ***The Drug Use Disorders Identification Test***

The DUDIT comprises 11 items and is a screening instrument used to identify a list of possible drugs that may be used by a person, the patterns of drug use, and various drug-related problems (i.e., substance abuse/harmful use or

dependence). To identify men with drug-related problems, a cut-off score of 6 or more is needed on the DUDIT, while for women a cut-off score of 2 points or more is required. For both genders, a score 25 or more indicates a high probability of dependence on one or more drugs (Berman, Bergman, Palmstierna & Schlyter, 2005). The Cronbach alpha for the DUDIT was 0.76 for this sample.

- ***Substance Abuse Questionnaire***

The Substance Abuse Questionnaire (SAQ) is a brief questionnaire on lifetime and current substance abuse, type of substances used and quantity of each substance used. The SAQ is a 10-item questionnaire developed by the principal investigator.

- ***ARV Adherence Assessment***

Two instruments were used to assess ARV adherence. One was the Morisky Scale to Assess Adherence to HIV Medications, a 4-item dichotomous response option scale. This self-report measure has shown to have sound concurrent and predictive validity when used in a patient population over 3-year and 5-year periods (Morisky, Green & Levine, 1986). The second scale was the ARV Adherence Questionnaire that was adapted and used in a previous South African study (Nachega *et al.*, 2004). The questionnaire assesses ARV adherence (various reasons for missing doses and stopping ARVs) using a Likert scale. Enquiry focused on recent adherence, beginning with less than three days to more than a month. The Cronbach alpha for the Morisky Scale was 0.62 and for the ARV Adherence Questionnaire it was 0.73 for this sample.

- ***Davidson Trauma Scale***

Patients were assessed for possible PTSD symptoms using the Davidson Trauma Scale (DTS). This is a 17-item questionnaire. Good internal consistency and good concurrent, convergent and divergent validity were reported in studies using the DTS (McDonald, Beckham, Morey & Calhoun, 2009; Sibrandij, Olff, Opmeer, Carlier & Gersons, 2008). The Cronbach alpha for the DTS was 0.96 for this sample.

- ***Center for Epidemiologic Studies Depression Scale***

The Center for Epidemiologic Studies Depression Scale (CES-D) was used to assess for symptoms of depression. This instrument is a 20-item self-rating scale and is modelled on DSM-IV criteria for major depression. The CES-D is scored from 0 (rarely or none of the time) to 3 (most of the time) regarding frequency of occurrence of each item in the previous seven days. Depression was assessed by the following cut-off scores on the CES-D: a score of < 16 is indicative of not being depressed, a score between 16 and 22 is indicative of mild depression, while a score of ≥ 23 is indicative of severe depression. This scale has been validated in studies in South Africa among different language and ethnic groups (Myer *et al.*, 2008). The Cronbach alpha for the CES-D was 0.93 for this sample.

- ***The Sheehan Disability Scale***

The Sheehan Disability Scale (SDS) was used to assess impairment in the domains of work, family and social life (Sheehan, 1983). This is a 3-item self-report measure with higher scores indicative of impairment and disability. Several

South African studies on people living with HIV have used this scale (e.g., Olley *et al.*, 2005, Olley, 2006, Olley *et al.*, 2003). The Cronbach alpha for the SDS was 0.66 for this sample.

- ***Risky Sexual Behaviour***

This scale measures sexual thoughts, feelings and behaviours associated with participants' previous or last use of substances. A subset of 11 questions assessing domains of sexual drive, risk-taking behaviour, sexual performance, sexual pleasure, involvement with drug use and treatment seeking for sexual behaviours associated with substance abuse, was chosen (Rawson, Washton, Domier & Reiber, 2002). The Cronbach alpha for the Risky Sexual Behaviour Scale was 0.90 for this sample.

- ***The Connor-Davidson Resilience Scale***

The Connor-Davidson Resilience Scale (CD-RISC) was used to assess resilience in participants as well as their stress-coping ability. The CD-RISC has 25 items and each item is rated on a 5-point scale. The scale has been tested on both the general population and clinical samples and has proven to have sound psychometric properties with good internal consistency, reliability and validity (Connor & Davidson, 2003). The Cronbach alpha for the CD-RISC was 0.94 for this sample.

- ***The Multidimensional Scale of Perceived Social Support Scale***

The Multidimensional Scale of Perceived Social Support (MSPSS) was used to assess participants' perceptions on the degree of support that they receive from

family, friends and significant others. The MSPSS is a 10-item scale (Cheng & Chan, 2004). The MSPSS has been used in other South African studies on people living with HIV (Olley, 2005; Olley *et al.*, 2006). The Cronbach alpha for the MPSS was 0.85 for this sample.

- **K 10**

The K 10 is a 10-item measure of psychological distress and is also used as measure of outcome following treatment for common mental health disorders (anxiety and depression). The K10 uses a 5-value response option for each question ranging from one indicative of 'none of the time' to five indicating 'all of the time'. Cut-off scores are used to indicate levels of distress with a score of 10-19 indicating the likelihood of being well, 20-24 indicating mild disorder, 25-29 indicating moderate disorder, and 30-50 indicating a severe disorder (Andrews & Slade, 2001). The Cronbach alpha for the K10 was 0.93 for this sample.

- ***The Mini International Neuropsychiatric Interview***

The MINI was used to establish psychiatric diagnoses. The MINI is a semi-structured questionnaire for major psychiatric disorders and has 17 Diagnostic and Statistical Manual IV Axis 1 psychiatric disorders (Lecrubier *et al.*, 1997). Earlier studies that were conducted to compare the MINI with other psychiatric diagnostic instruments, such as the Structured Clinical Interview for DSM-III-R Patients (SCID-P) and the CIDI, have shown that the MINI has high validity and reliability scores (Lecruiber *et al*, 1997; Sheehan *et al.*, 1997). The MINI has been used in several South African studies on HIV-infected samples (Olley *et al.*, 2005; Myer *et al.*, 2008; Olley *et al.*, 2006).

4.5 Main study questions

- To compare the AUDIT and DUDIT versus biomarkers as useful short screening tools for primary health care settings.
- To determine the extent and severity of substance abuse as measured by scores on the AUDIT and Drug Use Disorders Identification Test (DUDIT) (i.e. cut off scores on either measure indicating hazardous or harmful use of alcohol and/or drugs and possible dependence among patients attending HIV clinics).
- To compare substance users and non-users on the following domains: depression, psychological distress, psychopathology, PTSD, physical health status, HIV disease progression, poor adherence to ARV's, perceived social support, risky sexual behaviour, resilience and disability (work, social and family).
- To determine the predictors of hazardous or harmful use of alcohol and problematic drug use, psychological distress (anxiety and depression) and ARV adherence among PLWHA.

4.6 Specific hypotheses of the study

- PLWHA have a higher prevalence of hazardous and harmful use of alcohol and other drugs than the general population.
- Males living with HIV are more likely to be hazardous and harmful users of alcohol and other drugs than females living with HIV.
- PLWHA with hazardous and harmful use of alcohol and other drugs are more likely to be non-adherent to ARVs than PLWHA who are non-users.

- PLWHA who are hazardous and harmful users of alcohol and other drugs are likely to have lower CD4 counts than PLWHA who are non-users.
- PLWHA who are hazardous and harmful users of alcohol and other drugs are likely to be depressed than PLWHA who are non-users.
- PLWHA who were depressed were likely to have lower CD4 counts than PLWHA who were not depressed
- PLWHA who were depressed were likely to be non-adherent ARVs than PLWHA who were not depressed
- PLWHA with PTSD were likely to be hazardous and harmful users of alcohol and other drugs
- PTSD in PLWHA is likely to affect their work, social and family functioning.
- PLWHA
- PLWHA who are hazardous and harmful users of alcohol and other drugs are less likely to have social support than PLWHA who are non-users.
- PLWHA who are hazardous and harmful users of alcohol and other drugs are likely to engage in risky sexual behaviour.
- Psychosocial factors is a predictor/determinant of hazardous and harmful use of alcohol and other drugs
- Hazardous and harmful use of alcohol and other drugs in PLWHA is a predictor/determinant of poor ARV adherence which is a determinant of a decline in CD4 count.

4.7 Data analysis

All data was analysed using SPSS, version 18. A 95% confidence interval and a 5% level of significance were used to interpret statistical significance. All statistical tests were two-tailed. Descriptive analyses (means, standard deviations and frequencies) were used to describe demographic data and clinical characteristics. Univariate tests of association for categorical variables (chi-square tests) were used to examine bivariate associations between substance abuse and gender, opportunistic infections, TB and ARVs.

Univariate tests of association for categorical variables (chi-square tests) were used to examine bivariate associations between problematic drug use and gender, ARV adherence (stopping, missing a dose, being careless and forgetting to take ARVs), depression, psychological distress (depression and anxiety), PTSD, disability, substance abuse and psychiatric disorders as assessed on the MINI.

Student's t-tests were used, for continuous variables, to test for group differences on hazardous or harmful use of alcohol and gender, ARV adherence (stopping, missing a dose, being careless and forgetting to take ARVs), PTSD and disability. Pearson correlations were employed to assess the relationship between hazardous or harmful use of alcohol, CD4 count and social support.

Multiple linear regression analysis was conducted to examine the psychosocial determinants (gender, $p < 0.05$, employment status, $p=0.14$, level of education, $p < 0.63$, family income, $p < 0.06$ CES-D scores, $p < 0.05$ K-10 scores, $p < 0.05$ and family support, $p < 0.05$) were entered as independent variables) of hazardous or

harmful use of alcohol and the socio-demographic and clinical determinants (age, gender, $p < 0.05$ opportunistic infections, stopping ARVs, $p < 0.05$), alcohol consumption, family income, $p < 0.06$, HIV duration and level of education, $p < 0.63$ were entered as independent variables) of CD4 counts. Logistic regression was used to identify predictors of problematic drug use, major depression and ARV adherence. Variables entered into the regression models were selected on the basis of evidence from prior research as well as from the bivariate analyses undertaken in this study.

Following the regression analyses, a structural equation model (SEM) was developed for further analyses of data. The SEM was developed to examine the direct and indirect determinants of psychological distress, hazardous or harmful alcohol and/or drug use, ARV adherence and CD4 count.

The use of the SEM was based on the fact that while multiple regression analyses are useful for examining the determination of a single dependent variable (e.g. CD4 count) by an independent variable (e.g. hazardous and harmful use of alcohol) while simultaneously controlling for all other independent variables in the equation, however, the technique is limited by the specification of only a single dependent variable. Additionally, it only allows for the direct determination of the dependent variable by each of the independent variables. In reality, as is the case with complex behaviours such as ARV adherence, it is likely that multiple independent variables are contributing to multiple dependent variables, in both direct and indirect ways. So while demographic variables may directly determine hazardous and harmful use of alcohol, and hazardous and harmful alcohol use may be a direct determinant of ARV

adherence, it is also likely that demographic variables are impacting directly on hazardous and harmful use of alcohol and indirectly on ARV adherence. To test for such direct and indirect determination of multiple dependent variables by multiple independent variables, it is hence more appropriate to utilise a SEM.

Additionally, and importantly by use of powerful estimation techniques such as maximum likelihood estimation, SEM is able to provide a robust test of the multivariate normality of the variables in the model. This covers both categorical and continuous variables. As all model parameters such as variances, covariances and standard errors are fully estimated in the SEM when maximum likelihood estimation is used, any violation of multivariate normality will be detected and indicated in the model output in a number of ways. Firstly, the models iterative process will reflect such problems with continuous iterations without proper optimisation, that is, the model will either fail to converge or will require an excessive number of iterations to converge. Secondly, the standard errors estimated by the model will indicate biases indicative of violations of multivariate normality-these are supplied in the model output with significance tests to indicate such errors. Thirdly, the violations will be reflected in the calculation of Chi-square (used to determine the correspondence of the structural model to the measurement model). In general, violations of normality will result in inflated Chi-square values, which typically result in the model being rejected. These various tests of multivariate normality are available in SEM only when the model is estimated using maximum likelihood estimation.

For these reasons, as well as the fact that some of the variables in this study are categorical in nature, the SEM conducted on this data will be conducted using maximum likelihood estimation, and where relevant and necessary, model outputs which indicate non-normality will be presented and discussed. In instances where all model outputs are clear, that is, no special errors occur or are detected during the model estimation process, then only the model outputs and paths will be discussed.

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CHAPTER 5: PILOT STUDY

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A preliminary investigation of the AUDIT and DUDIT in comparison to biomarkers for alcohol and drug use among HIV-infected clinic attendees in Cape Town, South Africa

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Abstract

Objective: There is growing concern about the effect of substance use on HIV-treatment outcomes. The study objectives included: (i) evaluating whether the use of validated questionnaires (AUDIT and DUDIT) provide useful and consistent information of alcohol and drug consumption when compared with the use of biomarkers of alcohol in (urine and hair) and drugs in (urine) and (ii) assessing the feasibility of using self-report measures compared with urine and hair tests. **Method:** Participants were HIV-positive patients attending an HIV community health clinic in Kraaifontein, Cape Town. Hair and urine samples were collected and analysed for alcohol, in Fatty Acid Ethyl Esters (FAEE) and in Ethyl Glucuronide and (EtG), and drugs. Biological markers were compared with self-report measures of alcohol and drug consumption in terms of sensitivity, specificity. Forty-three participants completed the self-report measures, while 30 provided hair and urine samples. **Results:** On the AUDIT, 18 (41.9%) participants screened positive for hazardous or harmful drinking and 13 (30.2%) participants on the DUDIT screened positive for having a drug-related problem. Two of 30 participants (7%) tested positive for alcohol abuse on FAEE analysis. For EtG, 6 of 24 (25%) participants tested positive for alcohol abuse. On hair drug analysis, all 30 participants tested negative for cannabis, amphetamines, opiates, cocaine, PCP and methaqualone. On the urinalysis, 1 of 30 participants tested positive for cannabis and everyone tested negative for all other drugs included in the screening. **Conclusion:** Substance use among patients attending HIV clinics appears to be a problem, especially alcohol. Self-report measures seem to be a more cost effective option for screening of alcohol and drug abuse in resource poor settings.

Key words: Biological markers, substance abuse, HIV, South Africa.

