The Association Between Psychopathology And Substance Use In Young People

Amina Saban (née Jakoet)

Thesis Presented for the Degree of

DOCTOR OF PHILOSOPHY

in the Department of Psychiatry and Mental Health

Faculty of Health Sciences

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Supervisors: Professor Alan J. Flisher (deceased); Professor Leslie London and Dr Neo K. Morojele

This thesis is presented in fulfilment of the requirements for the degree of Doctor of Philosophy (Ph.D) in the Department of Psychiatry and Mental Health, Faculty of Health Sciences, University of Cape Town. The work on which this thesis is based is original research, and has not, in whole or in part, been submitted for examination for another degree at this or any other university. The contents of this thesis are entirely the work of the candidate, or in the case of multi-authored journal articles, constitute work for which the candidate was the lead author.

Amina Saban

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Thesis abstract

The co-occurrence of problematic substance use and non-substance use psychopathology is very common in psychiatry, and is generally referred to as comorbidity. The phenomenon has been the subject of debate and widespread research, yet remains poorly understood.

The thesis aimed to examine the association between psychopathology and substance use in young people in South African settings, to determine the nature and prevalence of comorbidity, and to identify sociodemographic factors that might influence the associations, as well as the influence of comorbidity on substance use treatment outcomes.

A comprehensive review of the recent literature on comorbid psychopathology and substance use identified facets of comorbidity from studies in community and substance use treatment settings, cross-sectional and longitudinal studies, and different demographic groups including females, males, and various racially classified social groups. The literature review highlighted deficits in knowledge of comorbidity in developing countries, including South Africa.

The association between psychopathology and substance use was examined through a series of empirical studies, each different from the other by the inclusion of a dimension which set it apart from the other studies. All the samples consisted of both males and females. Data were analysed using STATA to generate descriptive statistics and determine associations through regression analyses. The results of associations are presented as unadjusted and adjusted odds ratios, with 95% confidence intervals and p-values.

The first empirical study examined the association between psychopathology and substance use in a sample of Grade 8 (n=480) and Grade 11 (n=459) adolescents (ages 14-24 years), randomly-selected from 39 high schools in Cape Town. These students completed a self-administered questionnaire to obtain basic demographic information and lifetime prevalence rates of cigarette, alcohol, cannabis and inhalant use. Psychopathology scores were calculated using the Harvard Trauma Questionnaire, the Beck Depression Inventory and the Zung Self-Rating Anxiety Scale. Logistic regression, using survey design analyses, indicated significant associations between PTSD and all substances of use (with ORs ranging from 1.016-1.050), between depression and alcohol (OR=1.050; 95%CI 1.011-1.091), cannabis and inhalant use (OR=1.080; 95% CI 1.007-1.159), and between anxiety and cannabis use (OR=1.035; 95%CI 0.963-1.112). Evidence indicated a role for grade, gender, age and racially classified social group in these associations, and further investigation is recommended to examine this.

The second study examined comorbidity in a sample of young substance users who were in inpatient treatment for their substance use (n=95; ages 17-30 years). Patients were selected consecutively, in order of admission, from three substance use treatment centres in Cape Town. An interview schedule was used to elicit sociodemographic and substance use information. Psychopathology was assessed using the computer-assisted Diagnostic Interview Schedule (C-DIS) for Diagnostic and Statistical Manual (DSM) -IV. The results indicated a high prevalence of previously-undiagnosed psychiatric disorder (95.8%), with disruptive behaviour disorders predominating (antisocial personality disorder 87.4%; conduct disorder 67.4%; oppositional defiant disorder 33.7%). Substance use was characterised by daily use of cigarettes, and primary use of heroin and crystal methamphetamine. Evidence suggested marginal unadjusted associations between anti-social personality disorder and cannabis as first substance of use (p=0.061), between conduct disorder and cannabis as first substance of use (p=0.031), between specific phobia and cannabis as first substance of use (adjusted OR=4.74;

95% CI 0.99-22.66, p=0.051). It was suggested that the study be replicated with a larger and more representative sample and an appropriate control group, to clarify finer nuances in the results obtained.

In the third study, the substance use inpatients from the previous study were followed up in the year following their treatment (n=86) to establish associations between their psychopathology on admission, and their treatment and substance use status after discharge from their inpatient treatment programme. Follow-up interviews were conducted using an interview schedule to elicit substance use and treatment status information. The results indicated that single and male patients were more likely to complete the inpatient programme, while females were more likely to resume substance use and return to substance use treatment after the inpatient programme. Patients who sought treatment for heroin use were more likely still to be in treatment after the initial inpatient programme, than were those who sought treatment for substances other than heroin use. Patients who sought treatment for methamphetamine use were more likely to complete the inpatient programme, and were less likely to relapse or resume treatment, than were those who sought treatment for substances other than methamphetamine. Patients whose first substance of use was methamphetamine were less likely to relapse after inpatient treatment than were those whose first substance of use was not methamphetamine. No significant associations were found between psychopathology on admission and treatment completion or relapse after inpatient treatment. Methodological limitations of the study are discussed, as is the difficulty posed from the extremely high percentages of comorbidity, and suggestions are made for future research in light of evidence for the role of sociodemographic factors and substance use history in comorbidity, and substance use and treatment status after inpatient treatment.

The fourth and final study examined data from the nationally-representative South African Stress and Health (SASH) survey to determine associations between psychopathology and substance use. In this study, a subsample from the SASH survey, comprising 1766 community members aged 18 to 30 years, were interviewed using the Composite International Diagnostic Interview Version 3 (CIDI 3.0). Basic demographic information was elicited, together with lifetime and 12-month psychiatric diagnoses and lifetime substance use. The results indicated that substance users were more likely to have had anxiety disorders (ORs from 1.7 to 2.0 for lifetime anxiety) and major depression ORs from 1.8 to 5.6), compared with non-substance users. Evidence was obtained for associations between specific substances and specific psychiatric disorders, and particularly between mood disorders and substance use. Age, gender and racially classified social group emerged as factors to be further examined with respect to comorbidity. In light of the rigour with which this study was conducted, these results will make an important contribution to knowledge of comorbid psychopathology and substance use in South Africa. In addition, this study contributes to global information, by providing standardised data that can appropriately be compared with similar World Health Organisation (WHO) World Mental Health (WMH) initiatives elsewhere.

These studies thus all investigated associations between psychopathology and substance use in young people, providing strong evidence of associations in community settings, but less so in the setting of a substance use treatment population. The evidence appears to point in the direction of more likely associations between certain psychiatric diagnoses in relation to specific substances of use, possibly influenced by factors such as age, gender, racially classified social group and school grade. These results also highlight the need to consider methodological and conceptual issues when designing and executing research projects that involve comorbid psychopathology and substance use. It is clear that

further investigation will be needed to refine the results obtained and to establish greater clarity of the dynamic that exists when psychopathology and substance use co-occur.

In conclusion, this thesis has raised the profile of comorbidity research in Cape Town and in South Africa, has highlighted some important issues in the debate on comorbid psychopathology and substance use, has uncovered potential pitfalls of comorbidity research, and has provided a baseline from which further comorbidity studies can be developed.

Acknowledgements

Many people assisted me in developing and completing my doctoral thesis, and I shall always be thankful to them for their help.

In particular, I would like to thank my original thesis supervisor, Prof. Alan J. Flisher, for guiding me through the doctoral thesis process with kind consideration and respect. He made me feel that my work mattered both to him and to a greater body of knowledge. He instilled confidence in me when I doubted my own abilities and courage, and he was supportive of me when life events challenged my ability to work. Alan sadly passed away shortly before my thesis was completed, but I shall be forever grateful to him for his contribution to my work, my personal and my professional development.

My sincere thanks go to Dr Neo Morojele for her continual support and encouragement over many years, and to Prof. Leslie London for his generous assistance and time. Neo and Leslie offered to supervise my thesis when Alan passed away and I was left without a supervisor. Their offer came before I could request their assistance, at a time when I was experiencing anxiety and uncertainty about the future of my thesis. I shall always appreciate their support, generosity, and tireless efforts to meet my submission deadline, and I am truly grateful to them for their contribution to my thesis.

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Ria Laubscher deserves a special thank you for her kind assistance with completion of the statistical analyses for the treatment centre studies. Her patience and understanding, when challenges were encountered while completing these studies, are greatly appreciated. Thanks are also due to Dr. Carl Lombard for offering to assist at short notice when needed, to Greg Distiller for the structural equation modelling in the high schools study, to Francesca Little for statistical assistance with the high schools study, and to Anna Grimsrud for the statistical analyses of the SASH data set.

I wish to acknowledge the National Research Foundation and the University of Cape Town for their financial assistance in the early development of my thesis. The latter part of my research was kindly funded by the African Population and Health Research Centre (APHRC) through an African Doctoral Dissertation Research Fellowship. My association with the APHRC has assisted with advancing my general research skills, and nurtured my professional

development. I shall always be thankful for this. However, the opinions expressed in this thesis are my own and those of my co-authors, and are not necessarily shared by the funders.

In addition, I am thankful to my children, Ameer and Kamila, for never doubting my ability to complete my doctoral thesis successfully. Lastly,a special grateful thanks to my husband, Sadick, who was always enthusiastic about my research, and confident about my abilities as a researcher, and supported me financially and emotionally throughout my thesis process. Alhamdulillah.

Preface

This thesis includes manuscripts for journals in accordance with general provision 6.7 in the General Rules for the degree of Doctor of Philosophy (PhD) of the University of Cape Town, and with the approval in 2010 of the university Doctoral Degrees Board. The following papers are included as part of the thesis:

1. Saban, A and Flisher, A.J. (2010). The association between psychopathology and substance use in young people: a review of the literature. Journal of Psychoactive Drugs, 42(1): 37-47.
2. Saban, A., Flisher, A.J. and Distiller, G. (2010). Association between psychopathology and substance use among high school-going adolescents in Cape Town, South Africa. Journal of Psychoactive Drugs, 42 (4): pending.
3. Saban, A., Flisher, A.J. and Laubscher, R. (2010). The association between psychopathology and substance use: young substance users in inpatient treatment in Cape Town, South Africa. Drug and Alcohol Review, in review.
4. Saban, A., Flisher, A.J. and Laubscher, R. (2010). Comorbid psychopathology, substance use and treatment outcomes: a follow-up of inpatient substance users in Cape Town, South Africa. Journal of Groups in Addiction and Recovery, in review.
5. Saban, A., Flisher, A.J., Grimsrud, A., Myer, L., London, L., Morojele, N., Stein, D and Williams, D. (2010). The association between substance use and common mental disorders in young adults: results from the South African Stress and Health (SASH) survey. Drug and Alcohol Dependence, in review.

The candidate was the lead and corresponding author for all the included manuscripts, and drafted all versions of these manuscripts. All the co-authors critically reviewed and approved the submitted manuscripts. One exception was A.J. Flisher, who approved earlier drafts, but passed away before papers 3, 4 and 5 could be submitted for publication. The candidate designed the studies for papers 3 and 4, and alone conducted all the required interviews, and collected, captured and cleaned all the data for these papers. The candidate was integrally involved in the

data analyses and interpretation for all the papers, including the design of the secondary analyses for papers 2 and 5.

Abbreviations

<	less than
≤	less than or equal to
= >	implies
>	more than
≥	more than or equal to
↑	increase
→	leads to
↓	decrease
♀	female
♂	male
ADHD	Attention Deficit Hyperactivity Disorder
ADI	Adolescent Diagnostic Interview
ARC	Alcohol Research Centre
ASP	Anti-Social Personality
ASPD	Anti-Social Personality Disorder
AUDIT	Alcohol Use Disorders Identification Test
BDI	Beck Depression Inventory
BSI	Brief Symptom Inventory
CAPA	Child and Adolescent Psychiatric Assessment
CASI-I	Comprehensive Addiction Severity Index-Adolescents
CBC	Child Behaviour Checklist
CBCL	Child Behaviour Check List
CD	Conduct Disorder
CDDR	Customary Drinking and Drug Use Record
CDRS-R	Children's Depression Rating Scale-Revised
CES-D	Centre for Epidemiological Studies-Depression scale
CHQ	Child Health Questionnaire
CI	Confidence interval
CIDI	Composite International Diagnostic Interview
CIDI-SAM	CIDI-Substance Abuse Module
DICA	Diagnostic Interview for Children and Adolescents
DICA-R	DICA-Revised
DIS	Diagnostic Interview Schedule
DIS-C	Diagnostic Interview Schedule for Children

DSM	Diagnostic and Statistical Manual
DUSI	Drug Use Screening Inventory
ECA	Epidemiological Catchment Area
exptal	experimental
FU	follow-up
gp	group
HMO	Health Maintenance Organisation
incl	including
inpts	inpatients
ito	in terms of
K-SADS	Schedule for Affective Disorders and Schizophrenia-Kiddies version
MAST	Michigan Alcohol Screening Test
Mandrax (Mx)	methaqualone
MD	Major Depression
MDD	Major Depressive Disorder
MECA	Methods for the Epidemiology of Child and Adolescent mental disorders
n or N	sample size
NCS	National Comorbidity Survey
NESARC	National Epidemiologic Survey on Alcohol and Related Conditions
NIMH	National Institutes of Mental Health
NYS	National Youth Survey
OCD	Obsessive Compulsive Disorder
OR	odds ratio
POSIT	Problem Oriented Screening Instrument
probs	problems
PSUD	psychoactive substance use disorder
PTSD	Post-Traumatic Stress Disorder
RCSAST	Rutgers Collegiate Substance Abuse Screening Test
RCSG	Racially classified social group
RDC	Research and Diagnostic Criteria
ROC	Receiver Operating Characteristics
Rx	treatment
SADS-E	Schedule for Affective Disorders and Schizophrenia-Epidemiologic version
SAICA	Social Adjustment Inventory for Children and Adolescents
SASH	South African Stress and Health survey/study
SCID	Structured Clinical Interview for DSM
S-MAST	Short Michigan Alcohol Screening Test

SMFQ	Short Mood and Feelings Questionnaire
SRD	Self-Reported Delinquency
SUD	Substance Use Disorder
SUQ	Substance Use Questionnaire
SURF	Service Utilisation and Risk Factors Interview
TAQ	Traumatic Antecedents Questionnaire
tik	crystal methamphetamine
WHO	World Health Organisation
WMH	World Mental Health
wrt	with respect to
WURS	Wender Utah Rating Scale
X-S	cross-sectional
YASR	Young Adult Self-Report
yr	year
YRBQ	Youth Risk Behaviour Questionnaire
YSR	Youth Self-Report

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CHAPTER 7: DISCUSSION

CHAPTER 1

Introduction

CHAPTER 1

Introduction

While many users of substances such as tobacco, alcohol and cannabis do not experience substance-related problems, some individuals do develop problematic substance use (Diegenhardt et al., 2001). Some individuals might even meet criteria for diagnoses of substance abuse or substance dependence as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM) (Robins et al., 2002), and are treated within the ambit of psychiatry. Evidence from epidemiological studies [such as the Epidemiologic Catchment Area (ECA) (Robins et al., 1991), the National Epidemiologic Survey on Alcohol and Related Disorders (NESARC) (Grant et al., 2004), and the National Comorbidity Surveys (Kessler et al., 1994; 1996; 2005)] have reinforced a long history of clinical observations that suggest associations between problematic substance use and other psychiatric morbidity (Weinberg and Glantz, 1999). However, though recognition of the co-occurrence of disease symptoms and disorders has been longstanding, recent developments have altered the manner in which such co-occurrence is being treated (Angold et al., 1999).

Co-occurrence of diseases (individual and well-defined clinical entities) or disorders (behavioural and psychological syndromes that deviate from established norms) is generally referred to as 'comorbidity' (Angold et al., 1999), and is characterised by an overlap of disease or disorder symptoms. Thus, the co-occurrence of problematic substance use and psychiatric disorder constitutes a form of psychiatric comorbidity. Common forms of substance use and other psychiatric comorbidity include associations between alcohol use and anxiety disorders, antisocial personality disorders, affective disorders and schizophrenia (Hall and Farrell, 1997), smoking and depression (Goodman and Capitman, 2000), and between cannabis use and psychiatric disorder such as attention deficit disorder, conduct disorder, oppositional disorders, anxiety and depressive disorders (McGee et al., 2000). Comorbid substance use and psychiatric disorder is also recognised as a common occurrence (Volkow, 2000), amongst both clinically-derived and population-based samples, and amongst adults and adolescents (Weinberg and Glantz, 1999).

Comorbid substance use and psychiatric disorder, however, remains a phenomenon that is relatively poorly understood (Volkow, 2000), with various aspects being the subject of continuing discussion, including, i) whether comorbidity is a 'real' phenomenon, or an artefact of diagnostic symptoms, diagnostic techniques, chance, referral biases or sampling procedures (Wittchen, 1996a), ii) consistent use of terms such as 'comorbidity', 'co-occurring disorders', 'dual' and 'triple diagnosis' (Chambers 2008a, b), and distinguishing between concurrent, sequential and lifetime disorders or symptoms (Angold et al., 1999), iii) distinguishing between primary and secondary psychiatric diagnoses, and the temporal relationship between these, iv) explaining the common co-occurrence of seemingly unrelated disorders (Angold et al., 1999), v) the use of clinical samples to examine comorbidity when these samples have the potential to produce overestimates of comorbid diagnoses because they may be biased in favour of possibly more, and/or, more severe symptoms of disorders, unless a disorder is rare or most likely to precipitate treatment-seeking, and vi) the need for more longitudinal comorbidity studies, particularly with samples of children, adolescents and young adults.

However, notwithstanding the controversial nature of comorbidity, the importance of examining associations between substance use and psychiatric disorder remains indisputable. Firstly, such research will improve understanding of the aetiology of psychiatric and substance use-related disorders (Angold et al., 1999; Diegenhardt et al., 2001). Secondly, comorbid disorders have implications for both the treatment and management of the individuals involved. Thus, if persons with problematic substance use have an increased chance of having or developing an associated psychiatric disorder, or if people with psychiatric disorder have an increased risk of problematic substance use or substance use disorder, service provision will have to include assessment for co-occurring disorders and their subsequent treatment and management (Degenhardt et al., 2001).

Though research into associations between substance use and psychiatric disorder has been extensive, relatively few studies have addressed associations between specific substances of use and psychiatric problems or disorder (Degenhardt et al., 2001). In addition, information is lacking regarding the role of gender or age in comorbidity (Angold et al., 1999). Moreover, as shown by the literature review completed for this thesis, there is a paucity of comorbidity research from developing countries

compared with developed countries, with a particularly low research output in this field from Africa and South Africa. This thesis attempts to address these issues by increasing information on substance use and related psychiatric problems and disorders, and highlighting demographic and social factors that might influence such comorbidity, within the South African context.

More specifically, the thesis examines the association between psychiatric disorder and specific substances of use in a) a community sample of school-going adolescents and young adults, b) a sample of adolescents and young adult substance users in inpatient treatment for problematic substance use, and c) a community sample of young adults drawn from a representative sample of South African adults. In addition, the thesis includes a follow-up of the treatment sample of inpatient substance users, examining associations between identified psychiatric disorder and substances of use at baseline, and post-treatment status as defined by treatment completion, relapse and treatment resumption.

This chapter will elaborate on the importance of examining associations between psychiatric disorder and substance use. Specific reference will be made to the burden of disease posed by psychiatric disorder, substance use and associations between psychiatric disorder and substance use. The chapter will highlight the need to examine associated psychiatric disorder and substance use in young people particularly, and will discuss the challenges that conceptual, diagnostic and definitional issues pose to research in this area. Suggested explanations for associated psychiatric disorder and substance use, will be outlined. The status of research and knowledge regarding associations between psychiatric disorder and substance use will be discussed. The chapter will conclude with a rationale for the thesis and details of its aims and objectives, and a brief indication of the construction of the thesis and the contents of each chapter.

Substance use, psychiatric disorder and the global burden of disease

The report from the 2008 World Health Organisation (WHO) on the global burden of diseases (Hoelzer, 2009) indicated that cardiovascular diseases were the leading cause of mortality globally, and identified tobacco use as one of the risk factors in this statistic. Neuropsychiatric conditions

(including alcohol use and psychiatric disorder) were reported to be the leading causes of disability, accounting for a third of all years lost due to disability (YLD) in individuals aged 15 years and older.