Introduction

In South Africa, the overall prevalence rate for HIV is estimated to be 10.6%, with 17% of all persons between (15-49 years) being HIV positive. Currently, there are 5.2 million people living with HIV and the number of new infections estimated for 2009 was 413 000.¹ Although alcohol surpasses other drugs as the most abused substance in South Africa, in recent years there has been an increase in the use of heroin, crack cocaine and amphetamine-type stimulants.² This country had the 2nd highest prevalence of past year substance abuse (5.8%) compared to the 14 other participant countries in the World Mental Health Survey.³ According to the South African National HIV, Incidence, Behaviour and Communication Survey of 2008, 41.5% men and 17.1% women reported current alcohol use while 17% men and 2.9% women reported risky or hazardous and harmful drinking.⁴

Given the relationship between substance use and HIV infection, it is likely that many infected persons are also substance abusers. Substance abuse by persons living with HIV and AIDS (PLWHA) can lead to non-adherence to treatment, especially anti-retroviral therapy.⁵ PLWHA who have problematic substance use are also more susceptible to AIDS-related opportunistic infections and sub-optimal health compared to those who do not use substances.⁶ Despite this, there has been scant investigation of the relationship between substance abuse and HIV among PLWHA in South Africa. One study conducted among a convenience sample of 149 HIVHIV-positive patients receiving medical care at an infectious disease clinic in Cape Town found that 10.1% of the patients were alcohol dependent, with 22.7% of males reporting alcohol dependence compared to 4.7% of females.⁷ A more recent study,

also conducted in Cape Town, found that of the 465 HIV-positive patients enrolled for HIV treatment and care at primary health care clinics, 7% reported alcohol dependence/abuse.⁸

Often with stigmatized behaviours such as substance use, honesty is especially important.⁹ It seems that most patients attending HIV clinics will not talk about their substance use behaviour owing to stigmatization or fear of not being given antiretrovirals (ARVs).¹⁰ Untreated substance abuse may result in HIV treatment being ineffective secondary to compromised adherence and ongoing risk behavior which may result in re-infection. CD4 counts may also be reduced, drug resistance may occur and this may result in an earlier onset of death.¹¹ Health care professionals may also choose not to confront alcohol and drug-related behaviour and associated problems in patients due to their own negative attitudes towards alcohol and drug use.¹² However, objective testing of alcohol and drug usage may assist in identifying problematic drug and alcohol use early so that they may be addressed on an individual as well as a community level which, in turn, may improve treatment outcomes.^{12,13}

There is increasing recognition that self-report measures of alcohol and drug use can be useful aids in primary health care settings,¹⁴ but less is known about the accuracy of using self-report measures in HIV clinics. Patients with HIV may harbour fears that being open about their substance use may result in stigmatization by health workers and may compromise their eligibility to receive ARVs. Biological markers such as Fatty Acid Ethyl Esters (FAEE) and Ethyl Glucuronide (EtG) when used in addition to

self-report questionnaires, such as the Alcohol Use Disorders Identification Test (AUDIT) and Drug Use Disorders Identification Tool (DUDIT), could assist in the verification of self-reported drug and alcohol abuse.¹⁴

FAEE and EtG are metabolites of ethanol and are very specific biomarkers for alcohol. Both FAEE and EtG are deposited in the hair, enabling a longer window of opportunity for diagnosis of alcohol consumption.¹⁵ Analysis of these metabolites in hair and urine can be conducted with gas chromatography/mass spectrometry (GC/MS) to identify and quantify markers indicative of alcohol consumption.^{15,16} The analysis of urine for drug detection also uses the GC/MS technique and the HPLC/MS/MS technique can be used for detecting drugs in hair.¹⁶ This pilot study aimed to assess the relative utility of the AUDIT and DUDIT screening tool is compared with selected biomarkers for alcohol and drug-use disorders in HIV clinics. Specific objectives included: (i) evaluating whether the use of validated questionnaires [AUDIT and DUDIT] provide useful and consistent information when compared with biomarkers of alcohol and drug consumption in urine (drugs) and hair (alcohol and drugs) and (ii) assessing the feasibility (cost and practicality) of using self-report measures compared with urine and hair tests in HIV-clinic populations.

Materials and methods

Design

This pilot study used a cross-sectional research design.

Setting and participants

Data were collected in February and March 2010 at the Wallacedene Community Health Clinic (CHC) in Kraaifontein, Cape Town. The clinic is situated in one of the poorest communities in Cape Town, an informal settlement established between 1985 and 1989, with very high rates of HIV, TB, gang-related crime and alcohol and drug use. The clinic population is predominantly Coloured (mixed race) and “Black African and the clinic lacks basic resources, including not having enough rooms in which to attend to patients. HIV patients are attended to in a converted shipping container which serves as a clinic room. Often there is not enough space to accommodate all patients and they have to queue outside. The clinic provides HIV care, antiretroviral therapy, tuberculosis and other health care services free of charge. Study participants were HIV-positive patients who were 18 years and older, with 28 receiving antiretroviral therapy. Forty-three patients were recruited into the study. All 43 completed the self-report measures for alcohol and drug use (see below) and demographic data was obtained on all 43 patients. However, due to budgetary constraints, urine and hair samples were only obtained from the first 30 of the 43 patients that were willing to give their hair and urine samples.

Study procedures

A semi-structured diagnostic interview questionnaire (Mini International Neuropsychiatric Interview) was administered in English, Afrikaans and Xhosa and several self-report measures were completed.¹⁷ The interviews were administered by trained interviewers who had experience working within disadvantaged communities. The interviews were conducted in a school hall situated near the clinic, which afforded patients privacy for interviewing and collection of urine and hair samples.

Participants were interviewed for approximately 45 minutes, following which urine and hair samples were collected in a setting that allowed for privacy. Hair was cut approximately 1 mm from the scalp and then wrapped into foil with the root end marked. The hair sample was sealed in an envelope with a barcode. Samples were sent to Trimega Laboratories Limited in the United Kingdom to be analysed. At the time of this study, hair testing kits were not available in South Africa and laboratories did not have the necessary equipment to analyse hair samples. The urine samples were collected in a 50 ml container onsite which was then stored in a cooler box and subsequently sent to a laboratory in Pretoria, South Africa for analysis.

The decision to use hair analysis, a relatively expensive biomarker test, as compared to cheaper blood and urine analyses for the detection of alcohol and drug use was guided by several factors: first, hair analysis allows for the detection of drugs or alcohol over a longer period (up to 12 months) depending on the length of the hair strand. In contrast, blood and urine samples have a window of detection of several days to 2-3 weeks only; second, hair testing is considered the gold standard of biomarkers and has been shown to have higher levels of sensitivity and specificity for alcohol/drug detection than blood and urine tests; and third, we were interested in qualitatively assessing the feasibility and cultural acceptability of collecting hair samples in this community.

Completed questionnaires were checked every day, entered into an Excel spreadsheet and then exported to SPSS for cleaning and analysis. Participants received a voucher of R50 for their participation. Ethical approval to conduct this research was

provided by the Health Research Ethics Committee of the University of Stellenbosch, Cape Town. Written informed consent was obtained from all participants.

Assessment

Sociodemographic and clinical data

Demographic questions included age, gender, race, marital status, highest level of education attained, level of income and employment status. Clinical data included date of diagnosis of HIV and receipt of antiretroviral therapy (yes/no).

The Alcohol Use Disorders Identification Test (AUDIT)

The AUDIT screens for hazardous and harmful patterns of alcohol use and alcohol dependence. It is a 10-item, self-rating questionnaire developed by the World Health Organisation, and internationally validated for use in primary health and community settings. A total score of 8 or more on the AUDIT indicates hazardous and harmful alcohol use as well as possible alcohol dependence.¹⁴

The Drug Use Disorders Identification Test (DUDIT)

The DUDIT is a screening instrument used to identify patterns of drug use and drug related problems (i.e., substance abuse/harmful use or dependence). It consists of 11 items, and includes a list of different drugs. Drug-related problems are indicated by a score of 6 or more for men and a score of 2 or more for women. A score of 25 or more, for both sexes, is indicative of a high probability of drug dependence.¹⁸

Biomarkers

The biomarkers used in this study were urine and hair as discussed below. It is important to note that although biomarkers may indicate an objective report of alcohol or drug use, they are not 100% specific and sensitive in detecting alcohol abuse and drug abuse. A major drawback of FAEE's in hair is the use of hair products containing ethanol which will produce detectable amounts of FAEE in the hair which could bias the results.¹⁹ Also hair care treatments (bleaching, permanent waving, dyeing) can negatively affect hair EtG levels.²⁰ A gender bias could therefore exist when using FAEE and EtG analysis. Hair has a longer detection period (up to 12 months) depending on length of hair while urine samples have a window of detection period of several days to 2-3 weeks depending on the drug of abuse. The detection period for alcohol is (up to 2 weeks), for amphetamines (1 to 4 days), for opiates (2-5 days), for methaqualone (up to 2 weeks) and cannabis (up to 30 days) in urine. The window to detect a drug in a person's urine is dependent on several factors such as hydration, dosing, metabolism, body mass, urine pH, duration of use and a drug's particular pharmacokinetic.²¹

Urinalysis

Urine was tested for cannabis, amphetamines, opiates, cocaine, phencyclidine (PCP) and methaqualone, using the following cut-offs: 15 ng/mL for cannabis, 500 ng/mL for amphetamines 2000 ng/mL for opiates, 150 ng/mL for cocaine, 25 ng/mL for PCP and 300 ng/mL for methaqualone.

Hair alcohol analysis

A hair sample of approximately 3 cm length was taken from each participant to enable a 3 month diagnosis of alcohol consumption. Hair analysis was conducted using GC/MS technique.

Fatty Acid Ethyl Esters (FAEE) & Ethyl glucuronide (EtG)

FAEE is a metabolite of ethanol and indicates the amount of alcohol consumed. FAEE is derived from a range of fatty acids secreted in the body. The following cut-offs were applied: teetotallers (less than 0.20 ng/mg), questionable alcohol use (0.21-0.50 ng/mg), lower cut-off (0.51-0.99) and higher cut-off (1.00ng/mg and above). EtG is also a direct metabolite of ethanol which is formed in the liver and deposited into the hair follicles following the consumption of alcohol. The cut-off for EtG to indicate frequent excessive alcohol consumption is 30 pg/mg.¹⁵

Hair analysis for drugs

Hair analysis was used to test for amphetamine, cannabis, cocaine, ecstasy, methadone, methamphetamine and opiates. The following cut-offs were used: 3.0 ng/mg for amphetamine, 5.0 ng/mg for cocaine, 3.0 ng/mg for ecstasy, 5.0 ng/mg for methadone, 3.0 ng/mg for methamphetamine and 2.0 ng/mg for opiates.

Data analysis

Data were analysed using SPSS Version 18. "Sensitivity" "specificity", and "positive and negative predictive" values were determined (comparing self-report [DUDIT + AUDIT] with biological markers [in urine and hair]). It is strictly not correct to use the

terms sensitivity and specificity in this analysis as the biomarkers did not provide the perfect gold standard because of the differences in detection periods between the biomarkers and self-report measures. Student's t-tests were conducted to assess gender differences in AUDIT and DUDIT scores. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Demographic and clinical characteristics

The majority of the sample consisted of Black and Coloured females, reflecting the demographics of the population of persons living with HIV attending the public health clinic where the data were collected (Table I). The terms "white", "black", and "Coloured" refer to demographic groupings used in South Africa and do not signify inherent characteristics. Their continued use in South Africa is important for monitoring improvements in health and socio-economic disparities, identifying vulnerable sections of the population, and planning effective prevention and intervention programmes. Most of the participants were poor, unemployed, and relatively young, with an average age of 34 years (23-59 years). The majority (65%) were on ARVs at the time of data collection. The average time between diagnosis of HIV and data collection was 39.5 months (2 months-10 years).

Comparison of self-reported measures of problematic alcohol and drug use with urine and hair tests

All 43 participants completed the AUDIT. Of these, 18 (41.9%) scored at or above the clinically significant cut-off score of 8, indicating the likelihood of hazardous or harmful drinking. Of 30 participants tested for alcohol markers (FAEE and EtG) in

hair, 2 (7%) tested positive for alcohol abuse on FAEE and 6 (25%) tested positive for alcohol abuse on EtG.

Of the 43 participants who completed the DUDIT, 12 (28%) scored above the respective cut-off points on the DUDIT (≥ 2 for females; ≥ 6 for males) for over-the-counter drugs (OTC) and 1 tested positive for cannabis while none of the participants scored above the cut-off for other drugs. In contrast, using hair analysis, all 30 tested negative for cannabis, amphetamines, opiates, cocaine, PCP and methaqualone. Urinalysis revealed one positive test for cannabis which is consistent with the results of the DUDIT, with the remaining participants testing negative for amphetamines, opiates, cocaine, PCP and methaqualone.

Sensitivity and specificity analysis of the self-report measures versus the biological markers

A comparison of scores of AUDIT with FAEE and EtG is provided in Tables II a and II b. The sensitivity ($TP / (TP + FN) \times 100$) of the AUDIT against the FAEE and EtG to detect hazardous or harmful drinking in the participants was 100% and 83.3% indicating that the AUDIT is good at not missing people who have an alcohol problem as indicated by the biological markers (i.e., high rate of true positives). The specificity ($TN / (FP + TN) \times 100$) of the AUDIT using the FAEE was 53.6% and 61.1% when using the EtG. Thus, the AUDIT is only “fair” at detecting people who do not have an alcohol problem (i.e., moderate rate of true negatives).

The positive predictive value (PPV) ($TP / (TP + FP) \times 100$) for the AUDIT against the FAEE was 13% and on the EtG was 41.6%, indicating only a few of the participants who were screened positive were confirmed by the biological marker. The negative predictive value (NPV) ($TN / (TN + FN) \times 100$) on the FAEE was 100% and on the EtG was 91.6%, indicating that a high proportion of the participants who screened negative were in fact negative.

A comparison of scores of the DUDIT with the biological marker (hair) is provided in Table IV. The sensitivity, specificity, PPV and NPV of the DUDIT against the biomarker (hair) to detect harmful use or dependence of drugs in the participants were 0%, 70%, 0% and 100%, respectively. A comparison of scores of the DUDIT with the biological marker (urine) is provided in Table V. The sensitivity, specificity, PPV and NPV of the DUDIT against biomarkers in the urine to detect harmful use or dependence of drugs in the participants were 100%, 66%, 10% and 100%, respectively.

Discussion

The accuracy of the AUDIT was very high compared to a biological marker (hair) in the detection of an alcohol-related problem, but was only moderately good in detecting people who did not have an alcohol related problem. All participants, on both the DUDIT and hair testing, screened negative for a drug-related problem. The accuracy of the DUDIT was very high compared to urine analysis in the detection of a drug-related problem. Thus, these self-report measures are not likely to indicate that someone has a severe substance abuse problem if they do not have one.