Chronic diseases such as psychiatric disorder and substance use are recognised as simultaneously the most common, costly and preventable global health problems (Hoelzer, 2009). The burden of cost to the State associated with chronic illnesses is comparatively larger in countries where budgets for health funding and resources are smaller. In such under-resourced countries, the financial and social burdens of chronic diseases are further increased by limited available resources to deal with the needs of caregivers and service providers of individuals affected by chronic diseases (Adewuya et al., 2010).

In particular, the African continent's burden of disease (and specifically that of sub-Saharan Africa) has been linked to factors such as increased life expectancy, poverty, urbanisation, globalisation and lifestyle changes (de-Graft Aikens et al., 2010). In a recent review of the literature on the associations between poverty and mental disorders, Lund et al., (2010) concluded that there can no longer be any question as to whether poverty influences common mental disorders in low and middle income countries. Instead, these authors suggested that research must now be geared towards identifying which are the most important poverty factors that affect mental disorders. Furthermore, attempts to address the burden of disease in sub-Saharan Africa have been hampered by inadequate or insufficient relevant information because of the low research output regarding the burden of chronic disease in the region (de Graft-Aikens et al., 2010).

The WHO has recognised the need to gather information on the global burden of chronic diseases, and aims to invest in increasing both knowledge and understanding regarding these illnesses. The intention is to inform policy, particularly in developing countries, regarding the recognition of health priorities and the appropriate allocation of available resources. This approach is grounded in the view that health should be aspired to both for its own sake, and because it impacts on the economic growth and competitiveness of the countries involved (Baumberg, 2006).

The burden of psychiatric disorder

Generally, the burden of psychiatric disorder is larger than that of most chronic physical diseases because mental disorders often have an earlier age of onset than many physical chronic illnesses (Kessler et al., 2007). Problems associated with mental illness, for example violent behaviour, can cause injury to both the perpetrator and the victim of the violence, resulting in physical injuries that can increase the load on health services and providers, and could also result in reduced productivity due to the victim's absence from work. The consequent mental and emotional anguish suffered by the victims and perpetrators is more difficult to quantify, and might thus remain incalculable, unknown or be ignored (Desjarlais et al., 1995).

Similarly, non-natural deaths can result in significant distress in the dependants. Moreover, the underlying behavioural or mental problems of victims of non-natural deaths often go unrecognised. For example, the victim of a successful suicide attempt might be recorded as having had a non-natural death, and the role of a possible underlying depression in the suicide might remain unrecorded. As a result, statistics relating to the prevalence of mental disorders and other behavioural problems are often underestimates (Desjarlais et al., 1995).

According to Kessler et al. (2009), the occurrence of psychiatric disorder worldwide is generally very common (12.0-47.4%), irrespective of whether the country is a developed or developing country. According to the World Mental Health (WMH) surveys (Kessler et al., 2009), the most commonly-occurring lifetime psychiatric disorders in the community were the anxiety disorders (4.8-31.0%), followed by mood disorders (3.6-21.4%), the externalising disorders (0.3-25.0%) and substance use disorders (1.3-15.0%). Similar trends, but involving lower proportions, apply to the 12-month prevalence rates of these disorders.

The South African Stress and Health (SASH) survey, the South African arm of the WHO WMH surveys (Stein et al., 2009), found that 30.3% of a nationally representative sample had a mental disorder, with 11.2% and 3.5% having two or more, and three or more, disorders respectively. The most-commonly occurring lifetime disorders were the anxiety disorders (15.8%) followed by substance use disorders (13.3%) and mood disorders (9.8%) (Herman et al., 2009). The South African prevalence rates for the anxiety disorders thus loosely approximated the WMH mid-range, while the South African prevalence rate for mood disorders veered more towards the lower end of the WMH range. In South Africa the substance use disorder prevalence rate was closer to the WMH upper limit.

The SASH survey also reported that a quarter of individuals with severe or moderate psychiatric disorders had received psychiatric treatment in the year prior to interviews for the survey, with primarily mood and anxiety disorder consultations, while 13.4% of individuals with no psychiatric disorders had received treatment for psychiatric disorder (Seedat et al., 2009). These findings highlight the need gap between disease burden and actual utilisation of services, as well as the need for access to services, and provide some insight into the manner in which current available services are utilised.

Some attempts have been made, largely in developed countries, to calculate the burden of disease due to psychiatric disorder. Economic costs associated with psychiatric disorders have been estimated to approximate 79 billion dollars per annum in the United States of America, and 3% to 4% of Gross Domestic Product (GDP) per annum in the European Union (EU) member countries (Ngui et al., 2010)

However, there are many difficulties in obtaining valid cost estimates for the burden of psychiatric disorder. Wealthy and poorer countries differ in their ability to meet the costs associated with psychiatric disorder. Attempts to address this imbalance have been complicated by a lack of available data in most countries, and particularly in developing countries, with respect to the burden of disease

in general, psychiatric disorder in particular (Levinson et al., 2010) and the costs associated with these illnesses and their short-term or long-term effects (Kessler et al., 2009).

To address this deficit, the WHO embarked on the World Mental Health (WMH) surveys that currently provide information on the global burden of psychiatric disorder from 28 countries. These surveys generate data regarding the prevalence and severity of mental disorders and their correlates, as measured by the Composite International Diagnostic Interview (CIDI), and measures of the extent to which the mental disorders disable the affected individuals. Furthermore, the WMH surveys provide prevalence rates for individual disorders, thus allowing comparisons of prevalence rates across countries, and identification of disease areas where resources and intervention need to be prioritised.

The burden of substance use

Use of substances with psychoactive effects has long been part of cultures across the world (Anderson, 2006), and have historically included, among others, alcohol (from fermented fruits, grain, honey), nicotine (from tobacco or pituri plants), caffeine (from coffee beans), cocaine (from the coca plant), and heroin and opium (from poppy seeds). Global substance use estimates for 2002 indicate that 146.2 million adults used cannabis, 29.6 million used amphetamines and 13.3 million used cocaine globally, with an estimated 15.3 million people diagnosed with substance use disorders, and usage largely driven by a complex dynamic that includes, among other factors, affordability and availability of substances (Anderson, 2006).

Globally, tobacco use has been recognised as the 'most preventable cause of death', as 'a risk factor in six of the eight primary causes of death', is known to have doubled or tripled the mortality rate in smokers compared with non-smokers, and is estimated to have contributed to the deaths of 100 million people in the 21st century (Hoelzer, 2009:4). According to the latter report, tobacco use globally was most prevalent amongst men and individuals aged 18 to 25

years, declined in the United States, and had 70% of its consumption in lower income countries.

In comparison, alcohol use accounted for 4% of the global burden of disease, and for one-third of the male neuropsychiatric burden, and made its largest contribution to the burden of substance use in central and South America (Hoelzer, 2009). Alcohol was the substance of choice amongst US adolescents and young adults (aged 16 to 25 years), and played a contributory role in some cancers, epilepsy, motor vehicle accidents and homicides (Hoelzer, 2009).

Estimating the global economic and social cost of alcohol consumption has been complicated. Suggested reasons for this include methodological differences between studies, that identify who pays the costs involved, difficulties in calculating the economic 'benefits' of dying young from alcohol-related disorders, difficulties with attributing a causal role to alcohol in mortality, problems with calculating the indirect costs of alcohol use (for example, its contribution to an individual's reduced productivity), and the possibly differential impact of alcohol use in developed and developing countries (Baumberg, 2006). As a result, the true cost of alcohol use remains unknown, as are the estimates of measurement error in the calculated costs (Rehm et al., 2006). General consensus seems to hold, though, that the costs (social, economic or any other) of alcohol use outweigh the perceived benefits, and exert a substantial global economic burden (Baumberg, 2006).

In South Africa, details of various forms of substance use and abuse are recorded systematically and regularly as part of an ongoing surveillance programme, hosted by the South African Community Epidemiology Network on Drug Use (SACENDU, 2009). The SACENDU statistics report patterns of admission for treatment of problems relating to drug

and alcohol use in South Africa, at substance use treatment centres across the country, and provide an opportunity to track the changes in substance use admission patterns over time.

The SACENDU reports for January-June 2009 indicated that alcohol was the primary substance of abuse amongst individuals aged older than 20 years who sought treatment for their substance use while cannabis use was high across all age groups. Community studies found widespread use of cigarettes, alcohol, cannabis and inhalants amongst high school students in the Cape Town area of South Africa (Flisher et al., 2002; Patrick et al., 2009), while Taylor et al. (2003) similarly reported use of cigarettes, alcohol, cannabis, benzene, paint thinners, glue and petrol amongst rural high school students in the Kwazulu-Natal area of South Africa. These results were borne out by the South African (SA) National Youth Risk Behaviour Survey (NYRBS) of school-going students from Grades 8 through 11 (Reddy et al., 2007). The latter report also indicated increased rates of illicit drug use over time in this group, and suggested that this increase was largely the result of increased use of heroin, believed to have been driven by an increase in the heroin supply and a decrease in the price of heroin. Results from the SASH nationally-representative survey indicated that alcohol was the most common substance of use (38.7%) in the adult community, while 30% of those sampled used tobacco, and 8.4% used cannabis (van Heerden et al., 2009).

Use of substances such as alcohol and tobacco has been listed as responsible for approximately 4% of disability adjusted life years lost [World Health Organisation (WHO), World Health Report 2002]. Substance use, particularly amongst adolescents and young adults, has been linked to problematic behaviours such as risky sexual behaviour (Pahl et al., 2010), HIV (Myer et al., 2009b), dropout from school (Myer et al., 2009a), and unnatural deaths such as homicides, pedestrian victims of motor vehicle accidents, and victims of fire accidents (Matzopoulos and Lerer, 1995; Seedat et al., 2009). Risk factors for substance use identified in studies include poverty (with respect to illicit substances), lower educational

levels (with respect to tobacco use), higher income (with respect to tobacco use), single-parent households, and having family members who use substances (Anderson, 2006). Factors that appear to protect against substance use include harmonious domestic and family relationships, and adult supervision (Anderson, 2006), and intelligence, problem-solving ability and supportive family (Weinberg et al., 1998). However, there appears to be no single resilience factor that protects against substance use or its consequences (Weinberg et al., 1998).

Co-occurring psychiatric disorder and substance use

Information from the United States Substance Abuse and Mental Health Services Administration and United States National Comorbidity Survey indicated that individuals with psychiatric disorder were more likely to be dependent on substances (27%) than were individuals who had no psychiatric disorder (8%) (Buckley, 2007). Conversely, individuals who abused substances doubled their risk of psychiatric disorder compared with individuals who did not use illicit substances (Buckley, 2007). Co-occurring psychiatric disorder and substance use is seen to reflect both the risk of substance use in individuals with psychiatric disorder as well as the potential for substance use to trigger psychiatric disorder (Volkow, 2001). The commonness of this co-occurrence has been demonstrated by results from several different studies conducted in different geographical regions (Saban and Flisher, 2010).

However, despite the frequency with which co-occurring psychiatric disorder and substance use is encountered, the associations between the two remain "poorly understood", particularly with respect to the nature of the associations, their origins, and the manner in which they interact and influence each other (Volkow, 2001:1181). In addition, relatively few studies have rigorously examined associations between psychiatric disorder and specific substances of use (Jane-Llopis and Matytsina, 2006), while most of the studies have been conducted in

developed countries (Saban and Flisher, 2010). The findings from these developed countries might apply to developing countries, and co-occurring psychiatric disorder and substance use trends might not be specific to particular cultures. However, differences in prevalence rates of comorbidity in samples from the same populations, with no conclusive explanations for these differences, and varying study designs that make cross-study comparisons very difficult, indicate the need for further investigations into patterns of association between psychiatric disorder and substance use, with a particular view to obtaining cross-nationally comparable data (Jane-Llopis and Matytsina, 2006).

Epidemiology

Reported prevalence rates for any psychiatric disorder in individuals with alcohol use disorder or dependence have ranged from 28% for 12-month disorders in the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant et al., 2004), 48% for lifetime disorders in the National Comorbidity Survey (NCS) (Kessler et al., 1996) and the National Comorbidity Survey-Replication (NCS-R) (Kessler et al., 2005). The NESARC study also found a prevalence rate of 47% for alcohol problems or disorder in those with any psychiatric disorder. The comparative figures for alcohol use and alcohol dependence were 7% and 14% respectively in the National Household Survey on Drug Abuse amongst the general US population, 29% for alcohol problems and 36% for alcohol dependence in the NCS and NCS-R, and 16% for alcohol problems and 23% for alcohol dependence in the Mental Health Supplement to the Ontario Health Survey (Jane-Llopis and Matytsina, 2006). Co-occurring mental illness and substance use has also been more prevalent in treatment samples as compared with community samples (Kessler et al., 1996). A possible reason for this might be that the presence of more than one disorder might be more likely to result in treatment-seeking behaviour for either disorder (Angold and Costello, 1993). Evidence also indicates that psychiatric disorder is more likely to be associated with

substance dependence than abuse (Kessler et al., 1996) suggesting that psychiatric disorder might be more likely with increasing severity of the substance use.

Patterns of co-occurrence

The results of the National Comorbidity Survey (Kessler et al., 1996) showed statistically significant associations between mood or anxiety disorders (12-month and lifetime) and substance use and substance use disorders. Schizophrenia has been associated with multiple substance use, and mania has been associated with alcohol use (Goldsmith, 1999). Thought problems, attention problems, and delinquent and aggressive behaviour have been associated with tobacco use in adolescents and young adults (Ferdinand et al., 2001). Alcohol and other substance use (including cannabis) have been associated with conduct disorder in adolescents (Brown et al., 1996), use of opioids has been associated with antisocial personality disorder and major depression in adults (Brooner et al., 1997), and use of illicit drugs have been associated with increased risk of mood disorders in children and young adults (Kandel et al., 1997). Other evidence has indicated associations between bipolar disorder and substance use, as well as between attention-deficit hyperactivity disorder (ADHD) and substance use and related disorders in adolescents (Deas, 2006). There, is, thus, extensive evidence to suggest associations between psychiatric disorder and substances of use.

Associated factors

Various studies have examined factors that appear to play a role in the association between psychiatric disorder and substance use (Jane-Llopis and Matytsina, 2006). These factors can be categorised as individual biological or psychological characteristics, or factors that involve social or environmental aspects of the individual's life (Weinberg and Glantz, 1999). Factors examined have included gender (Goldsmith, 1999; Jane-Llopis and Matytsina, 2006), age (Jane-Llopis and Matytsina, 2006), school grade (Monshouwer et al., 2006), urbanicity

(Chong et al., 1999), socioeconomic status or economic deprivation (Jane-Llopis and Matytsina, 2006), homelessness (Goldsmith, 1999), ethnicity or racially-classified social group (Chatterji et al., 2009), biological markers or genetic factors (Ciccheti and Rogosch, 1999), and medical illnesses (Goldsmith, 1999). These factors have been examined with respect to their role as either risk or protective factors for psychiatric disorder or/and substance use.

Pathways to co-occurrence

Identifying the pathways that lead to co-occurring psychiatric disorder and substance use or substance use disorders is important for three reasons. Firstly, it can enable one to understand the mechanisms underlying associated disorders (Volkow, 2001). Secondly, it can assist in identifying temporal associations between disorders (Jane-Llopis and Matytsina, 2006), thereby facilitating the identification of possible causal associations. Thirdly, identified pathways can assist with the development of targeted interventions to prevent, treat or manage the co-occurring disorders and the individuals involved (Jane-Llopis and Matytsina, 2006).

Various pathways have been suggested to assist in understanding the development of co-occurring psychiatric disorder and substance use. The most common of these are i) temporality/causality, ii) self-medication, and iii) a genetic predisposition (Diegenhardt et al., 2001).

The temporal or causal theory holds that if one disorder precedes another, the preceding disorder could have caused the other disorder. However, Lillienfeld and Stolley (1994) proposed that demonstrating a temporal association between two factors is not enough to indicate causality. Instead, these authors suggest that when reviewing the evidence arising from the literature, temporality needs to be accompanied by additional factors before

causality can be accepted. These additional factors include the strength of the association, the consistency of the association, the specificity of the associated factors, and whether the observed association occurs in keeping with known scientific principles.

Establishing causality between psychiatric disorder and substance use has been hampered by inconsistent or contradictory findings. For example, the Pomerleau hypothesis (McGee et al., 1998) held that psychiatric disorder preceded cigarette smoking, played a role in inhibiting quitting smoking, and was accompanied by contributory socioeconomic factors like disadvantaged backgrounds. This hypothesis thus suggested the possibility that the psychiatric disorder might have caused the smoking initially by attempts to alleviate the symptoms of psychiatric disorder, and subsequently led to smoking-related disorders (McGee et al., 1998). The suggestion had earlier been supported by evidence from the National Health and Nutrition Examination Survey on the dynamics of depression and cigarette smoking (Anda et al., 1990). The NCS similarly found that mental disorders usually preceded substance use disorders (Kessler et al., 1996). However, data from the 1972-1973 Dunedin Multidisciplinary Health and Development Study indicated little evidence to support the Pomerleau hypothesis (McGee et al., 1998), while the International Consortium on Psychiatric Epidemiology found that the temporal order of co-occurring disorders differed for different countries (Jane-Llopis and Matytsina, 2006).

The self-medication hypothesis proposes that patients with mental health problems might attempt to alleviate the symptoms of these problems with substance use, for example reports of people claiming to feel more relaxed when drinking moderately or socially (Breslau et al., 1998). However, the empirical evidence associates consumption of alcohol with increased physiological indicators of tension, in moderate drinkers, heavy drinkers, and in young men who either had or did not have family histories of alcoholism (Breslau et al., 1998). In cases of acute alcohol withdrawal, consumption of alcohol was found to alleviate tension in the

short term, but ultimately the symptoms of anxiety persisted with continued drinking and only decreased with abstinence over time (Breslau et al., 1998). However, as mentioned by Jane-Llopis and Matytsina (2006: 532), "if all or most co-occurring substance use was motivated by need for self-medication, specific substances would probably be linked to specific conditions". However, very few conditions seem to have such specificity of associations, while substances of choice appear to be influenced by factors that include the cultural environment of the individual, the cost, and the availability of substances. Thus the self-medication hypothesis appears to be an unlikely explanation for all co-occurrence of psychiatric disorder and substance use (Jane-Llopis and Matytsina, 2006).

Genetic factors have been proposed as responsible for predisposing an individual to either the substance use, or the psychiatric disorder, or both. Though the evidence to support a genetic basis for comorbidity has in the past been considered unreliable (Schuckit et al.,1990), more recent reports of twin studies have demonstrated a role for genetic factors in patterns of comorbidity (Kendler et al., 2003), and also proposed a contributory role for shared environmental risk factors, such as family disruption, poor parental monitoring or low social class of rearing, in comorbidity (Kendler et al., 2003).

It has also been suggested that psychiatric disorders could play a role in changing the course of the prevailing substance abuse (Bukstein et al., 1989), with the emergence, occurrence or presence of a psychiatric disorder able to alter the manner, intensity, severity or type of substance abuse and its consequences. More recently, Chambers (2007) found that various psychiatric disorders were characterised by neurobiological conditions that resulted in the psychiatric symptoms. Though these psychiatric symptoms were often independent of any substance use, the author held that the neurobiological condition could pose a vulnerability to problematic substance use in the event of exposure to substance use. In these cases, the psychopathology and substance use would share a common neurocircuitry that would

predispose the individual independently to both the psychopathology and the problematic substance use.

These proposed pathways to the development of co-occurring psychiatric disorder and substance use seem to suggest that the development of such co-occurrence might be heterogeneous. It is possible that the co-occurrence might be influenced by factors such as individual, social, environmental and/or biological characteristics which protect or place the individual at risk for substance use and/or psychiatric disorder, and by the severity of either the substance use or the psychiatric disorder. Weinberg and Glantz (1998) have thus proposed that non-linear pathways that consider the interactive, dynamic and developmental aspects be explored to explain the aetiology of co-occurring psychiatric disorder and substance use. This view is based on the idea that, since co-occurring disorders develop over time and are thus integrally connected to the development of the individual, explanations for the co-occurrence should be sought through a developmental approach.

Intervention, management and treatment

Social stigma and cultural stereotypes accompany both problematic substance use and psychiatric disorder (Goldsmith, 1999). Individuals who enter treatment for either problem as adolescents or adults, usually have a history characterised by social dysfunction, problem behaviours and a lack of academic success, have exhausted, disgraced, disgusted or enraged their families and friends (Goldsmith, 1999), and are often poorly motivated or inadequately prepared for treatment (Riggs, 2003).

Research on the treatment of co-occurring psychiatric disorder and substance use has been reported relatively infrequently, considering the high prevalence of the phenomenon (70-80% in clinical samples) (Kaminer et al., 2007). Some suggested reasons for the low research output in this area have included problems with diagnosing the co-occurrence, the individuals

involved being "unstable" and difficult to recruit, or engage or retain in treatment, traditionally separated facilities for the treatment of psychiatric disorder and substance use problems, and separation of the major funding sources for psychiatric disorder and substance use (McHugo et al., 2006: 655).

Once diagnosed, co-occurring psychiatric disorder and substance use treatment usually require that the individual be stabilised and abstain from use of substances. Research-based interventions for substance use and related psychiatric disorder include medications, behavioural or psychosocial interventions, cognitive behavioural therapy, motivational enhancement therapy and community-based treatment programmes, with psychosocial approaches being the preferred initial treatment for substance use (Riggs, 2003). Other treatment modalities include multisystemic therapy, contingency management reinforcement and the Minnesota 12-step model (Kaminer et al., 2007).

Sequential or parallel treatment programmes for co-occurring psychiatric disorder and substance use have largely been found to be ineffective (Craig et al., 2008). As a result, it has been suggested that the co-occurring psychiatric disorder and substance use be treated simultaneously, with recognition of the possibility of interactions between substances of use and medications, lack of compliance with medication, and potential medication side-effects (Kaminer et al., 2007). Promising results, including symptom reduction and cost-effectiveness, have been obtained from some integrated interventions (Craig et al., 2008), but it appears that continuity of care would still be advised to ensure treatment retention (Kaminer et al., 2007).

Treatment outcomes

As previously mentioned, the co-occurrence of psychiatric disorder in substance users has been found to complicate the treatment of both the psychiatric disorder and substance use

through the potential for side-effects from medication and interactions between medications. The presence of concurrent psychiatric disorder in substance users has also been associated with increased relapse rates one year after completion of substance use treatment programmes (Compton et al., 2003). However, few studies have clearly identified the role of specific psychiatric disorder in relapse and other outcomes following treatment for substance use (Landheim et al., 2006). Furthermore, studies that have examined the role of co-occurring psychiatric disorder in substance use treatment outcome have largely examined short-term outcomes, while those that have examined longer-term outcomes (5 years and more) have been confined to limited samples (for example, individual facilities for the treatment of substance use) (Landheim et al., 2006). As a result, information on the long-term outcome of substance use treatment in individuals with co-occurring psychiatric disorder remains limited. Considering some of the problems experienced by individuals with either a psychiatric disorder or problematic substance use or a substance use disorder (for example psychosocial impairment, reduced productivity), it can be expected that the problems of individuals with co-occurring psychiatric disorder and substance use would be compounded (MacKay, 2005). However, it appears that, overall, difficulties associated with outcomes from treatment for co-occurring psychiatric disorder and substance use are often more than a summation of the challenges experienced due to each condition individually.

Compton et al. (2003), in a prospective study of substance users admitted to substance use treatment facilities in St Louis, Missouri in the United States of America, found that lifetime occurrence of antisocial personality disorder or major depression was associated with an increase in the number of illicit substances used one year after completion of substance use treatment. However, the association between psychiatric disorder and substance use treatment outcome varied with the kind of psychiatric disorder and gender. For example, the presence of phobic disorder was associated with reduced substance use at one-year follow-up, while

the co-occurrence of depression resulted in better treatment outcomes in females compared with males. Inconsistent results across studies were identified by Landheim et al. (2006). For example, one study found that, in women, depression was associated with increased alcohol consumption on follow-up (Schutte et al., 1997), while another study found the converse (Kranzler et al., 1996). Though these differences might reflect actual inconsistencies in the association between the psychiatric disorder and the substance use, it is possible that methodological differences (relating to, for example, the nature of the samples, follow-up period, the severity of the disorders) between the studies being compared could have contributed to the differences in the findings. It has also been suggested that substance use treatment outcome might be a function of the degree to which the co-occurring psychiatric disorder had been treated. Evidence has indicated that use of antidepressants was associated with a reduction in substance use, although this association was found to depend on the severity of the extant depression (MacKay, 2005).

It thus appears that the association between psychiatric disorder and outcome after substance use treatment might be influenced by several factors. These include sociodemographic factors such as i) age and marital status, with relapsers being more likely to be younger and single (Landheim et al., 2006), ii) gender, and iii) the kind of psychiatric disorder prevalent, with major depression, antisocial personality disorder and generalised anxiety disorder being associated with worse substance use treatment outcomes in males only (Compton et al., 2003) although the latter associations have not always been consistent (Landheim et al., 2006), iv) the severity of the psychiatric disorder, and whether the psychiatric disorder was current, 12-month or lifetime (MacKay, 2005). Relevant substance use factors include the kind of substances used, the severity of the substance use (MacKay, 2005), the onset of a substance use disorder (Landheim et al., 2006), the selection of outcome measures, and treatment for comorbid psychiatric disorder (MacKay, 2005).

The burden of co-occurring psychiatric disorder and substance use

Co-occurring psychiatric disorder and substance use has been shown to increase the prevalence of associated physical illnesses (Clark et al., 2009), and has been associated with increased utilisation of psychiatric disorder treatment services (Clark et al., 2009), with consequent potential increased costs in time (for example, due to lost productivity for the individual and the assisting family members) and money to the individual, the involved families, medical insurance and the State (Clark et al., 2009). Though some of these costs have proven difficult to calculate (Clark et al., 2009), evidence suggests that families of individuals with co-occurring psychiatric disorder and substance use provide the primary source of funding for treatment (Clark, 1994; Wynaden et al., 2006) and contribute additionally to the maintenance of the individuals by devoting time for their care (Clark and Drake, 1994; Ostman et al., 2000).

Definitional and diagnostic issues

The co-occurrence of more than one disorder is commonly referred to as "comorbidity", a term that is literally derived from Latin, with "co" meaning "together" and "morbus" meaning "disease" (Wittchen, 1996b). Comorbidity can be the co-occurrence, in one individual, of more than one type of the same disorder; for example, the occurrence of two types of substance use disorders, or the occurrence of two types of psychiatric disorder. Such comorbidity is commonly referred to as homotypic comorbidity. Comorbidity may also refer to the co-occurrence of two or more disorders of different types. For example, an individual might be diagnosed with both a substance-related disorder as well as a non-substance-related (and usually) psychiatric disorder. The latter co-occurrence is commonly referred to as heterotypic comorbidity (Degenhardt et al., 2001). According to this definition, comorbidity thus refers to the overlap of phenomena that meet criteria for diagnoses of disorder.

However, the term "comorbidity" is also commonly used very loosely to describe either an overlap of diagnostic classes, or "any type of association of psychopathological phenomena (symptomatic or asymptomatic overlap), irrespective of whether the phenomena met the criteria for a mental disorder", thus including overlap of diagnoses, or of symptoms or syndromes of disorders (Wittchen, 1996b: 9; 10).

Discussion of the definition of comorbidity has included whether to define comorbidity only when distinct diagnostic categories can be identified in terms of strict Diagnostic and Statistical Manual (DSM, Robins et al., 1989) or similar criteria, or whether symptoms of disorders should be considered as relevant to the diagnosis of comorbidity. Further discussion has involved what to call the phenomenon. Chambers (2008a, b) examined the options of whether to refer to comorbidity as 'dual diagnosis', co-occurring disorders' or 'double trouble' (Chambers, 2008a) or even 'triple diagnosis', where appropriate (Chambers, 2008b). Comorbid conditions have also variably been defined as a) those that occur at the same time (concurrent comorbidity), b) those that have occurred in tandem (sequential comorbidity), or c) those that have occurred at some time in the person's life, though not necessarily at the same time (lifetime comorbidity) (Degenhardt et al., 2001). In the absence of specifying the kind of comorbidity, cross-study comparisons (for example, comparisons of current versus lifetime comorbidity prevalence rates) can be inappropriate

Discussion of the definition of "comorbidity" has also opened debate on the reliability and validity of diagnostic criteria and categories of instruments such as the DSM (Robins et al., 1989). For example, Wittchen's (1996b) view held that the notion of comorbidity was a consequence of the specific diagnostic categories of the classification systems such as the DSM. Comorbidity would thus not exist if it were not for the DSM categories because the DSM draws borders to create artificial diagnostic categories (van Praag, 1996). The definition and diagnosis of comorbidity at this conceptual level are thus directly dependent on the

available and used diagnostic criteria and categories. As a result, different studies using different definitions could arrive at different diagnoses. This could increase or decrease the chances of deriving a comorbid diagnosis, once again with implications for the comparison of prevalence rates of comorbidity across studies.

The importance of researching co-occurring psychiatric disorder and substance use in adolescents and young adults

Adolescence has been identified as the developmental stage at which onset of psychiatric disorder (Kessler et al., 2005), experimentation with substances of use (Fergusson et al., 2001) and the initiation of substance use (Kandel, 1975) are most likely. These events (namely onset of a psychiatric disorder, substance use) can influence, or play a role in influencing, future events in the life of the adolescent. For example, adolescents or young adults who use substances are at risk of continuing their substance use into adulthood (Robertson, 1996) with potentially negative effects on their economic productivity, and social relationships. Furthermore, substance use has been associated with risk-taking behaviours in other areas of the lives of young (and older) people, including, for example, sexual inhibition leading to unwanted pregnancies and sexually-transmitted diseases (Myer et al., 2009b). In addition, use of one substance has often been found to be succeeded by use of other substances, with the increased possibility of future use of more dangerous substances, as well as the possibility of multiple substance use. (Dawes and Donald, 1994). Substance use in young people has also been associated with social dysfunction, school absenteeism and academic deterioration, possibly negatively affecting future achievement (Dawes and Donald, 1994), while the transition from adolescence to adulthood is also often marked by the onset of depression. (Reinherz et al., 2000). It is, therefore, necessary to address the adolescent events and characteristics, identified as risk factors for future problems, to develop appropriate

interventions that will minimise their potential negative effects on the lives of the individuals involved.

Additional evidence has indicated high prevalence rates of substance use amongst adolescents, and increasing evidence for associations between psychiatric disorder and substance use, although the prevalent symptoms might not always meet diagnostic criteria (Deas, 2006). Yet relatively few community studies have been conducted on adolescent substance use and associated psychiatric disorder (Langenbach et al., 2010). The studies on co-occurring psychiatric disorder and substance use in youth have largely been confined to specific mental disorders, and to substance use treatment outpatients or inpatients (Langenbach et al., 2010). This has resulted in limited information being available on comorbid substance use and psychiatric disorder in young people in inpatient treatment for substance use (Langenbach et al., 2010).

Further advantages for investigating comorbidity in young people would include that, with younger individuals, problems associated with recall regarding onset of symptoms might be reduced. Younger individuals have a longer opportunity to be followed up than older people. Thus well-designed cohort studies have opportunities to observe the course of disorders and treatment outcome for longer periods in younger people than would be possible with older people. Furthermore, investigating young people can provide opportunities for early diagnoses with the potential for early intervention and treatment.

Operational definitions

Specific terms have been operationalised for use in this thesis. Co-occurring non-substance use psychiatric disorder and substance use will generally be referred to as 'comorbidity', unless otherwise stated. The term 'psychopathology' will refer to psychiatric symptoms in those cases where a diagnosis had not been made or confirmed, and to psychiatric disorders

or mental illness in those cases where a diagnosis had been confirmed. The term substance use will be used to refer to any substance use, regardless of whether the substance use involves casual use, problematic use, misuse, abuse, or dependence, unless these latter terms are specified.

Rationale

The research for this thesis was conducted to explore the notion of comorbidity in adolescents and young adults within a South African context. In so doing, the thesis addresses a topic that has not been extensively researched in developing countries such as South Africa. The studies for the thesis also examine the occurrence and nature of comorbid psychopathology and substance use in adolescents and young adults, a group that has been recognised as under-researched with respect to comorbidity (Angold et al., 1999). Furthermore, this thesis addresses the need for increased knowledge about comorbidity in both community and treatment samples, and provides insights into factors that potentially influence substance use treatment outcomes in inpatient substance users.

Aims (Table 1)

The general aim of this thesis is:

To examine the association between psychopathology and substance use in adolescents (aged 14 to 17 years) and young adults (aged 18 to 30 years).

The specific aims of the thesis are:

1. To examine the frequency of occurrence, and nature, of psychopathology, substance use, and comorbidity in Cape Town high school students, young adult substance use inpatients, and in the broader South African community of young adults.

2. To examine the role of sociodemographic factors in comorbid psychopathology and substance use in Cape Town high school students, young adult substance use inpatients, and in the young adult South African population.
3. To examine the role of sociodemographic factors and comorbid psychopathology in the substance use inpatient treatment outcomes of young adults.

The thesis objectives are:

1. To quantify the occurrence of psychopathology, substance use and comorbidity in adolescents and young adults.
2. To measure strengths of association between specific psychopathology and specific substances of use.
3. To identify demographic and/or social factors that influence comorbidity.
4. To identify demographic and/or social, psychopathology and substance use factors that influence substance use inpatient treatment outcomes as defined by treatment completion, relapse and treatment resumption.

Development of the research

The intention was for the completed thesis to consist of a cross-sectional and longitudinal community study of Cape Town high school adolescents and young adults, and a cross-sectional and longitudinal study of Cape Town adolescent and young adult substance users in inpatient substance use treatment.

The thesis was embarked upon to examine associations between psychopathology and substance use in young people, and involved conducting an extensive literature review as well as empirical studies.

The literature review was conducted to gain an understanding of the issues pertinent to research in comorbid psychopathology and substance use in young people, and to identify areas of comorbidity research where questions remained unanswered.

For the empirical components of the thesis, the initial intention was to conduct secondary analysis studies involving school-going young people, and primary studies of treatment centre-based adolescents and young adults. The school studies were to take the form of a cross-sectional study of young people (Grades 8 and 11, and aged 18-24 years), followed by a longitudinal study of the original Grade 8 students in Grade 10 and again in Grade 12. The treatment centre studies were intended to involve a cross-sectional and, subsequently, a longitudinal, study of adolescent and young adult substance-using inpatients, in treatment for their substance use and of ages similar to those of the high school students, would be conducted. However, during the execution of the thesis plans, two main changes to the original protocol became necessary due to circumstances beyond the control of the researcher.

Firstly, the longitudinal study of school-going students was abandoned: it was found, after lengthy examination of the data, that the longitudinal data set for the high school students was inappropriate for the intended analyses due to its pattern of missing data, despite earlier statistical advice that the missing data could be imputed. Subsequent analyses identified that the gaps in the missing data were not random, but pertained largely to students who had earlier reported substance use. This finding had potential implications for the results of the study pertaining to associations between psychopathology and substance use, thus rendering imputation of the missing data inappropriate.

It was then decided that a secondary analysis of young adults from a different data set [namely, from the South African Stress and Health (SASH) survey] would be completed in place of the longitudinal analysis of the high school adolescents.

Secondly, the upper age limit for participants sampled for the treatment centres and SASH studies was extended to 30 years, thus exceeding the age of the oldest student in the high schools study. The reasoning was as follows: during the sampling of inpatients, the treatment centres selected as study sites experienced an unanticipated and dramatic decrease in inpatient admissions, particularly among adolescents and young adults, with one treatment centre electing to close its dedicated adolescent chemical dependency unit because of a lack of financial viability. Though the reason for this slump was not clear, it coincided with the global economic recession, and/or possibly parents could not afford to have their substance-using adolescent children in protracted inpatient treatment programmes. The implications of a reduced sample size were serious for the research plan, and decisions had to be made to accommodate the unanticipated circumstances. It was decided that, since the SASH study sampled only individuals who were aged 18 years and older, and the inpatient substance use treatment centres were not admitting many adolescents younger than 18 years, the age limits for the inpatient study sample would be extended. The upper age limit was set at 30 years for these samples (inpatient baseline and follow-up studies, and the SASH study), to approximate the ages considered for the literature review (already published by this time), and to ensure at least adequate sample sizes within the time constraints of the projects involved.

The different study samples in the thesis, therefore, consist of adolescents aged 14 to 17 years and young adults aged 18 to 24 years for the high schools study, adolescents aged 17 years and young adults aged 18 to 30 years for the substance use inpatient studies, and young adults aged 18 to 30 years for the SASH study. Thus, broadly speaking, the study samples consisted

of young adults, remaining faithful to the original plan of investigating comorbidity amongst young people.

Construction of the thesis

This thesis is built upon four separate studies. Each of the studies examines the association between psychopathology and substance use in young people, and includes a dimension that sets it apart from each of the other studies (Table 2). Table 1 summarises the studies completed for this thesis, detailing the aims and objectives of the various studies, and the status of the related journal articles.

Overview of chapters

Following this introductory chapter, Chapter 2 provides a review of the recent literature as it relates to the association between substance use and psychopathology in general. Particular emphasis is placed on the literature relating to the association between substance use and psychopathology from the perspective of identified adolescent and young adult substance users who have psychiatric problems, as opposed to reviewing the literature relating to the substance use problems of identified psychiatric patients. Chapter 3 describes a survey of high schools in Cape Town, South Africa, in which Grade 8 and Grade 11 students were compared with regards to the association between their substance use and psychopathology. In Chapter 4 a study that examined the association between substance use and psychopathology in individuals who attended inpatient treatment for substance use is presented. Chapter 5 is a follow up of those patients in Chapter 4 who had been in inpatient treatment for their substance use, and examines treatment outcomes in relation to comorbidity. Chapter 6 outlines the findings of the South African Stress and Health (SASH) survey in relation to the association between substance use and psychopathology in a representative, nationwide community survey. Chapter 7 is the final chapter of this thesis,

and presents over-arching conclusions from the studies conducted. In addition, this chapter highlights points of discussion from each study, discusses recognized strengths and limitations of the studies, and suggests recommendations for future research.

Thus, in summary, this thesis consists of an introductory chapter (Chapter 1), a literature review (Chapter 2), four empirical studies (Chapters 3, 4, 5 and 6), and a discussion chapter (Chapter 7).

Finally, to address the period between completion of the literature review (2008) and submission of the thesis for examination, Chapters 1 and 7 include discussion of more recent empirical studies, while the Introductions of each of Chapters 3 through 6 include updated reviews of more recent relevant literature.