However, the self-report measures tended to over predict the likelihood of a person having a substance related problem if hair and urine testing are used as the gold standard.

The discrepancy between biological hair analysis and self-report (AUDIT & DUDIT) findings may relate to the timing of substance use. Biological markers are able to detect use over a relatively short time period only (for hair: up to 3 months given the length of hair we obtained; for urine: maximum of two weeks and a minimum of 72 hours depending on the drug of use), while the AUDIT and DUDIT measure alcohol and drug use over a longer time frame (i.e. up to a year). Differences in time measurement may explain why the AUDIT and DUDIT detected higher rates of alcohol and drug use among participants.

The findings of this study like many studies have found that there is a high rate of substance abuse among people who are HIV positive.^{6,22,23} In South Africa a study conducted on HIV patients attending an infectious diseases clinic at Tygerberg Hospital in Cape Town in revealed that 10.1% of the patients were alcohol dependent.⁷ A cross-sectional study also conducted in Cape Town between October 2004 and December 2005 found that of the 465 HIV-positive patients enrolled for HIV treatment and care at primary health care services, 7% reported alcohol dependence/abuse.⁸ These findings are also consistent with a study²⁰ conducted in the emergency department of a university hospital in Germany that found the AUDIT to be superior in detecting alcohol abuse in comparison to biomarkers such as Gamma-Glutamyl-Transferase (GGT), Mean Corpuscular Volume (MCV) and

Carbohydrate-Deficient-Transferrins (GGT). However, a study¹⁶ conducted in Britain on parents with suspicious alcohol abuse in child protection cases that compared self-reported drinking data with FAEE to measure excessive alcohol consumption showed that FAEE has a longer time period of detection than CDT and GCT and hence has increased sensitivity and specificity. The comparison with the self-report measures indicated that FAEE can discriminate between moderate and excessive drinking compared to the CDT and GCT. However, it's important to note that these results should still be interpreted with caution as validated cut-offs cannot fully exclude false positive or false negative results caused by the use of hair care products and biological variability.¹⁶

In terms of practicalities, obtaining hair samples from Black and Coloured participants proved to be challenging. In many instances adequate hair samples were not obtained as hair was too short (less than 1 cm) and curly. In addition, most women had their hair plaited in braids which resulted in an inability to acquire a natural strand of head hair. For successful analysis of hair samples, it is recommended that the hair strand be at least 3-6 cm long.¹⁶

Furthermore, the cost of doing both urine and hair assays was very high in comparison with self-report measures. Hair assays cost approximately R1 593 (US\$ 212) per participant and the urine test cost R1 180 (US\$ 157) per participant. Urine tests were sent away for analysis as opposed to the dip-stick approach which is cheaper and gives an immediate result but is subject to other limitations.

Hair biomarkers although costly can be useful and beneficial in primary health care settings in assisting health care professionals in the early identification of patients

with substance abuse problems. Biomarkers can give important objective information regarding the severity of the substance abuse problem, help with diagnosis and assist in the monitoring of alcohol related medical conditions. Biomarkers could also serve as an objective measure of substance abuse treatment outcomes and provide patients with feedback about the effects of drugs and alcohol on their condition. Primary health care settings could benefit from these tests since early detection of substance abuse could result in considerable savings in medical costs and lessen the burden in primary health care settings where patients have alcohol and drugs problems that exacerbate their other medical conditions.²⁴

The AUDIT and DUDIT are two screening instruments that can be utilised in all treatment settings to screen for alcohol and drug use by health workers with varying levels of training and experience.^{14,18} There are cheaper biomarkers (blood, nails, and saliva) can be used in these settings as biomarkers do provide an objective means of testing for substance abuse. While both biomarkers and the AUDIT and DUDIT are not used routinely to screen for alcohol and drug use problems in primary health care clinics in South Africa, they are becoming increasingly recognised by clinicians as useful tools for the detection of alcohol and drug use.^{25.}

Study limitations

One of the main limitations of this study was that the window period for the biomarkers and self-reports did not match, with the self-report measures having a longer period of detection. This was an important lesson for future research that similar window periods on test should be used when conducting a comparison of

measures. Also cheaper biomarkers (blood, saliva, nails) can be used in future studies. Other study limitations include the small sample size and localisation of the study to one HIV clinic which makes generalisation of findings to other settings and populations difficult. However, it should be noted that this was a pilot study with the primary purpose of evaluating biomarker assay methods and their feasibility and cost. The sample, therefore, represents approximately 5% of the sample to be recruited in a larger study of HIV, mental disorder, and substance use comorbidity that followed the pilot study. Despite the limitations, the preliminary findings are important because it is the first study undertaken in a South African population of HIV-clinic attendees to investigate the use of self-report measures (AUDIT and DUDIT) and biological measures (hair and urine) in the detection of alcohol and drug use.

Conclusions

This study highlights the problem of substance abuse among patients attending HIV clinics, especially abuse of alcohol. Furthermore, the findings emphasise the importance of screening HIV patients for substance abuse and dependence. Addressing alcohol and drug related problems should be standard protocol for ARV treatment programmes for patients attending HIV clinics.²⁶ Similarly, health workers working in the field of substance abuse need to consider including HIV-intervention services into their programmes.^{27,28} Self-report measures (AUDIT and DUDIT) are a more viable option for screening of alcohol and drug abuse in resource poor settings than biological markers. Furthermore, combining biological markers with self-report

measures does not appear to add much value to these questionnaires used on their own.

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Table I: Demographic data and clinical characteristics

Demographic/clinical data	N	%
GENDER (n=43)		
Male	7	16.3
Female	36	83.7
RACE (n= 43)		
Black	36	83.7
Coloured	7	16.3
MARITAL STATUS (n=43)		
Unmarried	26	60.5
Married	17	39.5
EDUCATION (n=43)		
No formal education	2	4.7
Some form of education	41	95.3
EMPLOYMENT STATUS (n=43)		
Employed	17	39.5
Unemployed	26	60.5
INCOME (n=41)		
< R10 000	26	63.4
Between R10 000 & R110 000	15	36.6
Taking ARV's (n=43)		
Yes	28	65.1
No	15	34.9
MEAN TIME SINCE HIV		
DIAGNOSIS	39.5 mths ± 34.1 (sd)	
MEAN AGE	33.6 mths ± 7.8 (sd)	

Table II a: Hair alcohol biomarkers versus AUDIT

FAEE

	-	+		
AUDIT	-	True negative (TN) 15	False negative (FN) 0	15
	+	False positive (FP) 13	True positive (TP) 2	15
		28	2	

Table II b

EtG

	-	+		
AUDIT	-	True negative (TN) 11	False negative (FN) 1	12
	+	False positive (FP) 7	True positive (TP) 5	12
		18	6	

Table III: Hair drug biomarker versus DUDIT

		Hair drug biomarker	
		-	+
DUDIT	-	True negative (TN) 21	False negative (FN) 0
	+	False positive (FP) 9	True positive (TP) 0
		30	0

Table IV: Urine drug analysis versus DUDIT

		Urine	
		-	+
DUDIT	-	True negative (TN) 20	False negative (FN) 0
	+	False positive (FP) 9	True positive (TP) 1
		29	1

CHAPTER 6: RESULTS

6.1 Demographic and clinical characteristics

The sample of 1503 consisted almost entirely of black (89%) and Coloured (10%) participants reflecting the demographics of the population of PLWHA attending the public health clinics where data collection took place (Table 6.1). The mean age of participants was 35.8 years. Most of them were female (70%), single (63%), unemployed (66%), and had some high school education (60%). Only 1% had a tertiary education. The monthly income for most of them (61%) was less than R1 000 (US\$120) and 37% earned between R1 000 and R5 000 (US\$ 120 and US\$ 602).

6.2 Health status

The average time between diagnosis of HIV and data collection was 3.7 years (SD=3.1). The current mean CD4 count was 305.3 (SD=193.7, n=1478 records) and the CD4 nadir (lowest CD4 count in the previous 12 months) was 265.3 (SD=178.1, n=1 467 records). Most participants, 1 336 (89%), were on ARVs. Those diagnosed with TB (as indicated in patients clinical records) were 184 (12.2%), while 175 (12%) reported having an opportunistic infection at the time of data collection.

6.3 Cognitive functioning

All 1503 participants completed the IHDS, with 812 participants scoring between 8 and 10. Although a score of < 10 is indicative of a need for further assessment, on further probing there were two factors that were found to contribute to the relatively

low scores. These were anxiety on doing the assessment and communication errors (fieldworkers mishearing participants' pronunciation of the word recall items). After taking these factors into account, all 1 503 participants were found to be cognitively intact and were eligible for inclusion in the next tier of screening.

6.4 AUDIT and DUDIT

All participants (1503) completed the AUDIT and DUDIT screening tools. Of these, 10% percent scored between 0 and 7 indicating low-risk drinking or abstinence; 33% scored between 8 and 15 indicating hazardous drinking patterns, while 20% scored between 16 and 19 indicating harmful levels of drinking. Over a third (37%) scored between 20 and 40 indicating possible dependence (Table 6.2). There was a statistically significant relationship between gender and hazardous or harmful use of alcohol ($p = 0.000$). More males (52%) reported hazardous or harmful drinking than females (30%).

Thirteen percent scored above the respective cut-off points on the DUDIT for a drug-related problem (Table 6.2). There was a statistically significant relationship between gender and problematic drug use ($p = 0.000$). More males (26%) reported having a drug problem than females (7%).

6.5 Hazardous or harmful alcohol use and/or drug use, demographic characteristics and health status

There was a significant relationship between hazardous and harmful alcohol use and/or drug use and gender ($X^2 = 95.176, p < 0.05$). More than half of the males reported hazardous and harmful alcohol use and/or drug use compared to only a third of females. There was no significant relationship, however, between hazardous or harmful alcohol and/or drug use and opportunistic infections ($X^2 = 0.831, p > 0.05$). There was a statistically significant relationship between hazardous or harmful alcohol and/or drug use and TB ($X^2 = 4.308, p < 0.05$). Eighty-seven participants (14%) who reported hazardous or harmful alcohol and/or drug use had TB compared to 97 participants (11%) who did not have an alcohol and/or drug problem (Table 6.3).

6.6 History of substance use/problematic alcohol and/or drug use (lifetime and current substance use/abuse)

Of the sub-sample of 607 participants, more than half (n=316, 52%) reported ever using a substance in their lifetime. The most common substances ever used, were alcohol (n=294, 93%), followed by cannabis (n=37, 12%) and cigarettes (n=14, 4%). With regards to current use, alcohol (n=243, 77%) was the most common, followed by cigarettes (n=44, 14%) and cannabis (n=14, 4%). Although 50% of participants met the cut-off for problematic alcohol and/or other drug use, 117 (19%) thought that they had a problem with substance use, while only 10 (2%) of the problematic alcohol and/or other drug users reported ever receiving help for their problem.

Twenty-five percent of participants (n=149) reported that they would like help for their drug and/or alcohol problem.

6.7 Hazardous or harmful use of alcohol and/or drug use and HIV parameters (bivariate analyses)

Hazardous or harmful use of alcohol

Of the 607 participants who completed the AUDIT, 278 (46%) scored at or above the clinically significant cut-off score of ≥ 8 , indicating the likelihood of hazardous or harmful drinking.

Problematic drug use

Of the 605 participants who completed the DUDIT, 90 (15%) scored above the respective cut-off points for a drug-related problem.

Gender

There was a significant association between hazardous or harmful use of alcohol and gender ($t=4.988$, $p < 0.05$), with males being significantly more likely than females to engage in hazardous or harmful use of alcohol. There was a significant association between problematic drug use and gender ($\chi^2=43.185$, $p < 0.05$). More males (28.4%) reported problematic drug use than females (8.3%). In fact, males were three times more likely to be problematic drug users than females.

6.8 ARV adherence

ARV adherence comprised participants stopping ARVs, missing ARVs, being careless and forgetting to take ARVs. Stopping ARVs is defined as participants

stopping their medication because they felt better, felt sick or depressed, felt overwhelmed by the number of pills, worried about getting side effects from medication, actually getting side effects from medication and because they ran out of pills. Missing ARVs comprised not taking ARVs for the following reasons: they did not want others to see they were taking medication, they were away from home, they just forgot, because they were busy with other things. Stopping and missing ARVs were measured using the ARV Adherence questionnaire. Forgetting and being careless to take medication was defined as self-reporting about forgetting or being careless about taking ARV medication and were assessed using the Morisky Adherence scale.

There was a significant association between hazardous or harmful use of alcohol and stopping ARVs ($t=-5.364$, $p < 0.05$), missing ARV doses ($t=-7.737$, $p < 0.05$), forgetting to take ARVs (measured by the Morisky Scale; $t=6.264$, $p \leq 0.005$), and being careless about taking their ARVs ($t=7.773$, $p < 0.05$). Participants reporting hazardous or harmful use of alcohol were significantly more likely to stop, miss, forget and being careless about their ARVs than their counterparts without alcohol problems.

There was a significant association between problematic drug use and stopping ARVs ($\chi^2=5.915$, $p \leq 0.05$), missing ARV doses ($\chi^2=31.794$, $p < 0.05$), forgetting to take ARVs ($\chi^2=13.987$, $p < 0.005$), and being careless about taking ARVs ($\chi^2=19.852$, $p < 0.05$). Participants with problematic drug use were more likely to stop their ARVs and were three times more likely to miss taking their ARVs than

participants without drug problems. Problematic drug users (46.1%) were more likely to forget taking their ARVs than their counterparts without drug problems (25.5%) and were twice as likely of forgetting to take their ARVs than those without drug problems. Problematic drug users (39.5%) were significantly more likely to be careless about taking their ARVs than those without drug problems (17.6%) and were twice as likely to be careless about taking their ARVs than those without drug problems. There was a significant association between gender and missing ARV doses ($\chi^2=6.326$, $p < 0.05$). Males were more likely to miss taking their ARVs than females.

6.9 CD4 Count

There was a significant negative correlation between AUDIT total scores and CD4 counts. As the AUDIT total scores increased, CD4 counts decreased ($r=-0.106$, $p < 0.005$). There was no significant correlation between DUDIT scores and CD4 counts. There was a significant association between gender and CD4 counts ($t=-2.825$, $p < 0.05$) with females having significantly higher CD4 counts than males.