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Table 1: Aims and objectives of thesis projects

	STUDY 1	STUDY 2	STUDY 3	STUDY 4	STUDY 5
TITLE	The association between psychopathology and substance use: a review of the literature	Association between psychopathology and substance use amongst school-going adolescents in Cape Town, South Africa	Young substance users in treatment: the association between psychopathology and substance use	Comorbid psychopathology and substance use: a follow-up of inpatient substance users in Cape Town, South Africa	Association between psychopathology and substance use : results from the SASH survey
GENERAL AIM	To examine the association between psychopathology and substance use	To examine the association between psychopathology and substance use	To examine the association between psychopathology and substance use	To examine the association between comorbidity and substance use treatment outcomes	To examine the association between psychopathology and substance use
SPECIFIC AIMS AND OBJECTIVES	1. To synthesise findings from other comorbidity research. 2. To understand recent developments in, and current status of	1. To determine the occurrence and nature of psychopathology, substance use, and comorbidity	1. To determine the occurrence and nature of psychopatholo gy, substance use, and	1. To identify psychopatholo gy, substance use and demographic factors that	1. To determine the prevalence and nature of psychopathology , substance use, and comorbidity

	debate concerning, comorbidity. 3. To identify knowledge gaps. 4. To identify factors that influence comorbidity.	2. To examine the role of sociodemographic factors in comorbidity	comorbidity 2. To examine the role of sociodemographic factors in comorbidity	influence substance use treatment outcomes	2. To examine the role of sociodemographic factors in comorbidity
STATUS OF ARTICLE	Published Saban, A. and Flisher, A.J. (2010). The association between psychopathology and substance use in young people: a review of the literature. Journal of Psychoactive Drugs, 42(1): 37-47.	Published Saban, A; Flisher, A.J. and Distiller, G. (2010). Association between psychopathology and substance use among school-going adolescents in Cape Town, South Africa. Journal of Psychoactive Drugs, 42(4)	In review Drug and Alcohol Review	In review Journal of Groups in Addiction and Recovery	In review Drug and Alcohol Dependence

Table 2: Comparative summary description of thesis studies

	STUDIES			
DESCRIPTION	High school students (STUDY 2)	Baseline Inpatient substance users (STUDY 3)	Follow-up Inpatient substance users (STUDY 4)	South African Stress and Health (SASH) study (STUDY 5)
SAMPLE				
	Random	Consecutive	Consecutive	Random
	Local, Cape Town	Local, Cape Town	Local, Cape Town	National, South Africa
DEMOGRAPHICS				
Age	12-24 years	17-30 years	17-30 years	18-30years
Gender	Males and females	Males and females	Males and females	Males and females
Racially classified social group (RCSG)	All	White, Coloured, Indian	White, Coloured, Indian	All
Education	Grades 8 and 11	Highest level completed	Highest level completed	Highest level completed
Marital status	Not married	Married/Not married	Married/Not married	Married/Not married

Employment	Not applicable	Employed/Unemployed	Employed/Unemployed	Employed/Unemployed
PSYCHOPATHOLOGY				
Instrument[†]	Harvard Trauma Scale, Beck Depression Inventory Zung Anxiety Scale	C-DIS IV	C-DIS IV	CIDI
Diagnoses:	Current PTSD Current Depression Current Anxiety	Any 12-month	Any 12-month	12-month and lifetime Mood and anxiety disorders
SUBSTANCE USE				
Instrument	Questionnaire	Questionnaire and C-DIS IV	Questionnaire and C-DIS IV	CIDI

Substances	Ever smoked a whole cigarette Ever had more than sip of alcohol Ever used cannabis, inhalants	Any	Any	Ever smoked >100 cigarettes Ever used alcohol, cannabis, other or extra-medical drugs

† C-DIS IV: Computer-assisted Diagnostic Interview Schedule for Diagnostic and Statistical Manual IV

CIDI: Composite International Diagnostic Interview

CHAPTER 2

Literature Review

The Association between Psychopathology and Substance Use in Young People: A Review of the Literature[†]

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Abstract--This article reviews the recent literature on the association between psychopathology and substance use in young people. An electronic literature search, using PSYCINFO/PSYCLIT and PUBMED/MEDLINE, yielded 93 English-language articles for the period 1990-2008. Of these articles, 89 (95.7%) reported studies conducted in developed countries, 57 (61.3%) had community or population samples, 38 (40.9%) had sample sizes ranging from 500 to 2000 subjects, and 33 (36.7%) had sample sizes of between 50 and 500. The most commonly-used assessment tool (n =29, 31.2%) was the Diagnostic Interview Schedule. Evidence exists for associations between depression and cigarette smoking, between anxiety and cigarette smoking, and between anxiety and alcohol use. The strength of the associations is increased with greater frequency and quantity of substance use, and is influenced by the nature of the psychopathology, the specific substances of use, and demographic factors such as gender, age or developmental stage. The need for more longitudinal studies on community populations, and increased access to funds and resources for researchers in developing countries is highlighted.

Keywords--Psychopathology; Substance use; Comorbidity; Young people

Various studies have suggested that the co-occurrence of substance use and psychopathology can be reached via a variety of pathways. For example, evidence for a statistical association between substance use and psychopathology would imply that a dynamic links the prevailing conditions. Thus, the one condition might have caused the other, triggered an existing predisposition for the other, increased the risk of developing the other condition, or changed the course of the other condition. The most frequently cited explanations for co-occurring substance use and psychopathology include that of causality based on a temporal relationship, self-medication, where attempts are made to alleviate the symptoms of mental illness by using substances, risk factors for either the substance use or psychiatric illness, or that factors may mediate or moderate the association between co-occurring or comorbid substance use and psychopathology (Degenhardt, Hall & Lynskey 2001).

Several reviews address comorbid substance use and psychopathology. Many of these were published more than a decade ago (Bukstein, Brent & Kaminer 1989; el-Guebaly 1990; Woody, McClellan & O'Brien 1990; Wilens & Biederman 1993), or examine associations between specific psychopathologies and specific substances of use and abuse (Gerstley et al. 1990; Kushner, Sher & Beitman 1990; Angold & Costello 1993; Glassman 1993; Schuckit and Hesselbrock 1994). The more recent review articles on comorbid substance use and psychopathology confine themselves to a subset of substances and psychiatric disorders. For example, Rey et al. (2004) examine only cannabis use and juvenile psychiatric disorder; Upadhyaya et al. (2002) examine only adolescent cigarette smokers; Weinberg & Glantz (1999) examine only child psychopathology risks for drug abuse; Angold, Costello &Erkanli (1999) review only population comorbidity studies in relation to the psychiatric disorders that are regarded as common in children and adolescents; Armstrong & Costello (2002) review only community studies on adolescent substance use and psychiatric comorbidity; and Jane-Lopis & Matytsina (2006) review only studies from high-income countries.

We undertook this literature review to synthesise the findings of previous research, and to understand the recent development and current status of the broader debate concerning the association between substance use and psychopathology in general, with a view to identifying areas of research that require further investigation. This was done to provide a springboard from which to launch a series of studies in a developing country where the association between psychopathology and substance use has had limited investigation, particularly amongst the youth. With these aims in mind, the articles selected for review were not limited to particular substances or psychiatric disorders, or to specific settings or countries. Instead, this review highlights those issues relating to any comorbid psychopathology and substance use that are pertinent to adolescents and young adults, emphasizing the most common associations that have been identified in both community and clinical settings, and the salient factors that impact on these associations. As such, the present review explores the geographical locations in which empirical studies have been conducted, the sizes and kinds of samples used, the instruments used to assess psychopathology and substance use, the kinds of psychopathology and substance use investigated, the statistical analyses employed, and the outcomes discussed as they pertain to associations between psychopathology and substance use.

METHODS

We searched for English language articles, using the PUBMED/MEDLINE and PSYCLIT/PSYCINFO databases and the keywords "comorbidity and substance use", "comorbid substance use and psychopathology", "substance use and psychopathology" and "dual-diagnosis". Online links, related articles and the reference lists of relevant published articles were sourced, and key researchers in the field were consulted.

Articles were sourced from the period 1990-2008. The year 1990 was selected as the starting date for the literature search since Bukstein, Brent & Kaminer's (1989) review was completed the prior year, and appears to have identified and summarized the major role players

comprehensively, capturing the important conceptual and clinical issues relevant to the debate to-date.

The inclusion criteria for article selection were empirical studies, published in English between 1990 and 2008, that have been done in the area of substance use and associated psychopathology, using adolescent and young adult samples within the ages of approximately 14 to 25 years. All articles relating exclusively to the comorbidity of psychotic disorders with substance use were excluded from consideration for the present literature review, unless these articles referred to research that included the investigation of non-psychotic disorders as well. The psychotic disorders were excluded from the present review because the association between substance use and the psychotic disorders is very common and has been well-documented (Castle & Murray, 2004). In those studies that used clinical or treatment samples, articles that referred to patients in treatment for substance use were selected, as opposed to selecting articles relating to patients who were in treatment for psychiatric disorders. Sourced articles were reviewed with reference to the geographical location of the study, sample size, study design, types of psychopathology and substance use investigated, assessment instruments used, and study outcomes (Tables 1-3 are available on request from the primary author).

RESULTS

Ninety-three articles were found to be relevant for review.

Geographic location of research

The large majority of articles reviewed relate to studies that were completed on the North American continent, with 67 articles (72%) from the United States of America and two (2.2%) from Canada. Two articles each (2.2%) were from South Africa and the United Kingdom, five (5.4%) from Australia, four articles each (4.3%) from the Netherlands and New Zealand, three (3.2%) from Germany, and one article each (1.1%) from Brazil, Taiwan, Italy and Switzerland.

Sampling strategies

Most of the articles reviewed (n = 57; 61.3%) used community or population samples, while 28 (30%) articles used treatment samples. Eight articles (8.6%) used samples that included both community members and patients, while one study sample (1.1%) consisted of only substance-using army draftees. Fifty-five (59.1%) studies used a cross-sectional and 38 (40.9%) used a longitudinal design. Relatively few studies had sample sizes larger than 2000 (n = 22; 23.7%), but five studies (5.6%) had sample sizes between ten thousand and more than twenty thousand. Several of the studies (n = 38; 40.9%) had sample sizes ranging from 500 too 1999, while 33 (35.4%) had sample sizes of 50 to 500. Two of the studies (2.2 %) had sample sizes of fewer than 50 subjects with Horner and Scheibe (1997) having a sample size of 30.

Sample demographics

Race/Ethnicity.

In 20 (21.5%) articles, samples had a distinctly significant majority of one population group. Breslau, Kilbey &Andreski (1991), Rounsaville et al. (1991), Breslau, Kilbey &Andreski (1993), Dunn al. (1993), Kendler et al. (1993), Fals-Stewart & Angarano (1994), Grilo et al. (1995), Kandel et al. (1997), Biederman et al. (1997), Horner & Schiebe (1997), Breslau & Klein (1999), Costello et al. (1999), Disney et al. (1999), Greene & Biederman (1999), Reinherz et al. (2000) and Goodman et al. (2003) had samples that were largely or exclusively White. Compton et al. (2003) and Miller- Johnson et al. (1998) had samples that were largely African-American, Novins et al. (1996) had a sample consisting of only American Indian patients, while Obando et al. (2004) sampled only Costa Ricans. Though these samples were not necessarily biased, in that they might have truly been representative of the populations from which they were drawn, they provide for limited conclusions beyond the ethnic composition of the samples.

Age. The ages of subjects varied greatly. Some subjects were selected at birth for later follow-up in a longitudinal study (Fergusson, Lynskey &Horwood 1996; Hayatbakhsh et al, 2007) while some studies investigated subjects within a relatively narrow age range (14-15 years,

in Patton et al. 1998, or all 17 years old in Disney at al. 1999). Most of the studies (66.7%; n = 62) investigated largely children or young adults. Of the remaining studies, 29 (31.2%) had their age range lower limit in the adolescent or young adult sector.

Assessment and diagnosis. The most commonly used assessment and diagnostic instrument (n=29; 31.2%) was the Diagnostic Interview Schedule (DIS; children and adult versions). Thereafter the most common means of assessment were questionnaires, self-reports, rating scales and structured interviews (n=28; 30.1%). Some studies elected to make their assessments, particularly assessments of psychopathology, by means that require clinical judgement (Kendler et al. 1993), while other studies used instruments such as the DIS (King et al. 1996; Breslau et al. 1997; Kandel et al.1997; Roberts, Roberts & Xing 2007) and Composite International Diagnostic Interview (CIDI) (Kessler et al. 1997; Ross & Shirley 1997; Lieb et al. 2002; Zimmermann et al. 2003; Wittchen et al. 2007) which allow for use by lay interviewers. In some cases the same instrument was used to assess both psychopathology and substance use because the instrument allowed for this to be done (for example, Anda et al. 1990; Schuckit, Irwin & Brown 1990; Fals-Stewart & Angarano 1994; Merikangas & Klein 1994; Lieb et al. 2002; Zimmermann et al. 2003; Roberts, Roberts & Xing 2007; Wittchen et al. 2007). This occurred particularly in studies where the DIS or CIDI was used as the primary diagnostic instrument (for example, Glassman et al. 1990; Regier et al. 1990; Deykin, Buka & Zeena 1992; Breslau, Kilbey & Andreski 1993). In some studies, more than one instrument was used to assess either substance use (for example, Riggs et al. 1995) or psychopathology (for example, Sonne, Brady & Morton 1994; Kandel et al. 1997), or a subscale or module of an instrument like the DIS was used to assess the pathology or substance use of interest (for example, Henry et al. 1993; Fals-Stewart & Angarano, 1994).

In several studies, more than one instrument was used to assess psychopathology (for example, Dunn et al. 1993). This was the case both in those studies in which more than one kind of psychopathology was being assessed (for example, Dunn et al. 1993; Fals-Stewart &

Angarano, 1994), as well as in studies where there was one major pathology of interest (Sonne, Brady & Morton 1994). For example, in Boyle et al. (1992) any psychopathology was of interest, and the Youth Self Report and Child Behaviour Checklist as well as structured, self administered questionnaires were used to assess these disorders. Similarly, Sonne, Brady & Morton et al. (1994) used the SCID, as well as Hamilton's Depression Rating Scale and the Young Mania Rating Scale. More examples of multiple instrument use to assess either pathology or substance use are listed in Table 2.

Several studies investigated more than one type of substance use or abuse (for example, Deykin & Buka, 1992; Henry et al.1993; Biederman et al. 1995). Thus, one study might attempt to determine any substances of use (for example, King et al. 1996; Novins et al. 1996; Brooner et al. 1997), while another would test for only one type of substance of use or abuse (for example, Moscato et al. 1997; McGee, Williams & Stanton 1998; Patton et al. 1998). Other studies looked at a variety of different, but defined, substances of use, for example, tobacco, alcohol, cannabis (Degenhardt, Hall & Lynskey 2001). Still other studies, for example Ferdinand, Blum & Verhulst (2001), looked at some defined substances of use and abuse, namely tobacco and alcohol use, as well as any other drug use. It is, however, quite clear that, of those studies that investigated specific substances of use and abuse, tobacco (n=29; 32.2%) and alcohol (n=45; 50%) were the most frequently emphasized. Several studies used more than one instrument to assess substance use. Thus, for example, even though Kushner, Sher & Erickson (1999) assessed only alcohol use, they used the DIS as well as the Short Michigan Alcohol Screening Test (S-MAST).

Statistical analyses

The main statistical analyses used varied greatly, from some studies concentrating largely on descriptive statistics (for example, Rounsaville et al. 1991; Sonne, Brady & Morton 1994; Grilo et al. 1996), t-tests and chi-squared tests (for example, Araujo & Monteiro 1995; Hovens, Cantwell & Kiriakos 1994;) to others that used a variety of comparatively highly sophisticated statistical techniques (for example, Brook et al. 1996; Fergusson, Lynskey & Horwood 1996;

Kendler et al. 1993; Patton et al. 1998). Most commonly, regression analyses were used, while similar associations are illustrated using discriminant function analyses in a few studies (Brown et al. 1996; King et al. 1996; Brooner et al. 1997).

Findings

This section records the outcomes of the reviewed studies, with regards to the associations between psychopathology and substance use, and the identified salient sociodemographic and other factors that appear to impact these associations. Particular attention is paid to the roles of age and gender on comorbid associations, to associations between psychopathology and cigarette smoking, alcohol and cannabis use, as well as to temporal associations among these.

Age. Certain patterns have emerged across ages and stages of development. For example, according to Henry et al. (1993) pre-adolescent conduct problems and depressive symptoms (at age 11 years) predicted multiple drug use by age 15 years, with the depressive symptoms appearing to have a more significant role in this association than the conduct problems. Sonne, Brady & Morton. (1994) found that 20 years of age is significant in that those who used substances were more likely to develop mood disorders with onset before 20 years of age. On examining 12-18 year olds, Brook et al. (1995) found that childhood personality traits were associated with adolescent personality traits as they pertained to substance use. Similarly, Grilo et al. (1995) found that childhood conduct disorder was associated with adolescent substance use, while Ferdinand, Blum & Verhulst (2001) found that behavioural and emotional problems in adolescence related to substance use in young adulthood. It thus appears that developmental stage might play an important role in the association between psychopathology and substance use, and that the role of developmental stage could possibly exceed that of chronological age. However, unless stages in between those of the suggested developmental stages are also examined for an association of this nature in equivalent studies, the validity and relevance of the developmental stages in contrast to chronological age remain unclear.

Gender. Gender appears to play a significant role in the course and development of some pathologies. For example, Glassman et al. (1990) found that males are more likely than females to have ever smoked and been successful in smoking cessation, but that these gender differences tend to disappear in the presence of comorbid major depressive disorder or lifetime diagnosis of major depression (MD). More evidence for the role of gender in the association between psychopathology and substance use is provided by the following studies. Brooner et al. (1997) found that their male and female opioid dependents differed markedly, with females being more likely to have Axis I disorders and males more likely to have personality disorders. Henry et al. (1993) found that childhood conduct problems and depressive symptoms predicted adolescent multiple drug use in males, while in adolescent females, only childhood conduct problems were strongly associated with substance use. Hofstra et al. (2001) found that childhood aggressive behaviour predicted adult alcohol misuse or dependence in females, but not in males. Hovens, Cantwell & Kiriakos (1994) found that male substance abusers were more likely to have conduct disorders while female abusers were more likely to have anxiety disorders. Deykin & Buka (1997) found that in males, substance abuse preceded onset of PTSD while in females the reverse occurred. Costello et al. (1999) found a strong association between depression and substance use in males, as well as a strong association between conduct disorders and substance use in females. Similarly, Henry et al. (1993) found that only in females at age 15 years was there a strong association between conduct problems and multiple substance use. Moscato et al. (1997) found that females were more likely to have depressive symptoms while males were more likely to have alcohol problems. They also found that depressive symptoms preceded and predicted alcohol problems in females who initially had no alcohol problems, but that no such significant relationship existed in males. This result concurred with the finding of King et al. (1996) that depression leads to alcohol abuse in females.

Yet the role of gender in comorbid psychopathology and substance use remains unclear because of several conflicting findings. For example, Fergusson, Lynskey & Horwood (1996)

found no significant differences between males and females as regards comorbid depression and nicotine dependence, while Costello et al. (1999) found a strong association between depression and substance use but only in males. Similarly conflicting findings are illustrated by the findings of the following studies. Shrier et al. (2003) found that anxiety symptoms were most common in females but that these were not associated with substance use disorders. Fergusson, Lynskey & Horwood (1996) found no difference between males and females regarding their comorbid depression and nicotine dependence at age 16 years.

Association between psychopathology and smoking. Several of the studies reviewed have identified an association between depression and smoking. Of these, 11 studies were longitudinal studies which used community samples (Anda et al, 1990; Glassman et al., 1990; Breslau, Kilbey & Andreski 1993; Fergusson, Lynskey & Horwood 1996; Breslau et al. 1998; McGee, Williams & Stanton 1998; Patton et al. 1998; Brook, Cohen & Brook 1998; Johnson et al. 2000; Escobedo, Reddy & Giovino 1998; Kessler et al. 1996; King, Iacono & McGue 2004; Costello et al. 1999) while the remainder were cross-sectional studies which used community samples either in clinical settings (Riggs et al. 1995) and/or or from the community (Breslau, Kilbey & Andreski 1993; Kendler et al. 1993; Fernander et al. 2006; Kessler et al. 1996). Anda et al. (1990) found that with an increase in the level of depression (as measured by the CES-D score), the prevalence of smoking increased. They also found that those people with increased CES-D scores were less likely to have quit smoking and, as found by Glassman et al. (1990), were less likely to quit smoking over time. A strong association between major depression and smoking was reported by Kendler et al. (1993). Fergusson, Lynskey & Horwood (1996) identified a significant association between nicotine dependence and affective disorder, particularly for depression and depressive disorder, in 16 year olds. The presence of this association was later borne out by the results of Breslau et al. (1998), McGee, Williams & Stanton (1998), Brook, Cohen & Brook (1998) and Fernander et al. (2006) who similarly found associations between smoking and depression, while Escobedo, Reddy & Giovino (1998) reported that depressed

adolescents were more likely to initiate smoking, Patton et al. (1998) established an association between depression, anxiety and smoking initiation, and Johnson et al. (2000) found an association between anxiety disorders and cigarette smoking.

It thus appears that there is strong evidence for an association between depression and cigarette smoking, and possibly between anxiety disorders in general and cigarette smoking. It also seems clear that with increased levels of depression, there is likely to be an associated increased prevalence of cigarette smoking, an increased chance of smoking initiation, and a decreased likelihood of smoking cessation both in the short and long term.

***Association between psychopathology and alcohol use*.** Several studies explore the association between psychopathology and alcohol use. Some of these studies used cross-sectional community samples (Schuckit, Irwin & Brown 1990; Kendler et al.1993; Merikangas, Risch & Weissman 1994; Schmidt 1995; King et al. 1996;; Kessler et al. 1997; Kushner, Sher & Erickson 1999; Dixit & Crum, 2000; Rodgers et al. 2000; Hofstra, van der Ende & Verhulst 2001; Steinhausen & Metzke, 2003; Goodman et al. 2003; Grant et al. 2004), some used longitudinal community samples (Rohde, Lewinsohn & Seeley 1996; Brown et al. 1996; Moscato et al. 1997; Costello et al. 1999 and Ferdinand, Blum & Verhulst 2001), while Clark et al. (1997) used a convenience sample of a treatment experimental group and voluntary controls, and Dunn et al. (1993) and Compton et al. (2003) used cross-sectional treatment samples of substance users.