6.10 Hazardous or harmful alcohol and/or drug use and psychopathology

Major depression

There was a significant association between hazardous or harmful use of alcohol and major depression as assessed by the CES-D ($f=13.946$, $p < 0.05$) with hazardous or harmful users of alcohol being more likely to be depressed than those without alcohol problems. There was a significant association between problematic

drug use and depression as assessed by the CES-D ($\chi^2=12.753$, $p < 0.05$), with 31.1% with problematic drug use reporting mild depression, while 23.3% reported severe depression. In comparison, 19.8% without drug problems reported mild depression and 15.7% severe depression. The association between gender and depression was not significant.

Psychological distress (anxiety and depression)

There was a significant association between hazardous or harmful use of alcohol and psychological distress ($f=10.913$, $p < 0.05$) and problematic drug use and psychological distress as assessed on the K10 ($\chi^2=24.556$, $p < 0.05$). Hazardous or harmful users of alcohol were more likely to report psychological distress than those without alcohol problems. Of the participants with problematic drug use, 22.2% met the criteria for a moderate disorder compared to 8.9% of those with no drug use. Similarly, 22.2% met the criteria for a severe disorder compared to 15.9% without any drug problems. The association between gender and psychological distress was not significant.

Depression and CD4 counts

CD4 counts were not associated with clinically significant depression or psychological distress, respectively. Participants who met criteria for major depression (32.6%) were significantly more likely to stop ARVs ($\chi^2=23.674$, $p < 0.05$), while 58.1% were more likely to miss taking their ARVs ($\chi^2=23.691$, $p < 0.05$).

Post-Traumatic Stress Disorder and Disability

There was no significant association between total scores on the AUDIT or DUDIT and symptoms of PTSD as assessed by the DTS. However, there was a significant association between PTSD and work functioning ($\chi^2=16.192$, $p < 0.05$). Participants who met the criteria for posttraumatic stress disorder (19.7%) reported that their work functioning was moderately affected by trauma, while 4% of participants with no disorder reported that their work functioning was moderately affected. PTSD was significantly associated with worse social functioning ($\chi^2=66.972$, $p < 0.05$) and family functioning ($\chi^2=67.711$, $p < 0.05$). Of those participants with PTSD, who reported about their social and family functioning, 37.7% and 31.1%, were markedly affected, while 27.9% and 32.8% were extremely affected, respectively.

Social Support

There was a significant relationship between AUDIT total scores and family support ($r = -0.098$, $p < 0.05$). Participants with low levels of family support were more likely to be hazardous or harmful users of alcohol. There was no significant relationship between AUDIT total scores and support from significant others and friends or between problematic drug use and support from family, friends, or significant other.

Sexual risk behaviours

Of the participants reporting problematic alcohol and/or drug use, 51% reported engaging in moderate to high risk sexual behaviours (sexual performance, pleasure, drive, number of partners and risky sex influenced by the use of alcohol and drugs).

Thirty seven percent reported that their sexual thoughts, feelings and behaviours were often associated with using alcohol and/or drugs. Whereas 45% reported that their sexual drive and performance were improved by the use of alcohol and/or drugs, and 43% mentioned their sexual pleasure was enhanced.

6.11 Psychiatric disorders as assessed on the Mini International Neuropsychiatric Interview (MINI)

Eighty participants completed the MINI of whom 40 were substance abusers (according to cut-off points on the AUDIT and DUDIT) and 40 were non-substance users. Of the 40 participants using substances, 28 (70%) were diagnosed with alcohol dependence. One participant was diagnosed with alcohol abuse and four (10%) were diagnosed with drug dependence (excluding alcohol).

Substance abuse (53%) compared to no substance abuse (10%) was significantly associated with a diagnosis of a major depressive episode (current) ($\chi^2=6.373$, $p < 0.05$). Substance abuse (10%) was significantly associated with a diagnosis of panic disorder (current) ($\chi^2=4.321$, $p < 0.05$). Substance abuse (55%) was also significantly associated with a high suicide risk ($\chi^2=7.289$, $p < 0.05$). There were no significant associations between substance abuse and dysthymia, hypomanic episodes, manic episodes, lifetime panic disorder, social phobia (current), and PTSD (current).

6.12 Multivariate analysis

Predictors of hazardous or harmful use of alcohol

To examine the psychosocial determinants of hazardous or harmful use of alcohol, a multiple linear regression analysis was conducted, with gender, employment status, level of education, family income, CES-D scores, K-10 scores, and family support entered as independent variables. The results revealed that the overall model was statistically significant ($F=11.242$, $p < 0.005$). However, only gender, depression and psychological distress were found to be significant independent determinants of hazardous or harmful use of alcohol (Table 6.4).

Predictors of problematic drug use

Logistic regression was used to identify predictors of problematic drug use. Psychological distress was a significant predictor of problematic drug use ($p < 0.05$; 95% CI=1.03-1.74). This was an indication that as participants' anxiety and depression increased, they were more likely to abuse drugs. Gender was also a significant predictor of problematic drug use, with men being five and half times more likely to be problematic drug users than women ($p < 0.05$; 95% CI=3.45-9.37).

Predictors of major depression

Logistic regression was used to identify predictors of major depression. Alcohol consumption was a significant predictor of major depression with increased alcohol consumption (higher AUDIT scores) being associated with increased depression ($p < 0.05$; 95% CI=0.95-1.04). Family support was also a significant predictor of major

depression with a decrease in family support being associated with an increase in depression ($p < 0.05$; 95% CI=0.59-0.92). PTSD was a significant predictor of major depression with participants who experienced PTSD being ten times more likely to suffer from depression than those with no PTSD ($p < 0.05$; 95% CI=0.04-0.23) (Table 6.5).

ARV adherence

Logistic regression was used to identify predictors of stopping ARVs, missing ARV doses, and forgetfulness and carelessness about taking ARVs. Hazardous or harmful use of alcohol ($p < 0.05$; 95% CI=1.02-1.07), depression ($p < 0.05$; 95% CI=1.06-2.22), and resilience ($p < 0.05$; 95% CI=0.50-0.92) were significant predictors of participants stopping their ARVs. Hazardous or harmful use of alcohol ($p < 0.005$; 95% CI=1.03-1.07), depression ($p < 0.05$; 95% CI=1.12-2.13), and problematic drug use ($p < 0.05$; 95% CI=0.22-0.73) were significant predictors of missed ARV doses. Problematic drug users were twice as likely to miss taking their ARVs than those without a drug problem.

Hazardous or harmful use of alcohol ($p < 0.05$; 95% CI=1.03-1.07) and depression ($p < 0.05$; 95% CI=1.02-1.97) were significant predictors of forgetting to take ARVs. Hazardous or harmful use of alcohol ($p < 0.05$; 95% CI=1.05-1.09), depression ($p < 0.05$; 95% CI=1.15-2.42), psychological distress, and problematic drug use ($p < 0.05$; 95% CI=0.26-0.89) were all significant predictors of participants carelessness about taking ARVs ($p < 0.05$; 95% CI=0.26-0.89) (Table 6.6).

Predictors of CD4 count

To examine the socio-demographic and clinical determinants of CD4 count, a multiple linear regression was conducted with age, gender, opportunistic infections, stopping ARVs, alcohol consumption, family income, HIV duration and level of education entered as independent variables. The results revealed that the overall model was statistically significant ($F = 6.959, p \leq 0.05$). However, only age, gender, stopping ARVs, and HIV duration were found to be statistically significant determinants of low CD4 count. (Table 6.6).

Factors predicting psychological distress, problematic alcohol and/or drug use, ARV adherence and CD4 count

Based on the bivariate and multiple regression analysis, a structural equation model (SEM) was delineated, as shown in Figure 6.2. The results of the SEM analysis revealed that there were no residual errors and no data problems with the measurement model, thereby permitting the use of model indices and the interpretation of model results. The output indicated that the structural model provided a good fit to the data, as indicated by the following indices: CFI = 0.94 (a CFI of 0.90 and above is regarded as a well-fitting model), RMSEA = 0.037 (a RMSEA value of 0.03 and 0.05 is regarded as evidence of a good fitting model), and Chi-square = 65.3 with $df = 38$ and X^2/df ratio of 1.71 (a X^2/df ratio of 2 to 4 is considered as evidence of a good model). Furthermore, the Lagrange Multiplier Tests outputs confirmed the validity of the good fit indices and indicated that no further modifications were necessary to the model.

A number of significant direct predictive pathways were identified in the SEM. Firstly, PTSD was determined to be significant in predicting hazardous or harmful use of alcohol ($\beta = 0.08$, $p < 0.05$), with participants who experienced PTSD being more likely to have higher scores on the AUDIT (indicative of hazardous or harmful use of alcohol) than those without PTSD. Secondly, gender was found to be significant in directly predicting hazardous or harmful use of alcohol ($\beta = -0.23$, $p < 0.01$), with males being more likely to have higher scores on the AUDIT indicating hazardous or harmful use of alcohol than females. Thirdly, employment was also a significant predictor of hazardous or harmful use of alcohol ($\beta = 0.10$, $p < 0.05$). Participants who were employed were less likely to be hazardous or harmful users of alcohol than unemployed participants. Fourthly, psychological distress was found to predict hazardous or harmful use of alcohol ($\beta = 0.18$, $p < 0.01$). Participants suffering from psychological distress were more likely to have hazardous or harmful alcohol use than those who were not.

Hazardous or harmful use of alcohol ($\beta = 0.21$, $p < 0.01$), psychological distress ($\beta = 0.12$, $p < 0.01$) and gender ($\beta = -0.26$, $p < 0.01$) were predictive of problematic drug use. Participants who were male, hazardous or harmful users of alcohol and who suffered from psychological distress were more likely to be problematic drug users than participants who were female, did not suffer from psychological distress and were not using alcohol.

Hazardous or harmful use of alcohol was found to predict missing ARV doses ($\beta = 0.26$, $p < 0.01$) and stopping ARVs ($\beta = 0.13$, $p < 0.01$). Participants who were

hazardous or harmful users of alcohol were more likely to miss and/or stop taking their ARVs than those who did not use alcohol. Problematic drug use was found to predict missing ARV doses ($\beta = 0.16, p < 0.01$), but not stopping ARVs. Psychological distress (anxiety and depression) was significant in directly predicting missed ($\beta = 0.8, p < 0.05$) and stopped ($\beta = 0.11, p < 0.01$) ARV doses.

Missed ARVs was found to predict stopping ARVs ($\beta = 0.33, p < 0.01$) indicating that participants who missed taking their ARVs were more likely to stop taking their ARVs than participants who did not miss doses. Stopping ARVs ($\beta = -0.10, p < 0.01$) and gender ($\beta = 0.13, p < 0.01$) significantly predicted CD4 counts. Male participants and those who stopped taking their ARVs were more likely to have lower CD4 counts than female participants and those who did not stop.

PTSD was found to predict psychological distress ($\beta = 0.10, p < 0.05$) indicating that participants who experienced trauma were more likely to suffer from psychological distress (anxiety and depression) compared to those who did not experience any PTSD. Family support was also a significant predictor of psychological distress ($\beta = 0.10, p < 0.05$). Participants with lower levels of family support were more likely to suffer from psychological distress than those with high levels of family support.

A number of indirect predictive pathways were identified in the SEM, but only the following was found to be significant. Both PTSD and family support indirectly predicted CD4 count, mediated through psychological distress predicting hazardous or harmful use of alcohol and problematic drug use. This, in turn, predicted missing

ARVs and stopping ARVs, which subsequently predicted CD4 counts. Participants who experienced PTSD and who had no family support were more likely to be hazardous or harmful users of alcohol and inclined to use drugs. Therefore they miss or stop taking their ARVs, which can be postulated, leads to immunological deterioration and decreases CD4 counts.

6.13 Discussion

To our knowledge, this is the first large systematic investigation of hazardous or harmful alcohol and/or drug use among a representative sample of persons receiving treatment from HIV clinics in South Africa. The results indicate that alcohol and drug use is a significant problem among patients attending HIV clinics, with more males reporting hazardous or harmful alcohol and/or drug use than females. The prevalence of hazardous or harmful use of alcohol (37%) and problematic drug use (13%) are higher than levels documented in other studies on patients attending HIV clinics in South Africa (Olley, *et al.*, 2003; Myer *et al.*, 2008). The reporting of hazardous or harmful drinking among HIV patients is also higher than the findings of studies conducted on HIV patients in Nigeria (Goar *et al.*, 2011; Yunusa *et al.*, 2011). More than half of the males in this study reported problematic alcohol and drug use, which is consistent with other similar studies (Goar *et al.*, 2011; Olley *et al.*, 2003; Shacham *et al.*, 2011).

Our finding that 13% of participants had a drug-related problem is comparable to a previous study in which 9% of HIV-infected persons reported drug dependence in the previous 12 months, while 10% reported drug abuse (Turner *et al.*, 2006). Factors

related to drug use have been found to be a barrier to ARV adherence in this population. Another study among HIV-infected women found that 23% were crack users, while 42% used other drugs and they were less likely to take their ARV medication than their non-drug using counterparts (Sharpe *et al.*, 2004). This is consistent with a study in which drug users tended to have lower levels of adherence to ARVs than non-drug users (Yunusa *et al.*, 2011). However, both a systematic review and meta-analysis support the premise that PLWHA, who use drugs, can achieve good adherence to HAART provided that there is adequate psychosocial support, co-morbidities are addressed, and drug use and HIV treatment are properly managed (Malta, Magnanini, Strathdee, & Bastos, 2008; Malta, Strathdee, Magnanini, & Bastos, 2008). This is encouraging for service providers who provide ARV treatment to PLWHA.

In the present study, more participants with hazardous or harmful alcohol and/or drug use had a diagnosis of TB than those without, and hazardous or harmful use of alcohol directly predicted TB. A systematic review on the association between alcohol use, alcohol-use disorders and TB concluded that there is a causal link between heavy alcohol use and/or alcohol-use disorders and incidence of and re-infection (Rehm *et al.*, 2009). Alcohol use also worsens TB infection, leading to higher rates of defaulting on treatment and possible drug-resistant forms of TB. HIV-positive patients co-infected with TB and abusing substances can complicate their medical care and treatment. This triple diagnosis has implications for treatment providers who provide HIV treatment and care. A systematic review on the impact of alcohol-use disorders on HIV-treatment outcomes, adherence to antiretroviral

therapy and health-care utilization confirms there is decreased utilisation of health care among PLWHA with co-morbid alcohol-use disorders (Azar, *et al.*, 2010).

Male, unemployment, PTSD and psychological distress (anxiety and depression) were all direct predictors of hazardous or harmful use of alcohol. Hazardous or harmful use of alcohol was significant in directly predicting problematic drug use, which directly predicted missing ARVs. Hazardous or harmful use of alcohol and psychological distress were significant in directly predicting missing and stopping ARVs. Missing ARVs was, in turn, significant in directly predicting stopping ARVs, and stopping ARVs and male gender were significant in directly predicting CD4 counts.