The results of these studies indicate that, in general, there appears to be little doubt that anxiety symptoms commonly occur on cessation of alcohol drinking (Schuckit, Irwin & Brown 1990) However, as indicated by Roberts et al. (1999), these anxiety symptoms are often temporary and are specifically related to the abstinence and subsequent withdrawal. As such, the latter authors strongly recommend that one delay making a diagnosis of comorbid anxiety and problem drinking, as the anxiety symptoms commonly remit with time. Thus, it is important to distinguish between anxiety symptoms that are associated with, or constitute, a psychiatric

diagnosis of anxiety, and those anxiety symptoms that are commonly as a result of alcohol abstinence, and are temporary.

Regier et al. (1990) found that there was a greater association between anxiety disorders and other drugs than between anxiety and alcohol dependence. Nace, Davis & Gaspari (1991), when examining a group of 100 inpatient substance users found that those with personality disorders were more likely to abuse alcohol. Merikangas & Klein (1994) looked at non-hospitalised subjects with Major Depression, and found that anxiety disorders preceded alcoholism in 65% of those who were diagnosed with comorbid anxiety and alcoholism. Schmidt (1995) found that patients admitted for psychiatric problems such as anxiety, depression, hostility, phobia, somaticism, paranoia and obsessive-compulsive disorders were more likely than non-admitted community members to have been drinking heavily. In 1997, Biederman et al. reported that anxiety and depression were weakly associated with the development of subsequent problematic substance use. Clark et al. (1995) examined 43 adolescents who were hospitalized for alcohol abuse or dependence and found that, of these patients, 40% had at least one anxiety disorder, of which social phobia was the most common. This anxiety prevalence rate was also higher than that in the control group of volunteer community adolescents. Similarly, Araujo & Monteiro (1995) found an association between depression, generalised anxiety and alcohol use. In contrast, however, Shrier et al. (2003) found that anxiety symptoms in a convenient clinical sample were not associated with substance use disorders.

Some studies examined the association between psychopathology other than anxiety, and the use of alcohol. For example, Deykin, Buka & Zena (1992), on examining a group of alcohol and other substance users in treatment, found a greater association between substance abuse and depression as compared with that in the community. Dunn et al. (1993) found an association between depression and PTSD and alcohol use. Clark et al. (1997) found that alcohol dependence led to an increased prevalence rate of other psychiatric problems, and particularly that of major depression and PTSD, with the Major Depression and PTSD being able to either follow or

precede the alcohol use disorder. Biederman et al. (1995) found that the presence of ADHD with childhood onset increased the lifetime risk of drug or alcohol abuse or dependence. Brown et al. (1996) established an association between Conduct Disorder and alcohol and other drug use in a largely White sample of substance users in treatment.

Since the abovementioned studies used largely treatment samples, it is important to compare the results they obtained with the results of those studies that examined community non-clinical samples particularly since comorbid psychopathology and substance use is more likely to be found within a treatment setting, both as a result of Berkson's Bias and because people with one extant condition are mathematically more likely to seek treatment for a second condition (Du Forte, Newman & Bland 1993). Bearing this in mind, we find that Kendler et al.'s (1993) study of female twins reported a highly significant association between Major Depression and alcoholism, even though they were unable to establish which disorder was the preceding one. Breslau et al. (1997) found a similar association when examining mothers from three study sites in the USA. The latter authors concluded that a significant association exists between PTSD and lifetime occurrence of MD, anxiety disorders, alcohol abuse or dependence, and that PTSD increased the risk for first onset of MD and alcohol abuse or dependence. These results concurred with the earlier findings of Rohde, Lewinsohn & Seeley (1996) and the later findings of Dixit & Crum (2000). Rohde, Lewinsohn & Seeley (1996) found that other psychiatric disorders can lead to alcohol disorder, and that early age onset of alcohol disorder can increase the risk of developing comorbid depression and behavioural disorders. Dixit & Crum (2000) found that a history of depression increased the risk for heavy alcohol use.

Kushner, Sher & Erickson (1999) found that the presence of an anxiety disorder or alcohol abuse or dependence increased the likelihood of developing the other disorder concurrently. In contrast, Costello et al. (1999) found no evidence for an association between anxiety disorders and ADHD and the likelihood of substance use. Grant et al. (2004) found a strong association between all mood and anxiety disorders and drug dependence. Henry et al.

(1993) similarly found an association between conduct problems, depressive symptoms and multiple drug use that included alcohol. Boyle et al. (1992) found an association between conduct disorder and marijuana, but not with the use of tobacco and alcohol. Hofstra, van der Ende & Verhulst (2001) found an association between childhood aggressive behaviour and adult alcohol misuse, but only in females.

In summary, it thus appears that there is evidence for an association between anxiety and alcohol use, even though anxiety symptoms appear to be associated with cessation of heavy or prolonged alcohol use, while anxiety disorders are more likely to be associated with use of substances other than alcohol. In the event of comorbid anxiety and problematic alcohol use, it appears that the anxiety is more likely to have preceded the alcohol use. Heavy drinking and related disorders appear to be associated with psychiatric problems such as PTSD and depression, and, while major depression and alcoholism commonly co-exist, the order in which these disorders occur is unclear.

Association between psychopathology and cannabis. Four studies looked exclusively at cannabis in association with mental disorder (Rey, Andres & Krabman 2002; Monshouwer et al. 2006; Troisi et al., 1998; Hayatbakhsh et al. 2007). Troisi et al. (1998) examined the association between any psychopathology (but mainly depression) in a sample of 133 Italian male army draftees; Rey, Andres & Krabman (2002) sampled 1261 adolescents from the National Survey of Mental Health and Wellbeing (in Australia); Monshouwer et al. (2006) sampled 5551 adolescents from the Dutch Health Behaviour in School-aged Children schools survey, while Hayatbakhsh et al. (2007) did a secondary analysis of data obtained from the Mater University Study of Pregnancy (MUSP) and followed up newborns until age 21 years.

Troisi et al. (1998) found that the entire sample of cannabis users, abusers, and dependents suffered from a psychiatric disorder. These included Axis I and Axis II disorders, and mainly affective (depressive) disorders. This study makes specific mention of the possible effects of the nature of the sample and the circumstances under which the sample was selected. However,

despite the noted limitations of this study, the results indicate a distinct increase in psychiatric disabilities with increased use of cannabis. The Monshouwer et al. (2002) study specifically aimed to investigate the role of confounders in the association between cannabis use and mental health as measured by the Youth Self Report. Their results, too, demonstrated an increase in the strength of the association with increased frequency of cannabis use, but found that gender and age were not operative confounding factors in this association. More specifically, this study found a strong association between aggressive behaviour and cannabis use, while a weak association was found between cannabis use and depressive disorders. The findings of Rey, Andres & Krabman (2002) largely concurred with the findings of the other two studies, demonstrating an association between cannabis use and depression and behavioral disorders. The Hayatbakhsh et al. (2007) study found a significant association between anxiety/depression and cannabis use, but found that, though early cannabis use was significantly associated with anxiety/depression in young adults, anxiety/depression in adolescence did not predict early cannabis use, regardless of possible differences in socioeconomic and demographic factors.

Several other studies also specified examining the role of cannabis in the association between psychopathology and substance use, but included the role of other substances of interest in this association (Boyle et al. 1992; Henry et al. 1993; Miller-Johnson et al. 1998; Clark & Parker 1999; Costello et al. 1999; Kandel et al. 1999; McGee et al. 2000; Degenhardt, Hall & Lynskey 2001; Goodman et al. 2003; King et al. 2004; Wittchen et al. 2007), and varied in terms of the results reported. For example, Boyle et al. (1992) found a weak association between psychopathology and cannabis use; Wittchen et al. (2007) reported an association between cannabis use and all mood disorders; Henry et al. (1993) reported an association between conduct problems, depressive symptoms and multiple drug use; Miller-Johnson et al. (1998) reported an association between CD and substance use; Kandel et al. (1999) reported an association between substance use disorders and psychiatric disorders, while Goodman et al. (2003) demonstrated an increased risk for psychiatric disorder if cannabis had been used. Degenhardt, Hall & Lynskey

(2001) found an association between cannabis use and mental health problems but found no association between cannabis use and anxiety and affective disorders. This is in keeping with the findings of Costello et al. (1999) that there is no association between anxiety disorders (or ADHD) and the likelihood of substance use.

These results indicate that the association between psychiatric problems and cannabis use is beyond doubt. And despite some contradictory findings, there appears to be clear evidence for an increase in the strength of the association between psychopathology and cannabis use with increased use and increased frequency of cannabis use.

Temporal associations between psychopathology and substance use. Schmidt (1995) reported that in patient self-reports, some patients said that they drink alcohol because of their emotional problems while others say that their substance abuse caused their mental problems. Similarly, Rohde, Lewinsohn & Seeley (1996) reported that other psychiatric problems may lead to alcohol-related disorders while an increase in alcohol-related problems increases the likelihood of psychiatric disorder. These findings clearly demonstrate some of the conflicting results and seeming contradictions that have been highlighted in research on the temporal association between substance use and psychopathology.

Further examination of this literature reveals that Costello et al (1999) found that most psychiatric disorders preceded substance use, drug use preceded Major Depression in all the cases (Hovens, Cantwell & Kiriakos 1994), and that moderate nicotine dependence greatly increased the likelihood of developing Major Depression compared with an absence of nicotine dependence (Breslau, Kilbey & Andreski 1991). Chong, Chan & Cheng (1999) found that adolescents with psychiatric disorders were at risk for substance use disorders, but Patton et al. (1998) found that smoking did not predict mental health problems. More specifically, Costello et al. (1999) found no temporal association between anxiety disorders and ADHD and the likelihood of substance use, Kushner et al. (1999) found that anxiety disorders predicted alcohol use, that alcohol use did not predict anxiety disorders, and McGee, Williams & Stanton (1998) found that mental health is

only weakly predictive of smoking. Robins & Price (1991) reported that conduct problems can lead to substance abuse and depression or anxiety, or first to depression and then to substance use. Kendler et al. (1993) found that there was a highly significant comorbidity between major depression and alcoholism, yet there was no clear indication as to which disorder was the preceding one. Further work by Kendler, Neal et al. (1993) demonstrated a strong association between smoking and future episodes of major depression, but concluded that the smoking did not cause the major depression and neither did the major depression cause the smoking. As previously mentioned, Hovens, Cantwell & Kiriakos (1994) found that drug abuse preceded major depression in all their subjects. (The reliability and validity of the latter result should, of course be considered in light of the fact that the sample size was relatively small, namely n = 80.) The temporal association between substance use and psychopathology becomes further highlighted by noting that, for example, according to Sonne, Brady & Morton (1994), substance users had earlier onset of mood disorders and were more likely to have mood disorders before the age of 20 years. Brook, Cohen & Brook (1998) found that adolescent drug use leads to depressive and disruptive disorders in young adulthood. Kandel et al. (1999) found that adolescents with lifetime substance use disorders were at as high a risk for psychiatric disorders as adults, and Ferdinand, Blum & Verhulst (2001) found that adolescent behavioural and emotional problems related to substance use in young adulthood. Merikangas, Risch & Weissman (1994) found that anxiety disorders preceded alcoholism in 65% of their cases with both anxiety and alcoholism. These authors also concluded that, despite anxiety appearing more likely to precede alcoholism, it did not seem that alcoholism leads to anxiety. Grilo et al. (1995) found that early conduct disorder was associated with an increased risk of substance use disorders in later adolescence. Similarly, Pardini, White and Stouthamer-Loeber (2007) found that early adolescent conduct disorder symptoms increased the risk for increased alcohol use disorder symptoms and alcohol dependence by early adulthood. But these findings contradicted those of some other community and inpatient studies. For example, Brown et al. (1996) found that conduct disorder was

secondary to substance abuse. In contrast, Breslau et al. (1998) found that early conduct problems were associated with an increased risk for progression to daily smoking, indicating the possibility that conduct problems could lead to an increase in substance use, a finding that was echoed by Miller-Johnson et al. (1998). However, Breslau et al. (1998) also found that daily smoking could lead to an increased risk of first onset major depression, and that daily smoking was associated with an increased risk for first time panic attack (Breslau & Klein, 1999) with this risk being higher in current rather than past smokers. Yet Patton et al. (1998) found that even though smoking did not predict mental health problems, depression and anxiety predicted smoking initiation. Brook, Cohen & Brook (1998) found that adolescent drug use led to depressive and disruptive disorders in young adulthood, while Reinherz et al. (2000) found that early attention problems were predictive of drug disorders, and that early aggressive behaviour could lead to an increased risk of substance use disorders. Rey et al. (2002) reported that use of cannabis increased the chances of having emotional and behavioural problems, concurring with Goodman et al. (2003) who found that regular smoking, drinking or use of cannabis increased the risk for a psychiatric diagnosis.

These findings highlight the definitive existence of a temporal association between psychopathology and substance use, and simultaneously illustrate the conflicting findings of a variety of studies with respect to these temporal associations. However, what does seem clear is that the temporal association between psychopathology and substance use appears to be governed by the kinds of psychopathology and substance use involved, as well as factors such as gender, age or developmental stage, age of substance use onset, and frequency of use.

DISCUSSION

With regards to methodological strategies, this review illustrates an obvious predominance of studies on the association between psychopathology and substance use in the

developed countries compared with the developing countries, possibly reflecting the relative ease of access to funding and the required resources for the research of interest in the wealthier countries, and the need for improved access to funds for researchers in developing countries. The larger epidemiological studies appear to have gone to great lengths to ensure that the study samples were representative of the populations from which they were drawn. The smaller community studies, and some patient samples, appear to have relied on random selections from specific groups to ensure representivity, while some clinical samples were consecutive selections from available groups of interest. A multitude of diagnostic instruments have been used in recent research of the association between substance use and psychopathology. Predominance of use of the DIS might suggest a tendency to employ the assistance of lay interviewers, thereby reducing the need for, and possible increased cost associated with using, limited clinically-trained staff, while at the same time being able to obtain comprehensive, valid diagnoses. The variety of diagnoses of interest to researchers and the variety of terms used to describe the diagnoses of interest are also noted. For example, some studies include dependence and abuse of substances when referring to substance use, while others refer to substance use when both occasional and regular use is included. The difficulties of comparing the diagnoses of interest become more evident when the criteria for assessing diagnoses differ across studies (for example, Biederman et al. (1996) who used DSM III criteria to determine the existence of substance use disorders, and Costello et al. (1999) who used DSM IV criteria to assess the same diagnoses). It is also evident that the studies conducted used largely cross-sectional sampling strategies, indicating a possible tendency to limit costs and project duration that would usually be associated with longitudinal studies, while at the same time suggesting the need for more longitudinal studies and their added advantage of increasing the possibility of identifying causal relationships.

In unraveling the details of the association between psychopathology and substance use, it appears that attempts to establish which factor is the cause and which the effect remain largely unresolved. As previously mentioned, this might be an artifact of the study design, with cross-

sectional studies limiting a conclusion of causality, and longitudinal studies producing contradictory findings. A second factor appears to be that the temporal association between psychopathology and substance use might be specific to the nature of the psychopathology and/or substance use. A third factor might be that of age or developmental stage. Thus, in younger age groups the psychopathology might precede the onset of substance use while in older individuals the substance use might precede the psychopathology. Fourthly, the association might be influenced by gender so that the association might occur in one direction for males and specific disorders, and in the opposite direction for females with the same disorders. Lastly, it is possible that individuals' experience of particular associations in their psychopathology and substance use might be influenced by genetic predisposition and environmental factors in each case.

In short, it appears that, while there is little doubt that psychopathology and substance use are associated, the nature of this association might be subject to a variety of factors (genetic predisposition, environmental factors, gender, severity of symptoms) as well as the nature of the interplay between these factors.

One of the main challenges of comparing studies relating to the association between substance use and psychopathology appears to lie in the nature of the studies themselves. As is evident in this review, the studies examined differed on a variety of levels (demographically, sampling, kinds of pathologies and substances of use, assessment, data analyses). These differences impact on the kinds and generalisability of results reported, posing further challenges for attempts to establish associations between substance use and psychopathology.

Further attempts to explain associations between psychopathology and substance use include that of Upadhyaya et al. (2002) who proposed envisaging the association between cigarette smoking and psychiatric disorder as having a bidirectional relationship in which the one condition can alter and possibly worsen the other condition in terms of both its symptoms and outcome. Another model for understanding comorbid associations is provided by Marsden et al. (2000) who proposed that the association between psychiatric symptoms and substance use be

envisaged as "conditional" rather than as "directional", particularly in relation to opiate dependence, thus emphasizing the need to take into account the effects of factors other than the substance use or psychiatric symptoms which might impact on the association between the psychiatric condition and substance use, echoing Patton et al.'s (1998) views of "unmeasured liability".

It appears that stronger evidence exists for relatively clear associations between some comorbidly-occurring conditions and not for others. Certain substances of use and their related disorders also appear to have been investigated more frequently than have other substances of use and their related psychiatric conditions. This results in certain substances and their associated conditions having more, and often more definitive, information available than is found for some other substances. The gaps in knowledge can thus be expected to become exacerbated as more and new substances of use proliferate, particularly among the youth.

Conceptual issues and concerns

Two particular areas of concern need to be addressed with regards to the association between psychopathology and substance use, namely that of the definition of comorbidity, and the role of potential risk and protective factors. In the first instance, attempts to compare the findings of studies on comorbidity or associations between psychopathology and substance use require that the nature of the comorbidity be identified as being either lifetime, sequential or concurrent comorbidity so as to ensure equitable comparisons. Secondly, the role of substance use and psychopathology as potential risk factors for each other across different developmental stages must be identified, particularly since the possible effects of factors other than psychopathology and substance use appear to be significant in the development of either (or both) psychopathology or substance use.

Methodological issues and concerns

The above findings demonstrate both the similar and contradictory findings of studies which have examined the association between psychopathology and substance use. These

findings highlight the challenges which arise when trying to compare the findings of studies which used different, and different kinds of, samples, employed different research designs and data analyses, identified symptoms and obtained diagnoses of pathology by differing means, and were conducted in differing contexts at different times. The review of these studies also recognizes the pitfalls of adults trying to recall the onset of childhood illnesses and the implications that this has for longitudinal retrospective research. The studies identify the importance of distinguishing between behaviour patterns, symptoms of a disorder, and the diagnosis of a disorder, both in relation to psychopathology and substance use, because of the serious implications of seemingly innocuous behaviour patterns .

Strengths

This review provides a comprehensive and systematic analysis of recent literature relating to the association between substance use and psychopathology. It includes all non-psychotic disorders and all substances of abuse as discussed in the selected articles on empirical studies from both treatment and community populations. It highlights the roles of factors that have been examined in relation to the association between substance use and psychopathology. However, more importantly, this review identifies those areas of research where controversy rages and where important questions remain unanswered.

Limitations

This review has been limited to those English-language empirical studies that have been published and listed in PUBMED/MEDLINE and PSYCLIT/PSYCINFO. Thus articles that do not feature in these data bases, or are written in other languages, could have been missed, although it is hoped that some of the former have been accessed via cross-referencing of published reference lists. The review has also concentrated on adolescents and younger adults, thus excluding those studies that examined children or older adults exclusively. Lastly, the reviewed articles examined clinical samples of substance users who have comorbid psychopathology, and excluded samples of psychiatric patients with comorbid substance use.

CONCLUSION

The association between substance use and psychopathology is clearly not in doubt, and there appears to be global consensus on the need to investigate the finer details of this association. The review highlights some of the areas where focused research is required. It appears that more longitudinal studies are needed to ameliorate or eliminate the confounding effects of retrospective recall regarding the occurrence of significant events, and to gauge the development of the association over time. In addition, more studies need to be conducted on community populations to overcome the possible confounding effects of a multitude of comorbidly-occurring illnesses in patients who are already in treatment for one illness or another. There appears to be an over-arching need in research on comorbidity to standardize studies in a way to provide opportunities for meaningful comparison between studies. An increase in the number of studies that examine the association between substance use and psychopathology in adolescents and young adults would seal a recognized gap in current research in this area, particularly in developing countries. Once answers to the many questions filter through, it is hoped that the details of the association between psychopathology and substance use will become more defined, and that the information obtained will be used in meaningful ways to inform policy and effect implementation for the greater good of the management and treatment of the affected individuals.

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Please note: All tables are available on request from the primary author

Table 1: Reviewed articles: Demographic details

AUTHORS; STUDY LOCATION	STUDY DESIGN; TYPE OF SAMPLE	SAMPLE SIZE; AGE
Anda et al., **1990, USA**	Cross-sectional; Community sample	N = 2963; Ages 24-74yrs
Glassman et al., **1990, USA**	Cross-sectional; retrospective Community and Institutional sample; ECA Study sample.	N=3213 Mean age 42.5yrs; 18% betw. 18 and 24yrs
Regier et al.,**1990, USA**	Cross-sectional; Retrospective Community and Institutional sample; ECA Study sample	N=20 291; Ages ≥ 18yrs
Schuckit et al., **1990**; San Diego, **USA**	Consecutive; Treatment sample of primary alcoholics; Only ♂s, in treatment for alcoholism.	N= 171; Mean age 45.1±10.56yrs
Breslau et al., **1991;** Michigan, **USA**	Cross-sectional; random sample; all HMO members; 80.7% White	N = 1007; Ages 21-30yrs
Nace et al; **1991; USA**	Consecutive sample; Treatment sample of inpatient substance abusers	N = 100 Age > 18yrs
Robins and Price, **1991; USA**	Community sample; ♀♂s; Part of ECA Study; Multi-site	N=19482 Age ≥ 18 years
Rounsaville et al., **1991;** Connecticut, **USA**	Cross-sectional sample; Retrospective Treatment sample of inpatient and outpatient adults, seeking treatment for cocaine abuse; 64% White; 69% ♂	N = 298 Ages ≥ 18yrs Mean age 27.7yrs
Boyle et al., **1992;** Ontario, **Canada**	Cross-sectional; Population sample; FU after 4 yrs; Prospective cohort study. Sample from Ontario Child Health Study ; ♀♂	N = 726 12-16yrs old at baseline; FU ages 16-20yrs old
Deykin et al., **1992;** Massachusetts,**USA**	Cross-sectional; Treatment sample; very few on Medical Insurance	N=223; Ages 15-19yrs

Breslau et al., **1993;** **USA**	Cross-sectional; Random sample. Community sample; all members of an HMO; 80.7% White; 61.7% ♀.	N=1007; Ages 21-30yrs
Breslau et al., **1993;** **USA**	Cross-sectional Prospective study; FU after 14 months; 81% White; Community sample	N=995; Ages 21-30 yrs
Dunn et al., **1993;** **USA**	Cross-sectional; Treatment sample of substance users/abusers; Sample 74% White; All ♂s	N=265; Ages 23-73yrs (Mean age 44.33yrs)
Henry et al., **1993;** **New Zealand**	Cohort; Part of Dunedin Multi-disciplinary Health+ Development Study; Community sample	N=752; Baseline age=11yrs; FU at 15yrs.
Kendler et al., **1993;** **USA**	Cross-sectional; Retrospective; Community sample; All ♀; All twins	N=2163 Mean age 30.1 $\pm$ 7.6yrs
Kendler et al., **1993;** Virginia, **USA.**	Cross-sectional; Retrospective; Population sample; All twins; All ♀; All white	N = 1566; Mean age = 30.9 $\pm$ 7.1 years
Lehman et al., **1993;** **USA**	Cross-sectional; Consecutive; Treatment sample of dual and single diagnosis mentally ill patients and SUD patients. Inner city sample; all English-speaking	N = 314; Age 18-65 yrs.
Fals-Stewart &Angarano, **1994;** NY, **USA**	Cross-sectional; Treatment sample from substance use treatment centre; 70% White; mostly male	N = 217; Age range 17-50yrs; Mean age 25.6yrs
Hovens et al., **1994;** Burbank, LA, **USA**	Prospective; Clinical ♂♀; 2 groups(not matched for age or gender; i) Substance abusers ii) Non-abusers, but had a psychopathology;	N=80 Age $\leq$ 18yrs
Merikangas et al., **1994;** **USA**	Family study; Non-hospitalised subjects with MD, hospitalised subjects with MD; Normal community control group;Used data from a family study	N = 215 probands matched for sex and age
Sonne et al., **1994** South Carolina, **USA**	Cross-sectional; psychiatric patients	N = 50; Age $\geq$ 18yrs
Araujo&Monteiro, **1995;** **Brazil**	Cross-sectional; Only ♂s. Treatment sample, inpatients+outpatients.	N=166. Aged >15yrs

Biederman et al., **1995;** **USA**	Cross-sectional; Consecutive sample of adults; All subjects had childhood onset of ADHD. All positive for ADHD. Pre-existing study group used as comparison.	N=120; Age ≥ 18yrs;
Brook et al., **1995;** NY, **USA**	Cohort; Longitudinal; F-U over 4yrs; Community; 93% White;	N=976; Ages 5.5-22yrs old
Grilo et al, **1995;** Yale Psychiatric Institute, **USA**	Cross-sectional; Consecutive sample; ♂♀s. Psychiatric patients; (Private hospital); Mostly Caucasian	N=138; Ages 12-18yrs
Riggs et al, **1995;** **USA**	Consecutive Rx sample; admitted for substance use; All ♂.	N=99; Ages 13-19yrs
Schmidt, **1995;** California, **USA**	Cross-sectional; Psychiatric inpt + outpt sample for exptal gp; Community sample for control gp.	N=406 exptal gp; N=718 control gp. Age18+ yrs
Triffleman et al; **1995;** San Francisco, **USA**	Cross-sectional; consecutive;; Inpatient Rx sample; all substance abusers; all male.	N = 46; Mean age = 44.9yrs
Brook et al., **1996;** NY, **USA**	Cohort; Prospective; F-U after 8yrs, 10yrs, 16yrs; Community; 91% White	N=500; Ages 5-27yrs old
Brown et al., **1996;** SanDiego, California, **USA**	Prospective; Longitudinal over 2 yrs; Rx sample; mostly lower to middle-class; Rx sample of alcohol + other drug abusers; 80% White;	N=166; Ages 12-18yrs
King et al., **1996;** Urban, **USA**	Consecutive; Clinical sample; 87% Caucasian	N=103; Mean age 15.3yrs
Fergusson et al., **1996;** **New Zealand**	Longitudinal, 16 yr follow-up; Community sample	N=947; 0-16yrs
Novins et al., **1996;** **USA**	Cross-sectional; Treatment sample of pts in treatment for substance abuse; All American Indian pts; ♂♀s	N=64; Ages 11.7-19.7yrs
Grilo et al., **1996;** New Haven, Connecticut, **USA**	Cross-sectional; Treatment sample; All inpts in Rx for psychiatric problems; ♀♂; Mostly Caucasian; middle-class	N=165; Mean age 15.5yrs
Kessler et al., **1996**; **USA**	Cross-sectional; Community; Part of NCS	N=5877; Ages 15-24years
Rohde et al., **1996;** Oregon, **USA**	Longitudinal; Community High school sample; Urban+rural; Largely White, Middle class	N=1507; Ages 14-18yrs
Breslau, Davis et al., **1997;** **USA**	Stratified random sample; All ♀s; All mothers; 3 study sites, differing samples; Urban component of sample largely Black, single mothers who did not complete high school	N=801; Mean age 33.1yrs
Brooner, King et al., 1997;	Consecutive;	N= 716;

Baltimore, Md; **USA**	Outpatient treatment sample of opioid-dependents; ♂♀s, admitted to methadone maintenance clinic	Age range 20-58yrs; Mean age 34.8 ± 6.49 yrs
Kandel et al., **1997;** **USA**; **Puerto Rico**	Cross-sectional; Random population sample; ♂♀children and their parents; 78% Caucasian	N=1285; children aged 9-18yrs
Kessler, Crum et al., **1997;** **USA**	Retrospective;Household survey; Community; Sample data from National Comorbidity Survey	N=8098 with 82.4% response; 15-54yrs
Clark et al., **1997;** Pittsburgh, **USA**	Convenient Clinical Exptal group; Volunteer Community Control gp	N=251; Ages 14-18yrs old
Biederman, et al., **1997;** **USA**	Prospective; Urban F-U over 4yrs;Exptal gp=Clinical sample; All Caucasian; All ♂	N=260; Ages 6-17yrs old
Deykin+Buka, **1997;** Massachusetts,**USA**	Cross-sectional; Treatment sample of chemically-dependent adolescents	N=297(222=♂); Ages 15-19yrs.
Horner&Scheibe, **1997** **USA**	Consecutive; Treatment sample; Mostly Caucasian	N=30; 16♂; 14♀; Aged 14-19yrs
Moscato et al.,**1997;** Erie County, NY, **USA**	Longitudinal; FU at 3, 4, 7 yrs; Community sample	N=1306; Ages 19-85yrs
Ross & Shirley, **1997;** Ontario, **Canada**	Cross-sectional; Sample from Mental Health Supplement to the Ontario Health Survey; Only ♀s; Community sample	N=4285; Ages 15-64yrs
Breslau, et al.,**1998;** Michigan, **USA**	Longitudinal; Prospective; FU over 5yrs; Random sample; Treatment sample	N=974; Ages 21-30yrs
Escobedo et al., **1998**; **USA**	Longitudinal; Prospective; Community Part of Teenage Attitudes and Practices Survey (TAPS)	N = 9135 at baseline; N=7960 at FU; Ages 12-18 years
McGee et al., **1998;** **New Zealand**	Longitudinal; Community	N=773; Ages 5-15yrs
Miller-Johnson et al, **1998;** **USA**	Prospective, longitudinal sample; Community sample; ♀♂s; All African American	N=340; Grades 6, 8, 10
Patton et al., **1998;** **Australia**	Cohort; School students	N=2032; 14-15yrs
Brook et al., **1998;** NY, **USA**	Longitudinal; F-U over 9yrs; Community	N=975; 1-10yrs old at baseline
Troisi et al., **1998**; **Italy**.	Cross-sectional sample; All army draftees; All males; All cannabis-only users	N=133; No ages provided
Breslau and Klein, **1999;** Michigan, **USA**	Cross-sectional community sample; Prospective cohort; All members of Health Maintenance Organisation (HMO); FU over 5 years; 80% White; 62% ♀	N = 974 Ages 21-30yrs
Chong et al.; **1999;** **Taiwan**	Cross-sectional; Community sample; Random sample of Gr 9 students; ♀♂s; (PAST study)	N=774; Ages 14-16yrs (Mean age 15.23yrs)
Clark+Parker, **1999;** Pittsburgh, **USA**	Longitudinal; Mixed sample(Treatment group +Volunteers); Only ♂s; Divided into 2gps viz.	N=380; Ages about 11-16yrs

	i)Fathers with SUD, ii)Fathers without SUD;	
Costello et al., **1999;** North Carolina, **USA**	Longitudinal; Community sample; Rural; Mostly Caucasian	N=1420; Aged 9-16yrs
Costello et al., **1999**; **USA**	Longitudinal (predominantly rural); Community; Part of Great Smoky Mountains study; Largely Caucasian because population largely White. Representative sample	N=1420; Age closest to 9, 11 and 13 years; Age range 9-16 years, including ages at FU
Disney et al., **1999**; Minneapolis, **USA**	Cross-sectional sample; All reared-together twin pairs from the Minnesota Twin Family Study; 98% Caucasian	N = 626 pairs of twins; (674 ♀s; 578♂s). All 17yrs old; Mean age = 16.93yrs; SD = 0.57
Greene and Biederman, **1999;** Boston, **USA**	Longitudinal; FU after 4 yrs; Non-clinical Community sample related to a previous Treatment sample; All Caucasian; All upper or middle class SES.	N=186; ♂♀ siblings of a former research gp of boys; Baseline ages 9-18yrs; FU ages 12-22yrs
Kandel et al., **1999;** **USA**	X-sectional; ♂♀s; Community sample; Probability sample of children and caregivers taken from MECA study.	N=401; Ages 14-17yrs.
Kushner et al., **1999;** **USA** (Midwestern Univ.)	Prospective; Community sample of University students; Baseline = 1st yr university; FU at 4 and 7 yrs	N= 489; Mean age 18.6yrs
Roberts et al., **1999;** Cape Town, **SA**	Consecutive; Clinical	N=146; Mean 38.5±8.49yrs
Rao et al., **1999;** **USA**	Cross-sectional,; 7yr F-U; Clinical sample	N=63; Mean Age 15yrs
Johnson et al., **2000;** NY, **USA**	Prospective, Longitudinal; Community	688; Mean age 14-22yrs
Dixit&Crum, **2000;** Baltimore, **USA**	Prospective; 1-yr follow-up; Community; Part of ECA Study; only ♀s	N=1383; Ages !8yrs and older
Marsden et al., **2000**; **UK**	Cross-sectional; Treatment sample of substance users; Mostly ♂s	N = 1075 Age range 16-58yrs; Mean age 29.3 ± 6.7yrs
McGee et al., **2000;** **New Zealand**	Community sample; Longitudinal; FU every 2 years; Sample part of Dunedin Multi-disciplinaryHealth and Development Study (DMHDS); Economically advantaged group	N=1037; Ages 3-26yrs;
Rao et al., **2000;** LA County, **USA**	Longitudinal; Community Public High School sample; FU each yr for 5yrs; Only ♀s	N=155; Ages 17-19yrs
Reinherz et al., **2000;** **USA**	Longitudinal; Community sample; ♂♀; 98% White; mostly working- or lower middle class	N = 360; Ages 5 yrs; FU at 21 yrs

Rodgers et al., **2000;** Canberra, **Australia**	Cross-sectional; Population sample; Potential participants for the Stress and Wellbeing Project.	N = 2725 Aged 18-80yrs; Mean Age = 42.6yrs
Degenhardt et al., **2001; Australia**	Cross-sectional; Community	N=10641; 18+ years
Hofstra et al., **2001; Netherlands**	Longitudinal 10yr follow-up; Community ♀♂	N=1615; Ages 11-19yrs,
Ferdinand et al., **2001; Netherlands**	Prospective; Fu over 8 yrs; Community sample	N=787; Ages 10-14yrs
Dierker et al., **2002;** New Haven, Connecticut, **USA**	Prospective; Treatment sample from substance use clinic + anxiety clinic. Controls from Community	N= 133 probands, Ages 25-56yrs. N= 273 relatives, aged 18-80yrs
Rey et al., **2002; Australia**	Cross-sectional; Retrospective; Community sample from National Survey of Mental Health and Wellbeing	N = 1261 Ages 13-17 years
Compton et al., **2003; USA**	Random sample of admitted patients; Treatment sample of drug-dependents; Data from Drug Abuse and Risk of Study; 61% African-American; 66% ♂; 68% unemployed	N=425 FU N = 401(94%) Mean Age = 32.5yrs SD=6.5
Goodman et al., **2003; England,Scotland, Wales**	Cross-sectional; Community sample; 90% White	N = 2624 Ages 13-15yrs
Shrier et al., **2003;** Boston, **USA**	Cross-sectional; Convenience sample; Clinical; mostly non-white; 68% female	N=538 14-18yrs old
Steinhausen an Metzke, **2003; Switzerland**	Cross-sectional Community sample from the Zurich Adolescent Psychology and Psychopathology study (ZAPPS); Sample representative of population	N=794 Ages 13-20 years
De Graaf et al., **2004**; **Netherlands**	Longitudinal; Prospective; FU over 3 years. Sample from the Netherlands Mental Health Survey and Incidence Study (NEMESIS)	N=7076 at baseline. Ages 18-64 years.
Grant et al., **2004; USA**	Cross-sectional; sample of civilian, non-institutionalised individuals; Part of NESARC study	N=43093 Ages ≥ 18yrs
King et al., **2004**; **USA**	Longitudinal; Community; Twins study; Part of Minnesota Twin Family Study	699 twin girls; 655 twin boys; Ages 11yrs at baseline and 14yrs at FU; Age range 10-12yrs. Average age: 11yrs
Obando, et al., **2004** **USA**	Cross-sectional; Community	N=4967 high school students, 218 youths in Rx for substance use, 83 street youth; Ages 12-20yrs
Fernander et al., **2006;** Cape Town, **South Africa**	Cross-sectional sample;	N=620; High school students
Monshouwer et al., **2006**; **Netherlands**	Cross-sectional; Community; Part of Dutch Health Behaviour in School-aged Children (HBSC) schools survey	N=5551. Ages 12-16 years

Hayatbakhsh et al. **2007** **Australia**	Longitudinal; Community; Part of MUSP study	N=7223 at baseline; 3239 at 21yrs FU Ages birth, FU at 14yrs and 21yrs
Pardini et al., **2007** **USA**	Longitudinal; Community; Part of Pittsburgh Youth Study (PYS)	N=506; Only boys Ages Mean = 13.9yrs
Roberts et al. **2007** **USA**	Cross-sectional; Community	N=4500 Ages 11-17yrs

Table 2: Reviewed articles: Psychopathology and substance use details

AUTHORS; STUDY LOCATION	PSYCHOPATHOLOGY	DIAGNOSTIC TOOLS	SUBSTANCE USE	ASSESSMENT TOOLS
Anda et al., **1990, USA**	Depression	CES-D (Centre for Epidemiologic Studies-Depression Scale)	Cigarette smoking	Interview + quit ratio of CES-D to define smoking cessation
Glassman et al., **1990, USA**	Major depression (MD)	Diagnostic Interview Scheule (DIS)	Cigarette smoking	DIS
Regier et al.,**1990, USA**	Any	NIMH DIS	Alcohol + any other drugs	DIS
Schuckit et al, **1990**; San Diego, **USA**	Any	Alcohol Research Centre Interview (ARC) developed from SADS-L and DIS	Alcohol abuse and dependence	ARC
Breslau et al., **1991;** Michigan, **USA**	Any, including substance use disorders, and specifically nicotine dependence	NIMH-DIS(for DSM III-R diagnoses)	Any, but Nicotine primarily	NIMH-DIS for DSM III
Naceet al., **1991; USA**	Personality disorders	Structured Clinical Interview for DSM SCID II	Alcohol and anything else	Alcohol Use Inventory; MMPI; Health Daily Living Forum; Shipley Institute of Living Scale; Chemical Use Inventory; Satisfaction Questionnaire
Robinsand Price, **1991; USA**	Conduct problems used as childhood symptoms of anti-social personality; 10 DSM III diagnoses	DSM III-R	Any	DSM III-R
Rounsaville et al., **1991;** Connecticut, **USA**	Any	SADS-Lifetime and RDC	Cocaine and other	SADS-L and RDC
Boyle et al., **1992;** Ontario, **Canada**	Any	Youth Self Report (YSR); Child Behaviour.Checklist (CBC)	Tobacco, alcohol, marijuana, hard drugs	Self-report
Deykin et al., **1992;** Massachusetts, **USA**	Depression; Drug dependence	DSM III-R; NIMH-DIS	Alcohol; Other drugs	DSM III criteria; Family+Social History Interview
Breslau et al.; **1993; USA**	Neuroticism; Negative affect; Hopelessness; general emotional distress.	NIMH-DIS	Nicotine	NIMH-DIS

Breslau et al.; **1993; USA**	Major depression disorder (MDD)	NIMH-DIS	Nicotine (dependence)	NIMH-DIS
Dunn et al., **1993; USA**	Depression; PTSD; affective disorders; psychotic disorders; adjustment disorder; anxiety disorders; dissociative disorders	Shipley-Hartford Institute of Living Scale; Routine psychological examination; Dissociative Experiences Scale	Alcohol; Cocaine; Multiple substances	Self-reports
Henry et al., **1993; New Zealand**	Depression Conduct problems	Diagnostic Interview Schedule for Children- Child Version (DISC-C) DISC-C Oppositional Behaviour Subscale	Marijuana; Glue sniffing; Alcohol; Other drugs	Self-report Early Delinquency instrument(SRED)
Kendler et al., **1993; USA**	Major depression	Structured Clinical Interview for DSM III an RDC	Alcohol	DSM III criteria
Kendler et al., **1993;** Virginia, **USA.**	Major depression	Structured Clinical Interview for DSM III-R diagnosis	Cigarette smoking	Self-Report
Lehman et al., **1993; USA**	Axis I primary mental disorder, and psychoactive substance use disorder.	DSM-III-R SCID	Any	Addiction Severity Index; Modified SCID
Fals-Stewart & Angarano, **1994;** NY, **USA**	Psychoactive SUDs	DSM III-R SCID-R psychoactive subsance use and OCD modules; Yale-Brown Obsessive-Compulsive Scale and Symptom Checklist	Any, excluding nicotine or alcohol as primary drug of choice	SCID-R
Hovens et al., **1994;** Burbank, LA, **USA**	Conduct+/or oppositional defiant disorder (non-abusing group); Depression; ADDH	DSM III-R SADS-E Parent info via interview	Any	DSM III-R and Halikas criteria
Merikangas et al., **1994; USA**	Anxiety; Depression	Interviews using RDC criteria and modified DSM III symptomatic criteria	Alcoholism	Interviews using RDC criteria
Sonne et al; **1994** South Carolina, **USA**	Bipolar Affective Disorder	DSM-III-R-SCID; Hamilton's rating Scale for Depression; Young Mania rating Scale	Any	SCID
Araujo&Monteiro, **1995; Brazil**	Depression, Generalised anxiety, panic attacks, suicide attempts	DSM III SCID	Alcohol	DSM III SCID
Biederman et al., **1995; USA**	ADHD; Anxiety syndrome	Structured Clinical Interview for DSM III-R (SCID); Kiddies-SADS-E	Alcohol; Drug abuse	SCID