Of the 40 participants who were assessed with the MINI, 70% were diagnosed with alcohol dependence and 10% with drug dependence. The prevalence of alcohol-use disorders (abuse and dependence) is much higher than was previously documented in studies conducted in sub-Saharan Africa where hazardous or harmful use of alcohol was reported to range between 2.6% to 24.3% (Farley *et al.*, 2010; Yunusa *et al.*, 2011; Do *et al.*, 2010; Sebit *et al.*, 2003). Similarly, studies in South Africa have reported lower rates of alcohol abuse/dependence in PLWHA than in the current study, ranging from 7% to 12.9% (Olley *et al.*, 2003; Freeman *et al.*, 2007; & Myer *et al.*, 2008). Findings from international studies have also indicated lower rates of current binge drinking, (12.8%), problem drinking (2.8%), heavy drinking (31%) and alcohol dependence (10%) in PLWHA (Mohammed *et al.*, 2004; Sullivan *et al.*, 2008).

The rate of problematic drug use (15%) is comparable to a study by Turner, *et al.*, (2001) who reported that 9% of PLWHA met the criteria for drug dependence in the previous 12 months and 10% abusing drugs. This rate is considerably lower than international studies where current drug use in PLWHA is in the order of 46%-64% (Sullivan *et al.*, 2008; Mellins *et al.*, 2009). More males reported hazardous or harmful use of alcohol and/or drugs which is consistent with other studies conducted in South Africa, where a higher prevalence of problematic alcohol and/or drug use has been reported (Olley *et al.*, 2003; Freeman *et al.*, 2007; Schlebusch & Vawda, 2010).

Hazardous or harmful alcohol use and problematic drug use predicted missing and stopping their ARVs which, in turn, was associated with a decrease in CD4 counts. This is consistent with findings from a study by Cook *et al.* (2001) who reported that hazardous drinkers, heavy drinkers and binge drinkers were more likely to miss a dose of medication or to take medication off-schedule. Similarly, Parson *et al.* (2008) reported on their study that hazardous or harmful drinkers of alcohol were nine times more likely to not adhere to ARVs than their non-drinking counterparts. Ventakesh *et al.* (2010) also reported that alcohol users were over five times more likely to be non-adherent compared to participants who did not use alcohol. In their meta-analysis of the association between alcohol use and ARV adherence, Hendershot, *et al.* (2009) reported that alcohol users were 50%-60% less likely to be adherent to ARVs (OR = 0.548; 95% CI: 0.490 to 0.612) compared to those who abstained from alcohol or drank relatively less. Furthermore, they reported that several factors moderated the

association between alcohol and ARV adherence, such as a higher proportion of men being non-adherent, which is consistent with the findings of this study. Other moderating factors included the quantity of alcohol consumed, which was a more important predictor of non-adherence than frequency of drinking. A higher threshold for adherence (e.g. 100% vs. 90%) was associated with greater difficulties maintaining adherence, suggesting that alcohol use impacts on achieving perfect or near perfect adherence. This is a concern as 95% adherence to ARVs is ideal for viral suppression and patients taking less than 95% of their medication are at risk of developing viral resistance (National Antiretroviral Treatment Guidelines, 2004). PLWHA with an adherence of 95% or greater were reported to have higher CD4 counts, suppressed viral load, and lower hospitalization rates than PLWHA who were non-adherent (Paterson *et al.*, 2000). In addition, poor adherence to ARVs can lead to drug resistance and lower the effectiveness of ARVs leading to the progression of AIDS (Bangsberg *et al.*, 2000).

Dual diagnoses are common in PLWHA and have an impact on ARV adherence and decreased CD4 counts. In this study, 53% of substance abusers met the criteria for major depressive episode (current), 10% of substance abusers met the criteria for panic disorder and 55% of substance abusers were at risk for suicide as assessed by the MINI. Participants with anxiety and depression (as assessed by the K10) and problematic alcohol and/or drug use were more likely to miss or stop taking their ARVs and hence had lower CD4 counts than participants with no anxiety and depression and who did not have an alcohol and/or drug-related problem. Dual diagnoses have been reported in other studies of PLWHA. In one such study, Gaynes, *et al.* (2008) documented that 53% of the participants presenting with a

mood disorder in the previous month, also had an anxiety or substance use disorder. Of those with an anxiety disorder, 62% had a mood disorder or substance use disorder and of those with a substance use disorder, 63% also had a mood or anxiety disorder.

PLWHA with a dual diagnosis (alcohol problems and depressive symptoms) were twice as likely to discontinue ARVs six months later than those who reported having no depressive symptoms (Kim *et al.*, 2007). Depressive symptoms were also found to mediate the relationship between current smoking and ARV adherence (Webb., 2009). Participants in this study who suffered from PTSD and who had no family support were more likely to be hazardous or harmful users of alcohol, inclined to use drugs, and therefore, be non-adherent that leads to a low CD4 count. PTSD was also found to predict psychological distress (anxiety and depression) and significantly impair work, family and social functioning. These findings are consistent with a study by Olley *et al.*, (2005), who reported major depressive disorder, social anxiety disorder and suicidality to be associated with PTSD in PLWHA in South Africa. Their study further documented that PTSD was associated with work impairment and participants' alcohol use as a means of coping, which is also consistent with findings of this study.

In other studies, researchers have also documented that hazardous or harmful use of alcohol and/or drugs and mental health predict lower CD4 counts, poor adherence to ARVs and virologic failure (Berger-Greenstein *et al.*, 2007; Mijch *et al.*, 2006; Tegger *et al.*, 2008; Whetten *et al.*, 2005; DeLorenze, *et al.*, 2010). In addition to

substance abuse, psychological distress is a significant predictor of non-adherence and decreased viral suppression. Therefore, when treating the substance abuse problems in PLWHA, it is important to address mental health concerns as well ensure optimal adherence to ARVs.

In this study, hazardous or harmful alcohol use was a direct predictor of problematic drug use, which in turn, predicted poorer adherence and lower CD4 counts. These findings are consistent with the findings of a study in which problem drinking was reported to be associated with illicit drug use and binge drinking and non-adherence to HAART (Mohammed *et al.*, 2004). Similarly, other studies have documented that active drug users underutilized HAART compared to former and non-drug users and had sub-optimal virologic and immunologic responses to antiretroviral therapy (Lucas *et al.*, 2001).

There are a number of limitations that deserve mentioning. Firstly, the sample was drawn from the Cape Metropole area and may not be representative of the HIV-treatment seeking population across South Africa with regards to patterns of substance use and TB infection. Secondly, the reporting of alcohol and drug use was measured by self-reports and not confirmed by laboratory testing for alcohol and drug abuse. However, it should be noted that a pilot study among PLWHA comparing self-report alcohol and drug use with urine and hair tests reinforced the value of self-report data on alcohol and drugs (Kader, Seedat, Koch & Parry, 2012). Thirdly, only cross-sectional data were collected which weakens any causal attributions regarding the effect of hazardous and harmful use of alcohol on health

and other outcomes of PLWHA. Fourthly, the 303 screened for substance abuse and 304 with no substance abuse were not randomly selected. Fifthly, investigation of a larger sample of participants with problematic drug use is needed to undertake multivariate analysis with drug use as a predictor variable. Finally, ARV adherence was self-reported and patients could be biased in their response and more importantly patients did not know the names of their ARVs and often confused their ARVs with their other medication. This posed as a challenge in attempting to collect data on their level of adherence, more objective means of collecting ARV adherence data should be considered.

Despite these limitations, this study makes an important contribution in identifying multiple predictors of ARV adherence and CD4 count and the association with health outcomes of PLWHA. However, of importance and to our knowledge, this is the first large systematic investigation of problematic alcohol and drug use and psychiatric disorders in a representative sample of persons receiving treatment from HIV clinics in South Africa. Therefore, it can form the basis for replication studies in other parts of the country.

6.14 Conclusion

Based on the findings of this study it is evident that problematic alcohol and other drug use and psychiatric disorders result in substantial health problems among PLWHAs and contributes to the burden of HIV disease. The importance of screening patients with HIV for problematic alcohol and/or drug use and for psychiatric disorders is crucial. Untreated substance abuse and psychiatric disorders in this

population may result in HIV treatment being less effective owing to compromised adherence and on-going risk behaviour. With almost two million South Africans now receiving ARVs, this is an issue that requires urgent attention.

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Table 6.1: Demographic characteristics of the sample

	N	%
Mean Age (35.83) SD = 8.5		
Gender		
Male	452	30.1
Female	1051	69.9
Race		
Black	1337	89.0
Asian	1	0.1
Coloured	155	10.3
Other	10	0.7
Current marital status		
Single	950	63.2
Widowed	56	3.7
Separated	36	2.4
Divorced	47	3.1
Married or living with a significant other	414	26.5
Current living situation		
Live alone	180	12.0
Live with other adults, no children	282	18.8
Live with other adults and children	765	50.9
Live with children	274	18.2
Live in an institution or retirement home	2	0.1
Highest level of education completed		
No formal education	104	6.9
Completed primary school	256	17.0
Attended high school but did not complete matric	897	59.7
Completed matric	210	4.0
Attended university, college or technikon but did not graduate	16	1.1
Graduated from university, college or technikon	20	1.3
Current work situation		
Employed full time	274	18.2
Employed part time	196	13.0
Student	17	1.1
Unemployed	991	65.9
Disabled	21	1.4
Homemaker	3	0.2
Retired	1	0.1
Monthly family income		
Less than R1 000	916	60.9
R1 001-R5 000	556	37.0
R5 001-R10 000	15	1.0
R10 001-R20 000	3	0.2
Don't Know	13	0.9

Table 6.2: AUDIT and DUDIT

	Males		Females		Total		Chi-square	
	N	%	N	%	N	%	df	p
AUDIT							2	0.00
Does not consume alcohol	194	42.9	695	66.1	889	59		
No drinking problem	23	5.1	41	3.9	64	4		
Harmful or hazardous drinking	235	52.0	315	30.0	550	37		
DUDIT							2	0.00
Does not take drugs	333	73.7	975	92.8	1 308	87		
No drug problem	2	0.4	1	0.1	3	0.2		
Drug problem	117	25.9	75	7.1	192	12.8		

* Cut-off score on DUDIT is ≥ 2 for females and ≥ 6 for males

*Cut-off score on AUDIT is ≥ 8 for males and females

* Row percentages were used

Table 6.3: Substance abuse, gender, opportunistic infections and TB

	Non substance abuse		Substance abuse		P-value	df
	N	%	N	%		
Gender					0.000	1
Males	185	40.93	267	59.07		
Females	713	67.84	338	32.16		
Opportunistic Infections					0.362	1
Yes	99	11.02	76	12.56		
No	799	88.98	529	87.44		
TB					0.038	1
Yes	97	10.08	87	14.04		
No	801	89.02	518	85.06		

* Row percentages were used

Table 6.4: Mental health and ARV adherence

	N	%	*Male (%)	*Female (%)
Depression (CES -D)				
No depression	374	61.6	35.6	64.4
Mild depression	131	21.6	30.5	69.5
Major depression	102	16.8	23.5	76.5
Anxiety & Depression (K10)				
Likely to be well	329	54.2	36.5	63.5
Likely to have mild disorder	109	18.0	28.4	71.6
Likely to have moderate disorder	67	11.0	31.3	68.7
Likely to have severe disorder	102	16.8	24.5	75.5
Trauma				
No trauma	199	32.8	29.1	70.9
Trauma	61	10.0	24.6	75.4
Stopped taking ARVs				
Yes	101	16.6	34.7	65.3
No	436	71.8	31.0	69.0
Missed taking ARVs				
Yes	217	35.7	37.8	62.2
No	320	52.7	27.5	72.5

* 32.5% of the sample were males and 67.5% of the sample were females

Table 6.5: Socio-demographic and mental health determinants of hazardous or harmful use of alcohol: linear regression analysis

Independent Variables	B	t-value	p
Gender	-0.234	-5.873	0.000
Work	0.066	1.475	0.141
Level of education	-0.019	-0.471	0.638
Income	-0.081	-1.835	0.067
Depression (CES-D)	0.121	2.358	0.019
Anxiety & Depression (K10)	0.123	2.399	0.017
Family support	-0.030	-0.755	0.451

Dependent variable: AUDIT

Table 6.6: Predictors of major depression, problematic drug use and ARV adherence