Brook et al., **1995;** NY, **USA**	Personality, behavioural, attitudinal characteristics	Structured interviews	Any	Self-administered questionnaires
Grilo et al, **1995;** Yale Psychiatric Institute, **USA**	Axis I and II diagnoses	DSM III Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (Kiddies SADS-E) Personality Disorder Examination	Any	DSM III
Riggs et al, **1995;** **USA**	Depression; MD; Mood and anxiety disorders CD	DISC-C; Children's Depression Rating Scale using additional questionnaire to supplement DISC; Child Behaviour Checklist	Any	Comprehensive Addiction Severity Index-Adolescents (CASI-A); Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM)
Schmidt, **1995;** California, **USA**	Somaticism; obsessive-compulsive disorders; interpersonal sensitivity; depression; anxiety; hostility; phobia; paranoia; psychoticism. Caseness assessed.	Structured interviews; Brief Symptom Inventory (BSI)	Alcohol	Interview + questionnaire
Triffleman et al; **1995;** San Francisco, **USA**	Childhood trauma exposure	Traumatic Antecedents Questionnaire (TAQ); DSM III-R-SCID PTSD Module	Any	Addiction Severity Index
Brook et al., **1996;** NY, **USA**	Personality, Behaviour, Mental health	Structured interviews	Any	Self-administered questionnaires
Brown et al., **1996;** SanDiego, California, **USA**	Conduct Disorder; Anti-Social Personality Disorder (ASPD)	DSM III-R	Alcohol; Other drugs	Customary Drinking + Drug Use Record (CDDR)
King et al., **1996;** Urban, **USA**	Behavioural disorders Depression	DISC + Adolesc DISC. Children's Depression Rating Scale (CDRS-R); Hamilton rating Scale.	Any	DISC
Fergusson et al., **1996;** **New Zealand**	Depression	DIS-C; DSM-III-R	Nicotine dependence	Self-Report
Novins et al., **1996;** **USA**	Depression Anti-social behaviour and suicide	Beck Depression Inventory; Intake questionnaire	Any	Medical record review

	attempts			
Grilo et al., **1996;** Connecticut, **USA**	Conduct disorder; Substance use Disorder	KSADS-E	Any	KSADS-E; DSM III criteria
Kessler et al., **1996**; **USA**	Any affective or anxiety disorders.	WHO Composite International Diagnostic Interview(WHO-CIDI)	Any addictive disorders	CIDI
Rohde et al., **1996;** Oregon, **USA**;	Any	K-SADS; K-SADS-P; DSM III-R	Alcohol	DSM IV criteria
Breslau et al.; **1997; USA**	PTSD; Depression; Anxiety	NIMH-DIS using DSM III-R criteria	Alcohol abuse or dependence; Illicit drug abuse or dependence	NIMH-DIS using DSM III-R criteria
Brooner et al; **1997**; Baltimore, Md; **USA**	Any	Structured Clinical Interview of DSM III-R	Any	Addiction Severity Index (ASI)
Kandel et al, **1997; USA**; **Puerto Rico**	Anxiety; Mood and disruptive behavioural disorders; eating, elimination, tic disorders	NIMH DISC; Service Utilisation and Risk factors Interview (SURF)	Cigarettes; Alcohol; Other substances	DISC-2.3; Frequency of substance use determined using Self-Reports
Kessler et al., **1997; USA**	Anxiety disorders, affective disorders, conduct disorders	Modified CIDI	Alcohol, drug use	Modified CIDI
Clark et al., **1997;** Pittsburgh, **USA**	Any mental disorders, but anxiety disorders in particular	Schedule for Affective Disorders+Schizophrenia for School Age Children (K-SADS)	Any Alcohol	Structured Clinical Interview for DSM III Lifetime History of Alcohol Use Interview
Biederman, et al., **1997; USA**	ADHD +associated disorders	Structured clinical Interview for DSM III-R + K-SADS Epidemiologic Version	Alcohol; Drug abuse	DSM III criteria
Deykin+Buka, **1997;** Massachusetts, **USA**	PTSD	DIS	Alcohol + Other drugs	DSM III criteria for dependence
Horner&Scheibe, **1997** USA	ADHD	Wender Utah rating Scale(WURS); Self Evaluation (Teenagers) Self-Report; Child Attention Problems Scale	Any drugs	Interview + History-taking
Moscato et al., **1997;** Erie County, NY, **USA**	Depression; Alcoholism	CES-D	Alcohol	DSM III criteria
Ross & Shirley, **1997;** Ontario, **Canada**	MD; Mood disorders; anxiety disorders; bulimia; ASP	Modified version of WHO-CIDI	Alcohol; any drugs; Tobacco use	DSM III-R

Breslau, et al., **1998;** Michigan, **USA**	CD, MD + other psychiatric disorders	NIMH-DIS	Cigarettes; Alcohol	DSM III criteria
Escobedo et al., **1998**; **USA**	Depressive symptoms	Mellinger Depressive Symptoms Scale	Cigarette smoking	Standard questionnaire via pone or mail
McGee et al.,**1998; New Zealand**	Attention deficit disorder, conduct disorder, oppositional disorders, anxiety, depression	Self, parent teacher reports, DISC-C, Revised Behavior Problem Checklist	Smoking	Self-Report
Miller-Johnson et al, **1998; USA**	Depression; CD	Child Assessment Interview	Alcohol; tobacco; marijuana	National Youth Survey
Patton, et al., **1998; Australia**	Anxiety, depression	CIS	Cigarette smoking	Self report
Brook, et al., **1998;** NY, **USA**	Any	DISC	Any	Structured interviews
Troisi et al., **1998**; **Italy**.	Any, But mainly depression and anxiety	Beck Depression Inventory; Spielberger State-Trait Anxiety Index; Revised Toronto Alexithymia Scale; Structured Clinical Interview for DSM-III-R (SCID)	Cannabis	SCID
Breslau and Klein, **1999;** Michigan, **USA**	Panic attack; Panic disorder	NIMH-DIS	Smoking	DIS using DSM III-R criteria and CIDI from NCS Tobacco Supplement
Chong et al.; **1999; Taiwan** (PAST study)	Any, including SUD's	K-SADS-E (Chinese version)	Any, including alcohol, cigarettes, betel	DSM III-R
Clark+Parker, **1999;** Pittsburgh, **USA**	Any	K-SADS	Alcohol; cannabis	DSM III-R
Costello et al., **1999;** North Carolina, **USA**	Any	Child + Adolescent Psychiatric Assessment (CAPA)	Tobacco; Alcohol; Cannabis; other substances	CAPA interviews; DSM IV criteria
Costello et al., **1999**; **USA**	Any	Child and Adolescent Psychiatric Assessment (CAPA)	Tobacco, Alcohol; Cannabis and several other substances	CAPA
Disney et al.; **1999**; Minneapolis, **USA**	Any, but specifically ADHD, conduct disorder and adult anti-social behaviour	DSMIII-R and Diagnostic Interview for Children and Adolescents-Revised	Any	CIDI + computer-assisted substance use and abuse questionnaire
Greene+Biederman, **1999;** Boston, **USA**	Any, but especially.social impairment	Kiddie SADS-E from DSM III-R , Social Adjustment Inventory for Children+Adolescents (SAICA)	Any, especially cigarette smoking	DSM III-R

	Aggression	Child Behaviour Checklist (CBC) – Aggression Scale		
Kandel et al; **1999; USA**	SUD; Anxiety; disruptive behaviour; Mood disorders; Eating, elimination and tic disorders	NIMH-DISC-C for children and DISC-P for caregivers	Alcohol; Marijuana; Other substances, but not tobacco.	NIMH-DISC
Kushner et al., **1999; USA** (Midwestern Univ.)	Anxiety disorders	NIMH DIS DSM III	Alcohol	DIS + DSM III; Short Michigan Alcohol Screening Test (S-MAST)
Roberts et al., **1999;** Cape Town, **SA**	Anxiety	SCID	Abstinent alcohol-dependent	SADQ, Withdrawal Syndrome Scale
Rao et al., **1999; USA**	Major psychiatric disorder Temperament +Personality Features	Schedule for Affective Disorders and Schizophrenia -Lifetime Version. Multi-dimensional Personality Questionnaire (MPQ)	Any	DSM III criteria
Johnson et al., **2000;** NY, **USA**	Agoraphobia, generalised anxiety disorder, panic disorder	DISC-C	Cigarette smoking	DIS-C
Dixit&Crum, **2000;** Baltimore, **USA**	Depression	Diagnostic Interview Schedule (DIS)	Heavy alcohol use	Baseline+F-U interview asked "How many times you had ≥5 drinks in last month
Marsden et al; **2000**; **UK**	Any	Brief Symptom Inventory (BSI)	Any	Severity of Dependence Scale; Addiction Severity Index (ASI)
McGee et al., **2000; New Zealand**	ADD; Conduct disorders;anxiety disorders; depressive disorders (mentalhealth assessed from age 15 onwards). Mental disorders (age 18 and 21yrs)	DIS-C DIS	Cannabis, smoking; alcohol	Self-report
Rao et al; **2000;** LA County, **USA**	MDD; SUD	SCID; BDI	Any	Rutgers Collegiate Substance Abuse Screening Test (RCSAST)=a modified version of MAST
Reinherz et al., **2000; USA**	Lifetime Major Depression and drug disorders	DIS III-R	Any	DIS III-R
Rodgers et al.; **2000;** Canberra,	Depression; Anxiety	Self-administered questionnaire	Alcohol	Alcohol Use Disorders Identification Test

Australia				(AUDIT)
Degenhardt et al., **2001; Australia**	Anxiety, affective disorders, psychosis	CIDI, ICD 10, DSM IV	Tobacco, Cannabis, alcohol	Self-report
Hofstra et al., **2001; Netherlands**	Anti-social behaviour, aggression, anxiety disorders, Mood disorders, disruptive disorders	Child Behaviour Checklist (CBC)	Alcohol misuse/ dependence; drugs	CIDI; DIS
Ferdinand et al., **2001; Netherlands**	Behavioural, emotional problems	Child Behaviour Checklist (CBCL)	Tobacco, alcohol, drug use	Young Adult Self-Report (YASR)
Dierker et al., **2002;** Connecticut, **USA**	Depression	DSM III-R semi-stuctured Schedule for Affective disorders + schizophrenia (current + lifetime Versions)	Tobacco (cigarette use)	Diagnostic interview DSM III-R
Rey et al; **2002; Australia**	Depression, ADHD, Conduct disorder	Questionnaires; CHQ, CES-D; YRBQ; DISC-IV. Recent versions of DISC and CHQ, CBCL	Cannabis	YRBQ (Youth Risk Behaviour Checklist)
Compton et al.; **2003; USA**	11 conditions	Non-clinical psychiatric interview; DIS III-R; NIDA Risk Behaviour Assessment	Drug dependence; Alcohol dependence.	DIS
Goodman et al; **2003; England,Scotland, Wales**	Any	ICD-10 and DSM IV computer-assisted interview	Alcohol; cigarettes; cannabis	ICD-10 and DDSM IV
Shrier, et al., **2003;** Boston, **USA**	Depression; mania; eating disorders; delusional thinking; hallucinations; ADD; anxiety + conduct dis.	ADI	Alcohol and any other substance abuse	Self-administered SubstanceUse/Abuse scale using POSIT + ADI for substance use
Steinhausen an Metzke, **2003; Switzerland**	Problem Behaviour	Youth Self Report and other scales	Alcohol	Substance Use Questionnaire (SUQ)
De Graaf et al., **2004**; **Netherlands**	Any	CIDI (DSM-III-R)	Any	CIDI
Grant et al.; **2004; USA**	Mood and anxiety disorders	AUDADIS-IV	Alcohol; 8 classes of drugs	AUDADIS-IV
King et al., **2004**;	Externalising disorders (ADHD; CD;	Dagnostic Interview for	Tobacco, Alcohol,	DICA-R

USA	ODD); Internalising disorders (MDD). In girls, Anxiety disorders.	Children and Adolescents-Revised (DICA-R), based on DSM-III-R.	Cannabis	
Obando et al., **2004** **USA**	Depression	Short Mood and Feelings Questionnaire (SMFQ)	Any	Drug Use Screening Inventory (DUSI)
Fernander et al.; **2006;** Cape Town, **South Africa**	Depression	Beck's Depression Inventory (BDI)	Smoking	Self-administered questionnaire
Monshouwer et al., **2006**; **Netherlands**	Any	Youth Self Report (YSR)	Cannabis	Questionnaire
Hayatbakhsh et al. **2007; Australia**	Anxiety and Depression	Youth Self-Report (YSR)	Cannbis	Self-Report of 2 questions
Pardini et al., **2007** **USA**	Conduct Disorder ADHD Depression Anxiety	Self-Reported Delinquency Scale (SRD) DISC-P Short Mood and Feelings Questionnaire (SMFQ) Youth Self Report (YSR)	Alcohol Use Disorders	DIS
Roberts et al., **2007** **USA**	Anxiety, Mood Disorders, Disruptive Disorders, ADHD	DISC-IV	Any	DISC-IV

Table 3: Reviewed articles: Statistical analyses and outcomes of studies

AUTHORS; STUDY LOCATION	STATISTICAL ANALYSES	OUTCOMES
Anda et al., **1990, USA**	Cochran-Mantel-Haenszel test for Trend; Kaplan-Meier analysis for incidence of quitting	↑CESD=>↑smoking Depression=> less likely to quit smoking
Glassman et al., **1990, USA**	Prevalences; OR's; Lifetime prevalences	Similar rates of smoking among ♂♀in depressed group. Gender differences among non-depressed group. Depressed smokers less able to quit smoking. MDD influences rates of smoking. Smoking more common among depressed patients than in general population.
Regier et al., **1990, USA**	Prevalences, OR's; lifetime prevalences	Substance abuse in 83.6% of individuals with Anti-Social Personality Disorder (ASP). Greater association between Anxiety disorders and other drugs, than between anxiety and alcohol dependence. Strong association between substance abuse and affective disorder.
Schuckit et al., **1990**; San Diego, **USA**	Mostly descriptive statistics	High prevalence of anxiety symptoms amongst alcoholics. But anxiety diagnoses comparable to expected population rates.
Breslau et al., **1991;** Michigan, **USA**	OR's; Multivariate Logistic Regression	Significant association between mild nicotine dependence and MD, OCD, phobia, and any anxiety disorder. Moderate nicotine dependence => 5 X greater likelihood of developing MD than if no nicotine dependence. Generally, any nicotine dependence =>↑ likelihood of anxiety disorder.
Nace et al., **1991; USA**	t-tests with Bonferroni Correction; Chi-squared analyses	Subjects with personality disorders more likely to be involved in substance abuse. Personality disordered group had higher scores on depression, negative life changes, avoidance as means of coping, emotional discharge as means of coping.
Robins and Price, **1991; USA**	Receiver Operating Characteristics (ROC) curves	Conduct problems more prevalent among males. Conduct problems predict other disorders less well than externalising disorders. Conduct disorders might cause externalising disorders which then cause other disorders. Conduct problems can lead to substance abuse and depression or anxiety or first to depression and then substance abuse.
Rounsaville et al., **1991; USA**	Descriptive statistics	Affective disorders and alcoholism followed onset of drug abuse. Anxiety disorder and ASPD and ADHD preceded drug abuse.

Boyle et al.; **1992;** Ontario, **Canada**	Relative odds; Logistic Regression	Conduct disorder was associated with use of marijuana and hard drugs but not with use of tobacco and alcohol. Small relative odds between ADHD, substance use and between emotional disorder and substance use.
Deykin et al., **1992;** **USA**	OR's	Primary and secondary depression possible. Abusers have ↑ risk of depression cf community. This is possibly because of Berkson's Bias.
Breslau et al., **1993;** **USA**	Anova; Dunnett's t-test; Multiple regression; SAS General Linear models	Nicotine dependence strongly associated with all measured psychiatric diagnoses. Thus nicotine-dependent smokers more vulnerable to psychopathology than non-smokers or non-dependent smokers.
Breslau et al., **1993;USA**	OR's	History of MDD =>↑ risk of first incidence MDD at FU.
Dunn et al., **1993;** **USA**	Correlations; Anovas; t-tests; Stepwise multiple regression	Comorbid PTSD subjects more likely to score high on dissociative dysfunction. Blacks had higher dissociative dysfunction scores than Whites. Dissociative experiences common in this population.
Henry et al., **1993;** **New Zealand**	Logistic Regression	♂s:Conduct probs + Depressive symptoms (DP) at 11yrs predicted multiple drug use at 15yrs; but DP more important. CP + DP independently both predicted multiple Drug use. ♀s: aged 15yrs, only CP strongly associated with substance use. ♀s: CP + DP predicted self-medication at 15yrs.
Kendler et al., **1993; USA**	Bivariate twin analysis; Tetrachoric correlation matrices	Highly significant comorbidity between MD and alcoholism. No clear indication of which disorder is the preceding one.
Kendler et al., **1993;** Virginia, **USA.**	Regression analyses; Co-twin control method to discriminate causal from non-causal relationships.	Ever smokers had higher rates of MD than never smokers. Heavy smokers had higher rates of MD than light smokers. Increased risk for MD with increased levels of nicotine dependence. Strong association between smoking and future episodes of MD. Smoking did not cause MD and MD did not cause smoking.
Lehman et al., **1993; USA**	Description statistics; ANOVA; MANOVA	Dually diagnosed patients have more adverse life circumstances than patients with single diagnoses, whether mental or SUD's.
Fals-Stewart & Angarano, **1994;** NY, **USA**	Approximation to Poisson Distribution to examine proportion differences; ANOVA; Chi squared	↑prevalence of OCD as compared with population. OCD under-diagnosed.
Hovens et al., **1994;** Burbank, LA, **USA**	Student's t; Chi squared; Newman-Keuls; Kruskal-Wallis	Substance abusers had higher rates of conduct disorder; ADDH; dysthymia; MD; anxiety disorders; social phobia. Non-abusers had higher Incidence of oppositional disorders. Abusers had larger average number of psychiatric diagnoses; more likely to have multiple diagnoses. ♀abusers more likely to have anxiety disorders; ♂abusers more likely to have conduct disorders. ♂s more likely to be polysubstance abusers + school dropouts. Drug abuse preceded MD in all cases.