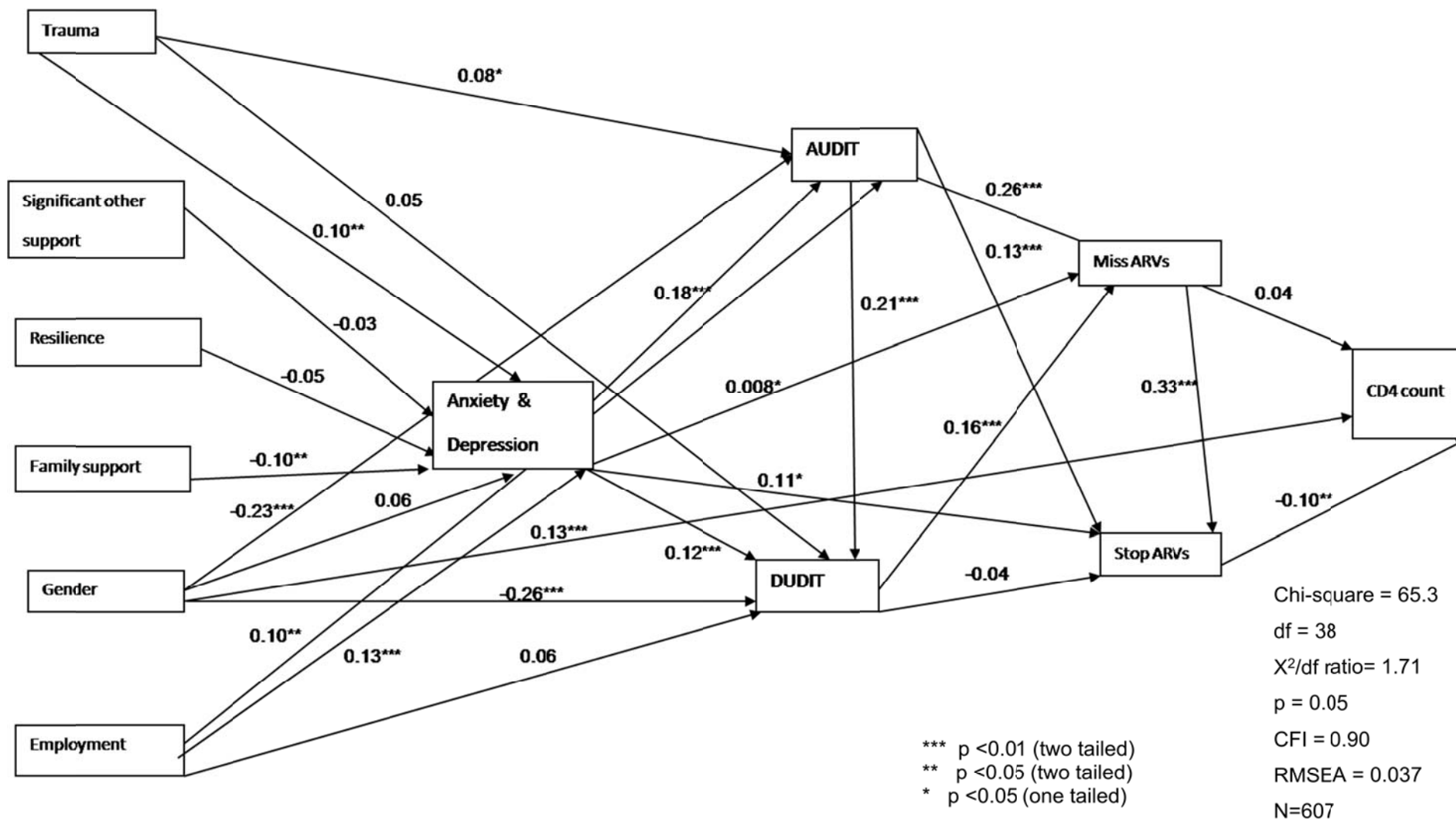
Variables	B	S.E.	df	Exp(B)	CI (95%)	p
Major depression:						
Age	0.000	0.024	1	1.000	0.954-1.048	0.995
AUDIT	0.044	0.018	1	1.045	1.010-1.082	0.012
Family support	-0.300	0.112	1	0.741	0.594-0.923	0.008
Resilience	-0.468	0.266	1	0.626	0.372-1.054	0.078
Work	-0.478	0.458	1	0.620	0.253-1.521	0.297
DUDIT	0.003	0.507	1	1.003	0.371-2.710	0.996
Trauma	-2.305	0.430	1	0.100	0.043-0.232	0.000
Problematic drug use:						
Depression (CES-D)	0.246	0.199	1	1.279	0.865-1.891	0.217
Anxiety & Depression (K10)	0.293	0.133	1	1.340	1.033-1.740	0.028
Gender	1.739	0.255	1	5.692	3.455-9.378	0.000
Work	-0.710	0.298	1	0.492	0.274-0.697	0.882
ARV adherence:						
Stopped ARVs:						
AUDIT	0.047	0.011	1	1.048	1.026-1.071	0.000
Depression (CES-D)	0.430	0.188	1	1.537	1.064-2.222	0.022
Anxiety & Depression (K10)	0.088	0.130	1	1.092	0.847-1.408	0.498
Resilience	-0.379	0.152	1	0.685	0.508-0.922	0.013
DUDIT	-0.022	0.327	1	0.979	0.516-1.857	0.947
Gender	-0.012	0.266	1	0.988	0.587-1.664	0.964
Missed ARVs:						
AUDIT	0.053	0.009	1	1.054	1.035-1.074	0.000
Depression (CES-D)	0.437	0.163	1	1.549	1.124-2.134	0.007
Anxiety & Depression (K10)	-0.018	0.112	1	0.982	0.788-1.224	0.871
Resilience	-0.126	0.129	1	0.882	0.684-1.136	0.330
DUDIT	-0.894	0.298	1	0.409	0.228-0.734	0.003
Gender	0.184	0.217	1	1.202	0.786-1.838	0.395
Forget to take ARVs:						
AUDIT	0.049	0.010	1	1.050	1.030-1.070	0.000
Depression (CES-D)	0.354	0.167	1	1.425	1.026-1.978	0.034
Anxiety & Depression (K10)	-0.037	0.116	1	0.963	0.767-1.210	0.749
Resilience	-0.066	0.136	1	0.936	0.718-1.221	0.628
DUDIT	-0.511	0.288	1	0.600	0.341-1.055	0.076
Gender	-0.181	0.232	1	0.835	0.529-1.316	0.437
Careless about taking ARVs:						
AUDIT	0.072	0.574	1	1.075	1.052-1.098	0.000
Depression (CES-D)	0.516	0.189	1	1.675	1.156-2.427	0.006
Anxiety & Depression (K10)	-0.276	0.136	1	0.759	0.581-0.991	0.042
Resilience	-0.150	0.154	1	0.861	0.636-1.165	0.331
DUDIT	-0.715	0.310	1	0.489	0.266-0.898	0.021
Gender	-.0352	0.268	1	0.704	0.416-1.190	0.190

Table 6.7: Socio-demographic and clinical determinants of CD4 counts:**Linear regression analysis**

Independent Variables	B	t-value	p
Age	0.088	1.965	0.050
Gender	0.128	2.824	0.005
Opportunistic infections	0.071	1.644	0.101
AUDIT	-0.016	-0.343	0.731
Stopped ARVs	-0.086	-1.936	0.053
Duration of HIV diagnosis	0.234	5.386	0.000
Family income	0.038	0.872	0.384
Level of education	0.012	0.267	0.789

Dependent variable: CD4 count

Figure 6.2: Factors predicting psychological distress, problematic alcohol and/or drug use, ARV adherence and CD4 count



CHAPTER 7: CONCLUSION AND RECOMMENDATIONS

To our knowledge, this is the first large systematic investigation of hazardous or harmful use of alcohol and/or drug use, ARV adherence and psychiatric disorders among a representative sample of patients receiving treatment from HIV clinics in South Africa. The findings of this study further confirm findings from other studies that hazardous or harmful use of alcohol and/or drugs are associated with poor ARV adherence, low CD4 counts, more rapid HIV-disease progression and poorer health outcomes in PLWHA (Farley, Miller, Zamani, Tepper, Morris *et al.*, 2010; Hendershot, Stoner, Pantalone & Simoni, 2009; Lucas *et al.*, 2001; Neblett *et al.*, 2011). Additionally, psychiatric disorders in this population were also associated with poor ARV adherence, low CD4 counts and poorer health outcomes as documented in other studies (Creuss *et al.*, 2003; Kim *et al.*, 2007; Barfod *et al.*, 2005). Problematic alcohol and/or drug use were significantly associated with a diagnosis of major depressive episode (current), panic disorder (current) and a high risk of suicide, as assessed on the MINI. Dual diagnosis was common in this population and was associated with poor adherence and lower CD4 counts.

With the increasing availability of ARVs in South Africa, the challenge is now to ensure that PLWHA who present with co-occurring disorders they are adherent to these life-prolonging medications. This can only be done if the health system focuses on providing a service that addresses all three conditions (HIV, substance abuse and psychiatric disorders) in an integrated manner. Separate service provision has proven to be less effective than an integrated treatment plan (Parry *et al.*, 2007).

The findings of this study underscore the need for a multidisciplinary approach to managing substance-use disorders and/or psychiatric disorders in PLWHA. Screening for substance use and psychiatric disorders should be standard practice and should be conducted routinely at primary health-care centres. Screening instruments will easily help detect substance abuse or psychiatric problems. Screening instruments are cost effective and can be easily administered by any health professional required they are given the proper training. For example, when using the AUDIT as a screening instrument; patients who are screened as low-risk drinkers should be given information about the risks of drinking. Medium-risk drinkers could be given simple advice, brief counselling and their drinking monitored at follow-up visits and patients who are high-risk drinkers could be referred to a specialist for further diagnosis and treatment (Babor *et al.*, 2001). In addition, treatment providers should inquire about drug use and poly-drug use before prescribing ARVs (Peretti-Watel, Spire, Lert, Obadai & the Vespa Group, 2006). For screening for a psychiatric diagnosis in patients the MINI can be utilised. The MINI is a useful tool in assessing for co-occurring disorders. This is especially important as most patients with HIV present with co-occurring psychiatric disorders. Furthermore, the MINI does not have to be administered by a specialist but other health professionals can also be trained in administering the MINI. The importance of intervention at PHC level is emphasised in the Western Cape Healthcare 2020 Plan especially since this is the first point of contact for the patient. Healthcare 2020 speaks to PHC providing a comprehensive package of care that includes preventive, promotive, curative and rehabilitative care and should be supported by other levels of care such as acute and specialised referral hospitals (Western Cape Government, 2011).

Primary health-care workers should also be cross-trained to identify these disorders and refer appropriately where necessary (Parry *et al.*, 2010). If psychopathology and problematic alcohol and drug use are picked up early in treatment and given the appropriate treatment and interventions are initiated timeously, this can improve ARV adherence and health outcomes could possibly be secured (Campos, Guimaraes & Remien, 2010). Recommendations have also been made to improve adherence using some form of Daily Observed Treatment System (DOTS) that could be rolled out to patients at primary health-care facilities and includes family and friends (Parry *et al.*, 2010). Furthermore, PLWHA should be referred for active case management to limit re-infection or non-adherence to medication.

7.1 Policy issues and implications

Planners and/or policy makers of HIV/AIDS programmes in developing countries have not given due attention to the prevalence of mental health problems and associated needs in PLWHA for various reasons, such as lack of resources, not recognizing the burden of mental disorders, stigma, and the low prioritisation of mental health generally (Freeman *et al.*, 2007). Currently, these services are offered independently of each other and are highly fragmented in South Africa. In the context of scarce resources, staff shortages, over-burdened treatment facilities, difficulty accessing treatment facilities, and poor planning and fragmentation of services, it is understandable that little focus has been placed on addressing HIV and important allied health-related problems such as alcohol and drug abuse and mental health in an integrated manner. The fact that HIV services are currently managed by the

Department of Health, while substance abuse services are managed by the Department of Social Development is further indication that insufficient progress has been made in ensuring proper integration of these problems at a policy level. Consequently, proper integration of services at a programmatic level is also affected. On a structural, policy and programmatic level, these matters need to be urgently addressed to provide a service that will ultimately be cost-effective and beneficial for the government and for individuals living with HIV/AIDS. If possible, referral to mental health services should be part of the infrastructure of local and district health-care centres in addressing the mental health needs of PLWHA. There should be close collaboration between HIV services and mental health services so that specialist mental health workers can provide supervision for HIV health-care workers dealing with mental health problems (Collins *et al.*, 2006).

This integration of services is further emphasized in the Healthcare 2020 Plan of the Western Cape government which states that the focus for future intervention and management of the burden of disease (HIV/AIDS, TB, injuries, non-communicable diseases including mental illness and women's and childhood illness) should focus on a comprehensive integrated burden of disease package of care to achieve the desired health outcomes. The document refers to an Ecological Model of Risk which targets risk factors through the following levels:

- a. "downstream" interventions which mainly focus on the individual and the biological and behavioral factors that impact on the burden of disease,

- b. “midstream” interventions which mainly focus on groups of people such as institutions and communities, and
- c. “upstream” interventions which focus on the broader society.

The document recognizes the importance of these levels of intervention being addressed in an intersectoral manner that includes various government departments, CBOs, NGOs, primary healthcare services and specialised hospital services (Western Cape Government, 2011). Hence an intersectoral and integrated approach in the holistic management PLWHA with a substance abuse problem and/or psychiatric disorder seems to be the most appropriate and cost effective approach to achieving the desired health outcomes.

Policy makers should focus on developing specific and integrated adherence treatment models, such as the development of effective ARV-adherence interventions, which specifically address management of co-occurring substance use and psychiatric disorders among PLWHA. This intervention model should be integrated into substance abuse settings (Gonzalez *et al.*, 2011). Parry *et al.* (2010) further suggest that integration of alcohol and HIV (and TB services) should be considered to ensure that patients are seen at a single facility. Cross-training staff at HIV, STI and TB clinics, substance abuse centres and at mental health in- and out-patient facilities should be considered. Cross-training should focus on the link between substance abuse, mental health problems and HIV/AIDS, and on screening. Brief interventions and appropriate referral for alcohol problems in HIV settings, and

screening for alcohol-related sexual risk and referral to VCT voluntary counselling and testing in substance abuse settings (Parry *et al.*, 2010).

An integrated and comprehensive treatment plan that provides interventions on an individual level and addresses the individual's cognitive and social functioning, gender, culture, economic and environmental circumstances is important. Equally important, is addressing basic survival needs (food, housing) and spiritual needs and combining this with mental health, substance abuse and long-term HIV care (Parry *et al.*, 2007).

Furthermore, greater attention should be focused on advocacy around alcohol and HIV. This could be done in the form of written articles (medical and nursing journals and popular magazines) that reach the broader society. The focus of these publications should be on the harmful effects alcohol has on HIV medication and adherence and disease progression (Parry *et al.*, 2010). In addition, information on the impact of mental disorders on the health status of PLWHA should also be provided with emphasis on the relationship between substance abuse, mental disorders and HIV. As part of continuing education, awareness and information, departments of health, departments of social development and other departments in government should invest in educational initiatives, such as the distribution of educational material to the public on the harmful effects that alcohol and drugs and psychiatric disorders in HIV/AIDS.

There are many challenges that also need to be addressed, both on an individual and societal level. Research has shown, in South Africa that, PLWHA have low levels of mental health literacy and stigmatize psychiatric conditions. PLWHA also have a negative attitude towards individuals with psychiatric conditions. Recommendations are that this should be addressed by developing interventions that are appropriate for addressing the low levels of mental health literacy and the stigmatization of psychiatric disorders as well as educating PLWHA about the importance of psycho-pharmacotherapy in the treatment of psychiatric disorders (Sorsdahl, 2010).

7.2 Future research needs

Although research has shown a clear link between mental disorders, substance abuse and HIV, this has mainly been in developed countries. Future research in South Africa should be focussed more on substance abuse and mental health problems experienced by PLWHA. Research should specifically focus on factors such as the substance abusing behaviours (quantity and frequency of use), personality traits, psychiatric symptoms, the socio-economic conditions and structural barriers and how these factors impact on HIV-medication adherence (Kagee & Delport, 2010; Coetzee *et al.*, 2011). More research should be conducted on the psycho-social factors such as poverty, unemployment, support structures/networks, social, political, cultural and individual factors that contribute towards mental illness and substance abuse. Interventions to address these problems would help policymakers to direct the allocation of scarce human and financial resources (Brandt, 2009). Epidemiological research needs to be conducted

on problematic alcohol use among newly infected HIV cases and to assess the risk for psychiatric disorders and substance use disorders between problematic drinkers and non-problematic drinkers.

The current study highlighted the impact of alcohol, drugs and psychiatric conditions on ARV adherence and CD4 count. While there seems to be much focus on alcohol and its harmful effects on ARV adherence and disease progression, of equal importance but a neglected area especially in South Africa is investigating the harmful effects of illicit drug use on ARV adherence and its impact on the health outcomes of PLWHA as shown in this study.

In addition, more qualitative research investigating PLWHA experiences that contribute towards them abusing substances and developing psychiatric conditions would be useful for the planning of intervention models. Research on the longer term effects mental disorders and treatment needs in PLWHA is also required (Brandt, 2009). Further exploration of the biological effects of alcohol and drugs and psychiatric conditions on the immune system and on the worsening of existing infections should be considered. As this study was a cross-sectional one, longitudinal studies that focus on the predictors of mental health and substance abuse and their association with poor adherence and disease progression should be conducted. This may help inform future interventions about ARV adherence and improve health outcomes (Chander *et al.*, 2006).

Further priority areas for research were identified at a technical meeting on alcohol and infectious diseases in Cape Town in 2012. Firstly, baseline information on patterns of drinking, risky HIV-sexual behaviours and information on treatment and adherence to ARVs and TB medication is required among HIV and TB patients. Secondly, randomised control trials (RCTs) are needed to evaluate alcohol focused-interventions that are evidence-based on reducing the risk of uninfected people acquiring HIV. Thirdly, RCTs evaluating evidence-based alcohol-focused interventions among persons initiating treatment for HIV and/or TB and their adherence to treatment is required (Parry, Ferreira-Borges, Poznyak, Lonroth & Rehm, in press).

Finally, more intervention studies are needed in South Africa, specifically a comparison of brief interventions vs. more long-term intensive interventions that address problems related to alcohol use, common mental disorders, and non-adherence as well as exploration of cost and feasibility issues in the treatment of PLWHA (Parry *et al.*, 2010).

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APPENDIX

QUESTIONNAIRES

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

Title of project: **The relationship between substance abuse, health status and health behaviours of patients attending HIV clinics**

Principal Investigator: Rehana Kader

Address: Alcohol and Drug Abuse Research Unit, MRC
Francie van Zijl Drive, Parow Valley
PO Box 19070
Tygerberg
7505

You are being asked to take part in a research project. Please take some time to read this form that will explain the project to you. If you have any questions or if you do not know what the study is asking of you please ask the people doing the study to help you. Your taking part is fully voluntary and you are free to refuse to take part in the study. If you say no that is okay. You have the right to stop being in the study at any time.

What is this study all about?

This study has two parts; the first part is looking at drug and alcohol use in patients who attend HIV clinics. The second part looks at how drugs and alcohol affects people living with HIV and your taking of anti retrovirals. This study will also try to learn about the link between people living with HIV and drugs and alcohol abuse. We also want to know if you have any emotional problems living with HIV.

Today we will start off by asking you about your drug and alcohol use. We will also ask you some private facts (e.g. your age, where you live, your level of schooling, etc). It will take you about 10 minutes to answer these questions.

Why have you been asked to take part in this study?

You were asked to be part of this study because this study wants to make drug and alcohol abuse and mental health services more easy to access when you come for your HIV treatment and care.

Will you benefit from taking part in this research?

There are no direct or private gains for you but the facts you provide will help us to improve health care at the clinics for you and others.

Are there any risks for you if you take part in this research?

There will be no harm or risks in you taking part in this study. You don't have to put your name on any of the forms used to collect data.

If you do not agree to take part, what options do you have?

You can refuse to be in this study. If you say no that is okay. You have the right to stop being in the study at any time.

Who will have rights to your clinical records?

The facts taken from your clinic files will be treated as private and will be kept in a locked cupboard. The facts will be used to write up a report but there will be no mention of your name.

Is there anything else that you should know or do?

If you have any questions about your rights as a subject, concerns or complaints, please call the Committee for Human Research at Stellenbosch University at 021-938-9207. If you have questions about the project you can also call Ms. Rehana Kader from the MRC at 021-938-0417.

Declaration by participant

By signing below, I agree to take part in a research study entitled (*The relationship between substance abuse, health status and health behaviours of patients attending HIV clinics*)

I declare that:

I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.

I have had a chance to ask questions and all my questions have been adequately answered.

I understand that taking part in this study is voluntary and I have not been pressurised to take part. I may choose to leave the study at any time and will not be penalised or prejudiced in any way. I may be asked to leave the study before it has finished, if the researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) on (*date*) 2011.

-----	-----
Signature of subject	Signature of witness

Declaration by investigator

I (*name*) declare that:

I explained the information in this document to

I encouraged him/her to ask questions and took adequate time to answer them.

I am satisfied that he/she adequately understands all aspects of the research, as discussed above

I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*)

Signed at (*place*) on (*date*) 2011.

Signature

The International HIV Dementia Scale

Memory-Registration – Give four words to recall (dog, hat, bean, red) – 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 – 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.

SECTION A: DEMOGRAPHIC INFORMATION

1. What is your gender?

Male	
Female	

2. What is your age? _____

3. What is your date of birth? _____

4. What is your current marital status?

Single	
Widowed	
Separated	
Divorced	
Married or living with a significant other in a marriage-like relationship	

5. What is your race/origin?

Black	
White	
Asian	
Coloured	
Other	

6. What is your current living situation?

Live alone	
Live with other adults(s), no children	
Live with other adults and children	
Live with children	
Live in an institution or retirement home	

7. Please select the highest level of education that you have completed:

No formal education	
Completed primary school	
Attended high school but did not complete matric	
Completed matric	
Attended university, college or Technikon but did not graduate	
Graduated from university, college or Technikon	

8. What is your current work situation?

Employed full time	
Employed part time	
Student	
Unemployed	
Disabled	

Homemaker	
Retired	

9. Which of the following best describes your approximate monthly family income from all sources, before taxes?

Less than R1 000	
R1001 –R5 000	
R5 001-R10 000	
R10 001-R20 000	
R20 001-R30 000	
R30 001-R40 000	
R40 001 and above	
Don't know	

SECTION B: HEALTH STATUS (from clinic records)

Clinic file no: _____

1. Date of HIV Diagnosis: Month_____ Year_____

2. CD 4 count (current): _____

3. Lowest CD 4 count in the last 12 months _____ Date _____

4. Are you on ARV's

YES	NO
-----	----

5. If yes, when did you start your treatment? Month _____ Year _____

6. Do you have TB?

YES	NO
-----	----

7. Date of TB diagnosis: Month_____ Year_____

8. When did you start your TB treatment? Month_____ Year_____

9. Do you have any opportunistic infections?

YES	NO
-----	----

10. If yes, what infections do you have? _____

AUDIT**The Alcohol Use Disorders Identification Test: THE AUDIT [English Version]**

Read questions as written. Record answers carefully. Begin the AUDIT by saying "Now I am going to ask you some questions about your use of alcoholic beverages during this past year." Explain what is meant by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Circle correct answer number.

1. How often do you have a drink containing alcohol?

(0) Never [**Skip to Qs 9-10**]

(1) Monthly or less

(2) 2 to 4 times a month

(3) 2 to 3 times a week

(4) 4 or more times a week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?

(0) 1 or 2

(1) 3 or 4

(2) 5 or 6

(3) 7, 8, or 9

(4) 10 or more

3. How often do you have six or more drinks on one occasion?

(0) Never

(1) Less than monthly

(2) Monthly

(3) Weekly

(4) Daily or almost daily

Skip to Questions 9 and 10 if Total Score for Questions 2 and 3 = 0

4. How often during the last year have you found that you were not able to stop drinking once you had started?

(0) Never

(1) Less than monthly

(2) Monthly

(3) Weekly

(4) Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?

(0) Never

(1) Less than monthly

(2) Monthly

(3) Weekly

(4) Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session? (0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily	<input type="checkbox"/>
7. How often during the last year have you had a feeling of guilt or remorse after drinking? (0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily	<input type="checkbox"/>
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking? (0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily	<input type="checkbox"/>
9. Have you or someone else been injured as a result of your drinking? (0) No (2) Yes, but not in the last year (4) Yes, during the last year	<input type="checkbox"/>
10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down? (0) No (2) Yes, but not in the last year (4) Yes, during the last year	<input type="checkbox"/>
TOTAL SCORE	<input type="checkbox"/>

DUDIT

DUDIT Drug Use Disorders Identification Test [English Version]

Here are a few questions about drugs. Please answer as correctly and honestly as possible by indicating which answer is right for you.

Name of drug used: (see list of drugs on back side)

1. How often do you use drugs other than alcohol?

(0) Never **[skip to question 10 & 11]**

(1) Once a month or less

(2) 2 to 4 times a month

(3) 2 to 3 times a week

(4) 4 times a week or more often

2. Do you use more than one type of drug on the same occasion?

(0) Never

(1) Once a month or less

(2) 2 to 4 times a month

(3) 2 to 3 times a week

(4) 4 times a week or more often

3. How many times do you take drugs on a typical day when you use drugs?

(0) 0

(1) 1-2

(2) 3-4

(3) 5-6

(4) 7 or more

4. How often are you influenced heavily by drugs?

(0) Never

(1) Less than once a month

(2) Every month

(3) Every week

(4) Daily or almost every day

5. Over the past year have you felt that your longing for drugs was so strong that you could not resist it?

(0) Never

(1) Less than once a month

(2) Every month

(3) Every week

(4) Daily or almost every day

6. Has it happened, over the past year that you have not been able to stop taking drugs once you started?

(0) Never

(1) Less than once a month (2) Every month (3) Every week (4) Daily or almost every day	<input type="checkbox"/>
7. How often over the past year have you taken drugs and then neglected to do something you should have done?	
(0) Never (1) Less than once a month (2) Every month (3) Every week (4) Daily or almost every day	<input type="checkbox"/>
8. How often over the past year have you needed to take a drug the morning after heavy drug use the day before?	
(0) Never (1) Less than once a month (2) Every month (3) Every week (4) Daily or almost every day	<input type="checkbox"/>
9. How often over the past year have you had guilt feelings or a bad conscience because you used drugs?	
(0) Never (1) Less than once a month (2) Every month (3) Every week (4) Daily or almost every day	<input type="checkbox"/>
10. Have you or anyone else been hurt (mentally or physically) because you used drugs?	
(0) No (2) Yes, but not over the past year (4) Yes, during the past year	<input type="checkbox"/>
11. Has a relative or a friend, a doctor or a nurse, or anyone else, been worried about your drug use or said to you that you should stop using drugs?	
(0) No (2) Yes, but not over the past year (4) Yes, during the past year	<input type="checkbox"/>
TOTAL SCORE	<input type="checkbox"/>

Name of drug/over the counter medication: _____

Active ingredients in drug/over the counter medication: _____

LIST OF DRUGS

(Note! Not alcohol)

Cannabis	Ampheta- mines	Cocaine	Opiates	Hallucinogens	Solvents/ inhalants	GHB and others
Marijuana Hash Hash oil	Methampheta- mine Phenmetraline Khat Betel nut Ritaline (Methylpheni- date)	Crack Freebase Coca leaves	Smoked heroin Heroin Opium	Ecstasy LSD (Lisergic acid) Mescaline Peyote PCP, angel dust (Phencyclidine) Psilocybin DMT (Dimethyltryptamine)	Thinner Trichlorethylene Gasoline/petrol Gas Solution Glue	GHB Anabolic steroids Laughing gas (Halothane) Amyl nitrate (Poppers) Anticholinergic compounds

PILLS – MEDICINES

Pills count as drugs when you take

- more of them or take them more often than the doctor has prescribed for you
- pills because you want to have fun, feel good, get "high", or wonder what sort of effect they have on you
- pills that you have received from a relative or a friend
- pills that you have bought on the "black market" or stolen

SLEEPING PILLS/SEDATIVES			PAINKILLERS		
Alprazolam	Glutethimide	Rohypnol	Actiq	Durogesic	OxyNorm
Amobarbital	Halcion	Secobarbital	Cocclana-Etyfin	Fentanyl	Panocod
Apodorm	Heminevrin	Sobril	Citodon	Ketodur	Panocod forte
Apozepam	Iktorivil	Sonata	Citodon forte	Ketogan	Paraflex comp
Aprobarbital	Imovane	Stesolid	Dexodon	Kodein	Somadril
Butabarbital	Mephobarbital	Stilnoct	Depolan	Maxidon	Spasmofen
Butalbital	Meprobamate	Talbutal	Dexofen	Metadon	Subutex
Chloral hydrate	Methaqualone	Temesta	Dilaudid	Morfin	Temgesic

Diazepam	Methohexital	Thiamyal	Distalgesic	Nobligan	Tiparol
Dormicum	Mogadon	Thiopental	Dolcontin	Norflex	Tradolan
Ethchlorvynol	Nitrazepam	Triazolam	Doleron	Norgesic	Tramadul
Fenemal	Oxascand	Xanor	Dolotard	Opidol	Treo comp
Flunitrazepam	Pentobarbital	Zopiklon	Doloxene	OxyContin	
Fluscand	Phenobarbital				

Pills do NOT count as drugs if they have been prescribed by a doctor and you take them in the prescribed dosage.

QUESTIONNAIRES [English Version]

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT: The relationship between substance abuse, health status and health behaviours of patients attending HIV clinics

PRINCIPAL INVESTIGATOR: Rehana Kader

ADDRESS: Alcohol and Drug Abuse Research Unit, MRC
Francie van Zijl Drive, Parow Valley
PO Box 19070
Tygerberg
7505

CONTACT NUMBER: 021-9380417

You are being asked to take part in a research project. Please take some time to read this form that will explain the project to you. If you have any questions or if you do not know what the study is asking of you please ask the people doing the study to help you. You are taking part of your own free will and you are free to refuse to take part in the study. If you say no that is okay. You have the right to stop being in the study at any time.

What is this study all about?

This study looks at how drugs and alcohol affects people living with HIV and who are taking anti retrovirals. This study will also try to learn about the link between people living with HIV and drugs and alcohol abuse. We also want to know if you have any emotional problems living with HIV.

Why have you been asked to take part in this study?

You were asked to take part in this study because this study wants to make it easy for you to get help with your drug and alcohol and mental health problems.

Will you gain from taking part in this research?

There are no direct or private gains for you but the facts you provide will help us to improve health care at the clinics for you and others.

Are there any risks if you take part in this research?

There will be no harm or risks in you taking part in this study. Some of the questions might make you feel awkward as they ask about private issues like your own drug use,

your sexual actions and any emotional problems you have. There will be a person to counsel you if you need to talk more about your problems. You will not be asked to put your name on any of the forms used to collect details about you.

If you do not agree to take part, what options do you have?

You can choose if you want to be in this study. If you say no, that is okay. You have the right to stop being in the study at any time.

Who will have rights to your clinic files?

Any facts taken from your clinic files will be treated as private and will be kept in a locked cupboard. The facts will be used to write up a report but there will be no mention of your name.

Will you be paid to take part in this study and will there be any costs for you?

You will be given a R50 voucher for your time. There will be no costs for you, if you do take part in this study.

Is there anything else that you should know or do?

If you have any questions about your rights, your concerns or complaints, please call the Committee for Human Research at Stellenbosch University at 021-938-9207. If you have questions about the project you can also call Ms. Rehana Kader from the MRC at 021-938-0417.

Signed by subject

By signing below, I agree to take part in this study

Signed at (*place*) on (*date*)
2011.

Signature of subject

Signature of witness

SUBSTANCE ABUSE QUESTIONNAIRE
(Drugs and/or Alcohol)

NSA

If the person does not abuse drugs and/or alcohol please tick the box on the right hand corner and move on to the next questionnaire.

Have you ever used/abused any substances (drugs and/or alcohol)?

Yes	No
-----	----

What was the substance? -----

How old were you when you first used drugs and/or alcohol? -----

Do you smoke cigarettes?

Yes	No
-----	----

If yes, how many cigarettes do you smoke on a typical day? -----

At what age did you start smoking cigarettes? -----

Have you ever received treatment for drugs and/or alcohol?

Yes	No
-----	----

Do you think you have a problem with drugs and/or alcohol?

Yes	No
-----	----

Would you like to get help to deal with your drug and/or alcohol problem?

Yes	No
-----	----

Refer to guidelines below before asking this question.

	(i) Current substances by name (<i>write in one per line</i>)	(ii) Routes of administration (<i>circle all relevant codes</i>)					(iii) Frequency past month (<i>circle one code</i>)				(iv) Age at 1 st use (years)	Quantity In a typical day of using	Type of drug used
		1	2	3	4	5	a	b	c	d			
1 st most frequently used		1	2	3	4	5	a	b	c	d			
2 nd most frequently used		1	2	3	4	5	a	b	c	d			
3 rd most frequently used		1	2	3	4	5	a	b	c	d			
4 th most frequently used		1	2	3	4	5	a	b	c	d			

(ii) Route: 1=swallow, 2=smoke, 3=snort/sniff, 4=inject, 5=other

(iii) Frequency: a=daily, b=2-6 days per week, c=Once per week or less often, d=not used in past month

ARV ADHERENCE SELF ASSESSMENT

If the person is not on ARV's please tick the box on the right hand corner and move on to next questionnaire

Instructions for Patient: Circle on the line below at the point showing your best guess about how much of each drug you have taken in the last 3 to 4 weeks.

0% means you have taken none of the drug

50% means you have taken half of the drug

100% means you have taken every single dose of the drug

DRUG (ARV) A: 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

DRUG (ARV) B: 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

DRUG (ARV) C: 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

DRUG (ARV) D: 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Morisky Scale to Assess Adherence to HIV Medications:		
Dichotomous Response Options		
Subjects were asked:	NO	YES
"Thinking about the medications PRESCRIBED (ARV's) to you by your doctor(s), please answer the following questions."		
Do you ever forget to take your medications?		
Are you careless at times about taking your medications?		
When you feel better, do you sometimes stop taking your medications?		
Sometimes if you feel worse when you take your medications, do you stop taking them?		

No Trauma

Instructions for Davidson Trauma Scale

Please read this to the patient.

Have you ever experienced or witnessed or had to deal with an extremely traumatic event that included actual or threatened death or serious injury to you or someone else?

Examples of such events include: serious accidents, sexual or physical assault, kidnapping, fire discovering a body, sudden death of someone close to you, war or natural disaster, or the experience of being diagnosed with/having HIV.

If the person did not experience a traumatic event then please tick the box on the right and corner and move on to the next questionnaire.

If yes, then you should follow it up with this question:

If you have experienced more than one of these traumas, then please select the one that has affected you the most.

What was the trauma experienced: _____

If the person has experienced a trauma now please turn to the next page and answer the questions.

DAVIDSON TRAUMA SCALE

In the past week, how much trouble have you had with the following symptoms?	
FREQUENCY	SEVERITY OF DISTRESS
0 = Not at all (leave severity column blank)	0 = None
1 = Once only	1 = Minimal
2 = 2-3 times	2 = Moderate
3 = 4-5 times	3 = Marked
4 = Everyday	4 = Extreme

1. Have you ever had painful images, memories, or thoughts of the event? _____
2. Have you ever had distressing dreams of the event? _____
3. Have you felt as though the event were recurring? Was it as if you were reliving it? _____
4. Have you been upset by something which reminded you of the event? _____
5. Have you been physically upset by reminders of the event? (This includes sweating, trembling, racing heart, shortness of breath, nausea, diarrhoea) _____
6. Have you been avoiding any thoughts or feelings about the event? _____
7. Have you been avoiding doing things or going into situations which remind you of the event? _____
8. Have you found yourself unable to recall important parts of the event? _____
9. Have you had difficulty enjoying things? _____
10. Have you felt distant or cut-off from other people? _____
11. Have you been unable to have sad or loving feelings? _____
12. Have you found it hard to imagine having a long life span fulfilling your goals? _____
13. Have you had trouble falling asleep or staying asleep? _____
14. Have you been irritable or had outbursts of anger? _____
15. Have you had difficulty concentrating? _____
16. Have you felt on edge, been easily distracted, or had to stay "on guard"? _____
17. Have you been jumpy or easily startled? _____

No Trauma

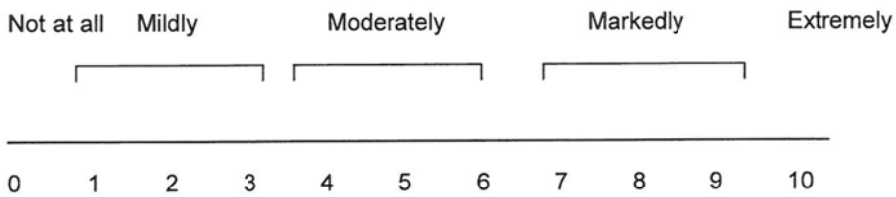
Instruction: If person did not experience any TRAUMA in the previous questionnaire than please tick the box on the right hand corner and move on to the next questionnaire

Sheehan Disability Scale (SDS) [English Version]

Please circle the number that best describes the way you have felt over the **past week**

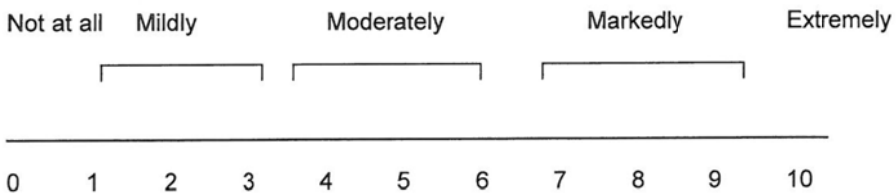
Work

These symptoms have disrupted your work

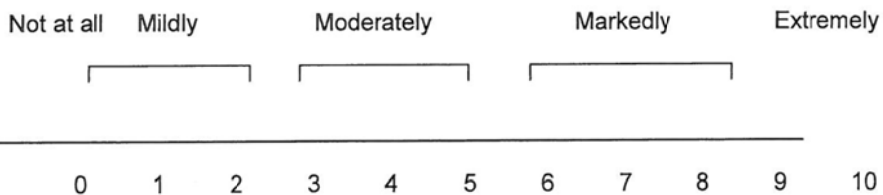


Social Life

These symptoms have disrupted your social life



Family life/Home responsibilities



13 May 2011

CES – D				
Please TICK the block for each statement that best describes how often you felt or behaved in this way DURING THE PAST WEEK:				
During the PAST WEEK	Rarely or none of the time (LESS THAN ONE DAY)	Some of the time (1-2 DAYS)	Occasionally or Moderately (3-4 DAYS)	Most of the time 5-7 DAYS
D1. I have been bothered by things that usually don't bother me				
D2. I did not feel like eating, my appetite was poor				
D3. I felt that I could not shake off the blues (sadness) even with help from my family or friends				
D4. I felt that I was not as good as other people				
D5. I had trouble keeping my mind on what I was doing (concentration)				
D6. I felt depressed and sad				
D7. I felt that everything I did was an effort				
D8. I have no hope for the future				
D9. I thought my life has been a failure				
D10. I felt fearful or afraid				
D11. My sleep was restless				
D12. I was unhappy				
D13. I talked less than usual				
D14. I felt lonely				
D15. People were unfriendly				
D16. I did not enjoy life				
D17. I cried frequently for no reason.				
D18. I felt sad				
D19. I felt that people disliked me				
D20. I could not get "going" during the day				

K10

For all questions, please put a tick in the appropriate response circle.

In the past 4 weeks:	None of the time	A little of the time	Some of the time	Most of the time	All of the time
----------------------	------------------	----------------------	------------------	------------------	-----------------

- | | | | | | |
|--|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| 1. About how often did you feel tired out for no good reason? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 2. About how often did you feel nervous? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 3. About how often did you feel so nervous that nothing could calm you down? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 4. About how often did you feel hopeless? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 5. About how often did you feel restless or fidgety? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 6. About how often did you feel so restless you could not sit still? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 7. About how often did you feel depressed? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 8. About how often did you feel that everything is an effort? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 9. About how often did you feel so sad that nothing could cheer you up? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| 10. About how often did you feel worthless? | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

Connor-Davidson Resilience Scale
(CD-RISC) [English Version]

Please indicate how much you agree with the following statements as they apply to you over the last month. If a particular situation has not occurred recently, answer according to how you think you would have felt.

	In the last month:	Not true at all	Rarely true	Sometimes true	Often true	True nearly all the time
1	I am able to handle unpleasant or painful feelings like sadness, fear and anger.	0	1	2	3	4
2	I have at least one close and secure relationship which helps me when I am stressed.	0	1	2	3	4
3	When there are no clear solutions to my problems, sometimes fate or God can help.	0	1	2	3	4
4	I can deal with whatever comes my way	0	1	2	3	4
5	Past successes give me confidence in dealing with new challenges and difficulties.	0	1	2	3	4
6	I try to see the humorous side of things when I am faced with problems.	0	1	2	3	4
7	Having to cope with stress can make me stronger.	0	1	2	3	4
8	I tend to bounce back after illness, injury, or other hardships.	0	1	2	3	4
9	Good or bad, I believe that most things happen for a reason.	0	1	2	3	4
10	I give my best effort, no matter what the outcome may be.	0	1	2	3	4
11	I believe I can achieve my goals, even if there are obstacles.	0	1	2	3	4
12	Even when things look hopeless, I don't give up.	0	1	2	3	4

13	During times of stress/crisis, I know where to turn for help	0	1	2	3	4
14	Under pressure, I stay focused and think clearly.	0	1	2	3	4
15	I prefer to take the lead in solving problems, rather than letting others make all the decisions.	0	1	2	3	4
16	I am not easily discouraged by failure.	0	1	2	3	4
17	I think of myself as a strong person when dealing with life's challenges and difficulties.	0	1	2	3	4
18	I can make unpopular or difficult decisions that affect other people, if it is necessary.	0	1	2	3	4
19	I am able to handle unpleasant or painful feelings like sadness, fear and anger.	0	1	2	3	4
20	In dealing with life's problems, sometimes you have to act on a hunch, without knowing why.	0	1	2	3	4
21	I have a strong sense of purpose in life.	0	1	2	3	4
22	I feel in control of my life.	0	1	2	3	4
23	I like challenges.	0	1	2	3	4
24	I work to attain my goals, no matter what roadblocks I encounter along the way.	0	1	2	3	4
25	I take pride in my achievements.	0	1	2	3	4

NSA

SEXUAL RISK BEHAVIOUR QUESTIONNAIRE [English Version]

Instruction: If person is not a substance abuser than please tick the box on the top right hand corner and move on to the next questionnaire.

	YES	NO
1. My sexual thoughts, feelings, behaviors are often associated with using drugs/alcohol.		
2. My sexual drive is increased by the use of drugs/alcohol.		
3. My sexual performance is improved by the use of drugs/alcohol.		
4. My sexual pleasure is enhanced by the use of drugs/alcohol.		
5. Use of drugs/alcohol has made me become obsessed with sex and/or made my sex drive abnormally high.		
6. I'm more likely to have sex when using drugs/alcohol.		
7. I'm more likely to have sex with someone other than my primary mate when using drugs/alcohol.		
8. I'm more likely to practice risky sex under the influence of drugs/alcohol.		
9. I have become involved in sex acts that are unusual for me when I am under the influence of drugs/alcohol.		
10. Use of drugs/alcohol is strongly associated with sex that I believe it will be difficult for me to separate my use of this substance from my sexual behavior.		
11. I believe I need treatment for my sexual behavior as it is linked to my use of drugs/alcohol.		

Multidimensional Scale of Perceived Social Support

Instructions: We are interested in how you feel about the following statements. Read each statement carefully. Indicate how you feel about each statement.

<p>If you DISAGREE then please Circle:</p> <p>“1” if you Very Strongly Disagree</p> <p>“2” if you Strongly Disagree</p> <p>“3” if you Mildly Disagree</p>	<p>If you are NEUTRAL then please Circle:</p> <p>“4” if you are Neutral</p>	<p>If you AGREE then please Circle:</p> <p>“5” if you Mildly Agree</p> <p>“6” if you Strongly Agree</p> <p>“7” if you Very Strongly Agree</p>
--	--	--

- | | | | | | | | | | |
|-----|--|---|---|---|---|---|---|---|-----|
| 1. | There is a special person who is around when I am in need. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | SO |
| 2. | There is a special person with whom I can share my joys and sorrows. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | SO |
| 3. | My family really tries to help me. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fam |
| 4. | I get the emotional help and support I need from my family. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fam |
| 5. | I have a special person who is a real source of comfort to me. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | SO |
| 6. | My friends really try to help me. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fri |
| 7. | I can count on my friends when things go wrong. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fri |
| 8. | I can talk about my problems with my family. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fam |
| 9. | I have friends with whom I can share my joys and sorrows. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fri |
| 10. | There is a special person in my life who cares about my feelings. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | SO |
| 11. | My family is willing to help me make decisions. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fam |
| 12. | I can talk about my problems with my friends. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Fri |