		Social phobia + ADHD preceded substance use. Conduct disorder before, during or after onset of substance use. No correlation between number or severity of drug use + severity of psychiatric diagnoses. Substance Use=>↑psychiatric comorbidity + ↑severity of psychopathology.
Merikangas et al., **1994; USA**	Proportional Hazards model. Co-transmission analysis used trivariate multifactorial threshold model	Anxiety disorders preceded alcoholism in 65% of persons with both anxiety and alcoholism. Does not seem that alcoholism leads to anxiety. But alcoholism and anxiety appear to share some underlying transmissible factors.
Sonne et al; **1994** South Carolina, **USA**	Mostly descriptive statistics; Chi squared	Substance users had greater morbidity associated with their mood disorders than non-substance users. Substance users had earlier onset of mood disorders and were more likely to have onset of mood disorders before age 20yrs. Most common comorbid non-substance use diagnosis = PTSD in substance users.
Araujo&Monteiro, **1995; Brazil**	t-test; chi squared	Alcoholics more likely to have 2 or more additional psychiatric diagnoses, and to have a family history of depression.
Biederman et al.; **1995; USA**	ANOVA; Chi squared; Logistic Regression	Presence of ADHD =>higher lifetime risk of drug or alcohol abuse or dependence. positive association between number of comorbid disorders and risk for SUD's in both ADHD and normal comparison subjects. Anti-social disorders are important risk factors for SUD's in non-ADHD patients. Association between SUD's and depression and anxiety.
Brook et al., **1995;** NY, **USA**	Correlations; hierarchical regression	Childhood personality attributes assoc with adolescent personality traits. Personality traits related to drug use.
Grilo et al, **1995; USA**	Chi squared; descriptive statistics	Early CD associated with ↑risk of SUD in later adolescence. Study data contradicted findings of some other community and inpatient studies.
Riggs et al, **1995; USA**	Chi squared; t-tests; Pearsons correlations	Depression associated with increased substance use. Patients with CD had earlier onset of depression. Boys with depression had earlier onset of CD. Depression group had higher prevalence of ADHD and anxiety disorders.
Schmidt, **1995;** California, **USA**	Logistic regression	Inpatients more likely than outpatients to report having been drinking during event that precipitated psychiatric admission. Admitted patients more likely to have been drinking more heavily than patients not admitted. Inpatients more likely to have drunk more than outpatient admissions. Patient self-reports appear to be contradictory, namely, some say they drink because of emotional problems; others say substance abuse causes their mental problems.
Triffleman et al; **1995;** San Francisco,**USA**	Correlations	Childhood trauma exposure strongly positively associated with substance dependence disorders. But study cautions that relationship might be more complicated, eg with other factors increasing risk for trauma and subsequent substance abuse.
Brook et al., **1996;** NY, **USA**	Latent variable structural equation modeling	Childhood aggression related to drug use and delinquency.
Brown et al., **1996;**	X^2; Discriminant Function Analysis; Analysis of Covariance;	CD highly prevalent Amongst abusers in Rx. ♂ abusers engage in more CD behaviour than ♀abusers. CD associated with poorer

SanDiego, California, **USA**	Anova's	prognosis after treatment for abuse. CD secondary to abuse. Primary CD => ↑ risk of poor abuse outcome and↑ risk of progression to ASPD.
King et al., **1996;** Urban, **USA**	Ancova; Mancova; Discriminant Function Analysis	In ♀s depression=>alcohol abuse. Comorbid alcohol abuse+depression=>♀s psychosocial adjustment problems + more likely to engage with ♂s
Fergusson et al., **1996; New Zealand**	Logistic regression, log-linear modeling	Strong comorbidity between depression and nicotine dependence at 16yrs, and did not vary significantly for ♂ and ♀.
Novins et al.,**1996; USA**	Bivariate analyses	High prevalence of SUD + psychiatric comorbidity. High drop-out from treatment.
Grilo et al., **1996;** New Haven, Connecticut, **USA**	Mostly descriptive statistics	Substance use disorders coexist more often with conduct disorder in absence of ADHD. Patients with CD had earlier age at 1st psychiatric contact than patients with coexisting CD and SUD. Anxiety disorders more common in conjunction with CD and comorbid SUD, than with SUD alone
Kessler et al., **1996**; **USA**	OR's; Logistic Regression; Age-of-onset curves; Balanced Repeated Replications	All the mental disorders are consistently more associated with dependence rather than abuse. Mental disorders usually occur first (preceding addictive disorders) except in men with affective disorders and alcohol use disorders.
Rohde et al.; **1996;** Oregon, **USA**;	Descriptive statistics; Multiple Regression	Other psychiatric disorders=>alcohol disorder; Early age onset of alcohol Disorder=>↑chance of comorbidity; Depression, disruptive behave disorders, drug, tobacco use strongly comorbid with alcohol use disorders. Alcohol Use disorder=>psychopathology ↑alcohol problems=>↑likelihood of psychiatric disorder.
Breslau et al.; **1997; USA**	Cox Proportional Hazards models for censored survival data	Significant association between PTSD and lifetime occurrence of MD, any anxiety disorders, alcohol abuse or dependence. PTSD increased risk for first onset MD and alcohol abuse or dependence.
Brooner et al; 1997; Baltimore, Md; **USA**	Prevalence rates with OR's; ANOVA's; Descriptive discriminant analyses	MD and ASPD most common lifetime diagnoses. 39% comorbidity mostly involved personality disorders. Most had substance use other than opioid dep. ♀s more likely to have Axis I diagnoses. ♂s more likely to have personality disorders
Kandel et al, **1997; USA**; **Puerto Rico**	Logistic regression	Frequent substance users had higher prevalence of psychiatric disorders. ↑use associated with ↑risk of psychiatric disorder.
Kessler et al., **1997; USA**	Logistic regression, Bivariate survival models	Earlier disorders are stronger predictors of alcohol dependence than alcohol abuse. This prediction is stronger in ♀s.
Clark et al., **1997;** Pittsburgh, **USA**	Configural Frequency Analysis	Alcohol dependence=>↑prevalence rates of other mental disorders, especially major depression+PTSD. MD+PTSD preceded or followed alcohol use disorders.

Biederman, et al., **1997; USA**	Bivariate descriptive tests	Conduct+bipolar disorders=>psychoactive SUD independently of ADHD status. Anxiety+Depression weakly=>PSUD
Deykin+Buka, **1997; USA**	X^2; OR's	↑ risk of PTSD amongst abusers of substances. ♀s have greater risk of PTSD due to greater susceptibility to high risk trauma. In ♂s abuse well-established before PTSD onset. Reverse applied to ♀s.
Horner&Scheibe, **1997; USA**	Correlations, Mann-Whitney U; 2x2 Anovas	There is an over-representation of ADHD among adolescent substance abusers in treatment. ADHD subjects have more severe substance use than controls.
Moscato et al., **1997;** Erie County, NY, **USA**	Logistic regression	Sample had higher proportion of ♀s with depressive symptoms at baseline + FU. Higher proportion of ♂s had alcohol problems at baseline+ FU. ♂♀ initial levels of depressive symptoms predicted subsequent levels of depressive symptoms. ♀♂ prior alcohol problems predicted subsequent alcohol problems. ♀ depressive symptoms predicted subsequent alcohol problems over 3 and 4 yr period, but not over 7yr period. ♂alcohol problems did not predict depressive symptoms. No evidence that alcohol problems predict depressive symptoms in ♀s.
Ross & Shirley, **1997;** Ontario, **Canada**	Multiple regression; Chi squared	Problem drinkers with comorbidity more likely to drink heavily; be current daily smokers; to have used tranquillizers or anti-depressants. Cannabis associated with problem-drinking with or without psychiatric comorbidity. Comorbid problem drinkers more likely to be diagnosed with alcohol abuse or dependence, and develop alcohol-related problems at a younger age. Binge drinking more common in problem-drinkers with psychiatric comorbidity.
Breslau, et al., **1998;** Michigan, **USA**	Hazards ratios	Early conduct problems assoc with ↑risk for progression to daily smoking. Early conduct problems =>↓smokers' potential for cessation o smoking. Early conduct problems =>↑risk of 1st onset MD. Daily smoking =>↑ risk for 1st onset MD. Prior alcohol use disorder not significant in any of the models used.
Escobedo et al., **1998**; **USA**	Multivariate analyses	Females more likely than males to report depressive symptoms. Depressed adolescents more likely to initiate smoking. Increase in frequency of depressive symptoms associated with increased rates of smoking initiation in males and females.
McGee et al., **1998; New Zealand**	OR's; Logistic Regression, Chi-squared	Mental health only weakly predictive of smoking
Miller-Johnson et al, **1998;USA**	Anova (repeated measures)	Earlier CD assoc with risk for increased levels of substance use. Early substance use assoc with/predicts later use.↑ substance use in youth with comorbid CD and depression.
Patton, et al., **1998; Australia**	Multiple logistic regression, Cox proportional hazards model	Smoking did not predict mental health problems, but depression + anxiety predicted smoking initiation. ↑psychiatric morbidity=>↑risk for smoking initiation if peers were mostly smokers.
Brook, et al., **1998;** NY, **USA**	Chi squared +Fisher's Exact	Adolescent drug use=>depressive+disruptive disorders in young adulthood. ↓drug use might later ↓psychiatric disorders.

		No correlation between level of substance use + rates of anxiety disorder. Tobacco most strongly related to depression.
Troisi et al., **1998**; **Italy**.	Fisher's Exact; Univariate and Multivariate analyses	Users had difficulty in identifying or expressing emotions. Increase in Cannabis use leads to increase in psychiatric disabilities.
Breslau and Klein, **1999;** Michigan, **USA**	Cox Proportional Hazards Models for censored survival data, with daily smoking as a time-dependent covariate.	Daily smoking associated with increased risk for first time occurrence of panic attack. Risk of panic attack higher in active than in past smokers.
Chong et al.; **1999; Taiwan** (PAST study)	OR's; Mmultivariate logistic regression	Among SUD cases disruptive behaviour disorders (incl CD and ADHD) most common comorbid psychiatric disorders, followed by anxiety and depressive disorders. Other diagnoses, including psychoses, very rare. Adolescents with psychiatric disorders at risk for SUD's.
Clark+Parker, **1999;** Pittsburgh, **USA**	Survival analysis	ADHD not associated with substance .related problems. Negative affect disorders not associate with SUDs.
Costello et al., **1999;** North Carolina, **USA**	Generalised Estimating Equation modelling	Early onset substance use=>↑likelihood of later substance use. No association between anxiety disorders or ADHD +likelihood of substance use. Most psychiatric disorders preceded substance use. Anxiety disorders=>earlier onset of later substance use/abuse. ♀s: strong association between CD + substance use. ♂s: strong association between Depression + substance use.
Costello et al., **1999**; **USA**	Prevalences	Depression strongly associated with substance use and abuse. Depressed boys more likely to abuse substances than non-depressed boys. Presence of psychiatric disorder meant earlier or same time onset of substance use when compared with those who did not have a psychiatric disorder. Psychiatric illness preceded substance use.
Disney et al.; **1999**; Minneapolis, **USA**	Hierarchical Logit analysis	Presence of ADHD or conduct disorder => largest rates of substance use and abuse in both ♂♀s. ADHD not significantly associated with substance use or abuse except in presence of comorbid conduct disorder. ADHD is a possible risk factor for nicotine dependence. Conduct disorder = strong risk factor for substance use or abuse across genders.
Greene+ Biederman, **1999; USA**	Logistic Regression	Social impairment predicts smoking and less severe SUDs. Conduct Disorders predict more severe SUDs.
Kandel et al; **1999; USA**	WALD statistics for ORs	Current SUD more likely to co-occur with another psychiatric disorder. This disorder is most likely to be a disruptive behaviour disorder or an anti-social personality disorder for both adolescents and adults. Adolescents with lifetime SUD are at as high a risk for psychiatric disorders as are adults. Comorbidity of SUD and psychiatric disorders highest among 15-24 yr olds.
Kushner et al., **1999;**	Odds ratios; Logistic Regression; Path analysis	Having anxiety disorder or alcohol abuse/dependence=>↑likelihood of developing the other diagnosis concurrently.

USA (Midwestern Univ.)		Anxiety disorders predicted alcohol abuse but not vice versa. But anxiety disorder increased risk of new alcohol abuse disorder and vice versa.
Roberts et al., **1999;** Cape Town, **SA**	Correlations, Non-parametric tests	Anxiety symptoms temporary, related to intoxication + withdrawal. Delay making diagnosis of anxiety after abstinence and only do so if symptoms persist.
Rao, et al., **1999; USA**	Student, t; Anova; All 2-tailed tests	Depressed adolescents had earlier onset of SUD. Comorbid depression + SUD assoc with Psychosocial morbidity.
Johnson et al., **2000;** NY, **USA**	Bivariate associations, Logistic regression	Anxiety disorders not assoc. with later smoking. Cig smoking may ↑ risk for later anxiety disorders.
Dixit&Crum, **2000;** Baltimore, **USA**	Logistic regression to predict heavy drinking at F-U from baseline depression	History of depression=>risk of heavy alcohol use. ↑depressive symptoms=>↑risk of heavy alcohol use
Marsden et al; **2000**; **UK**	Cluster Analysis; Cluster profiles described single chi- squared and Anova; Multiple Linear Regression	Psychiatric symptoms on admission seemed related to nature of substance use. Prevalent psychiatric Rx and more severe depression => more severe psychiatric symptoms
McGee et al., **2000; New Zealand**	OR's; Logistic regression; Chi-squared	In males aged 15yrs, mental disorder and earlier substance use predicted later substance use. Earlier smoking and cannabis use predicted later cannabis use and mental disorder for ages 18 and 21 yrs, especially in males. Smoking at age 18yrs increased risk for anxiety-depressive disorders + alcohol dependence
Rao, et al; **2000;** LA County, **USA**	Descriptive statistics; Survival analysis; Multiple Regression	SUD before study=>SUD at FU. More ♀s with MDD had lifetime SUD. Baseline MDD=>SUD at FU. MDD before study did not=> SUD at FU; but SUD before study =>more likely MDD at FU. FU SUD=>worst BDI score. Lifetime SUD=>depression more likely. SUD=>school dysfunction.
Reinherz et al., **2000; USA**	Multiple Regression models	Sibling's drug or alcohol use ↑ risk of both depression and drug disorders. In ♀s, those who were anxious or depressed at age 9 yrs were more likely to develop depression or SUD. Mothers' assessment of early behaviour. Difficulties not predictive of drug disorders. Early attention problems predictive of drug disorders. Early aggressive behaviour => ↑ risk of SUD's in ♀♂s. ♂s more likely to develop SUD's and ♀s more likely to develop depression.
Rodgers et al.; **2000;** Canberra, **Australia**	Logistic Regression	Non-drinkers had higher depression and anxiety cores than low-consumption drinkers. But, non-drinkers included EX-Drinkers which could have pushed up the scores. Heavy drinkers reported more symptoms than light drinkers. Possible U-shaped assoc. between drinking and psychopathology.

Degenhardt et al., **2001; Australia**	Bivariate regression, Multiple logistic regression	Tobacco, cannabis ↑ mental health problems. Cannabis not associated with anxiety + affective disorders. Tobacco, cannabis, alcohol use => ↑ other substance use problems
Hofstra et al. **2001; Netherlands**	Correlations between Time1 and Time 6; Linear Regressions	Aggressive behaviour in childhood predicted alcohol misuse/dependence in adult ♀but not in ♂.
Ferdinand et al., **2001; Netherlands**	Fisher's Exact; Logistic Regression; OR's	Adolescent behavioural + emotional problems related to substance use in young adulthood
Dierker et al., **2002; USA**	Logistic regression; Chi-squared	Only alcohol use disorders were significantly associated with regular heavy smoking.
Rey et al; **2002; Australia**	Descriptive an Logistic Regression	Use of cannabis increased the chances of having emotional and behavioural problems. Increased depression scores increased the chances of having used cannabis. ADHD doe not seem to increase risk of cannabis use.
Compton et al.; **2003; USA**	Descriptive statistics; Multivariate regression models	Comorbid substance use and ASPD increased the chances of worse Rx outcome. Generalised anxiety disorder also led to worse outcome. Comorbidity generally leads to worse RX outcome in ♂s. Not so clear cut in ♀s.
Goodman et al; **2003; England,Scotland, Wales**	Logistic Regression	Having a psychiatric disorder was assoc. with increased risk of regular smoking. Existence of a depressive disorder doubled risk of regular dinking and lifetime cannabis use. Increased risk for psychiatric diagnosis if a regular smoker or drinker, or had used cannabis.
Shrier et al., **2003;** Boston, **USA**	Chi squared; Anova; Multivariate Logistic Regression	♀s greater no. of symptom types; more likely to report depression, eating disorders. Anxiety symptoms most common in ♀s; not assoc with SUDs. ♂s↑severity substance use=>↑conduct disorder ↑SUD's=>↑likelihood psychiatric symptoms+ no. of symptoms.
Steinhausen an Metzke, **2003; Switzerland**	Qualitative and Multivariate Analysis of Covariance (MANCOVA)	Abstainers were mainly female. Females drank less than males. Disproportionate number of males among heavy drinkers. Problem drinkers more likely to have emotional and behavioural problems. The older the person, the more likely that s/he was to have emotional and/or behavioural problems.
De Graaf et al., **2004**; **Netherlands**	Descriptive statistics and Logistic Regression	Males were more likely to develop substance use comorbid with mood disorders than were females. Only gender was associated with comorbidity. Appears that rapid comorbidity is triggered not so much by previous life events as by life events that occur during the first disorder.
Grant et al.; **2004; USA**	Cross-tabulations; OR's	All mood and anxiety disorders were more strongly related to alcohol and drug dependence than to drug abuse. Mania most strongly associated with SUD's than any other mood or anxiety disorder.
King et al., **2004**; **USA**	Generalised Estimating Equations (GEE); Prevalence rates; OR's, Chi squared; Log-Linear analyses.	Externalising psychopathology increases risk for early initiation of alcohol, nicotine and cannabis use, and predicts higher level of SU. ADHD weakest predictor of SU. Males and females at similar risk for SU in early adolescence, but internalising pathways for SU might operate from later adolescence.

Obando et al., **2004 USA**	Descriptive statistics and Logistic Regression	Depressive symptoms contribute significantly to overall substance involvement. But there are risk factors that differ for school children vs youth in Rx vs street youth.
Fernander et al., **2006;** Cape Town, **South Africa**	Logistic Regression	Depression associated with smoking in ♀s only.
Monshouwer et al., **2006**; **Netherlands**	Multivariate Linear Regression	Cannabis use strongly associated with delinquent and aggressive behaviour. Association stronger with more recent use and with increased frequency of use. Association with thought problems in regular users of cannabis.
Hayatbakhsh et al., **2007; Australia**	Logistic Regression	Smoking at 14yrs increased risk of anxiety/depression in young adulthood. Cannabis use in adolescence significantly associated with anxiety/depression in young adults, but anxiety/depression in adolescence did not predict early cannabis use.
Pardini et al., **2007 USA**	Regression analyses	Early adolescent CD symptoms leads to increased alcohol use disorder symptoms and alcohol dependence by early adulthood. Increased depressive symptoms combined with high CD symptoms increased the risk for alcohol use disorders in adolescent males. Early adolescent psychopathology only modestly related to alcohol abuse in the absence of dependence. Increased CD symptoms led to increased risk for later alcohol use problems. Increased anxiety/withdrawal in early adolescence led to decreased risk for alcohol use disorders in adulthood.
Roberts et al., **2007 USA**	Logistic regression	Comorbidity between SUDs and othe psychopathology vary i.t.o. substance of use, abuse vs dependence, and type of psychiatric disorder. Strong association between substance use (especially dependence) and multiple comorbid disorders.

CHAPTER 3

Association between psychopathology and substance use among school-going adolescents in Cape Town, South Africa

Association between psychopathology and substance use among school-going adolescents in Cape Town, South Africa

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Abstract

Background. Limited information exists regarding the association between psychopathology and specific substance use in young people both globally and locally. We examined the association between psychopathology and substance use in high school students to determine the nature of the associations and the role of demographic factors in these associations. **Method.** Grade 8 (N = 480) and Grade 11 (N = 459) students from 39 high schools in Cape Town, South Africa, completed a self-administered questionnaire. Psychopathology information was obtained from total scores on the Harvard Trauma Questionnaire, Beck Depression Inventory and the Zung Self-Rating Anxiety Scale. Lifetime prevalence rates were calculated for tobacco, alcohol, cannabis and inhalant use. Associations between psychopathology and substance use were determined using regression analyses and structural equation modeling. **Results**. On adjusting for demographic characteristics, significant associations were found between PTSD and all substance use, between depression, alcohol, cannabis and inhalant use, and between anxiety and cannabis use. The associations of PTSD and depression with alcohol and cannabis use, and between anxiety and cannabis use, were moderated by grade. **Conclusions**. Although psychopathology and substance use were associated with each other, these associations occurred in accordance with substance and grade. Roles for gender, age and ethnicity emerged in the associations, but further investigation is recommended to examine these.

Keywords - psychopathology, substance use, comorbidity, adolescents

The association between psychopathology and substance use has been extensively researched, particularly within the last three decades. There is consensus that psychiatric problems and substance use are almost inextricably associated with one another, and that such comorbidity is as common in adolescents and children as it is in adults (Angold et al. 1999; Saban & Flisher 2009).

However, limited information is available on the association between psychopathology and specific types of substance use (such as alcohol, cannabis and inhalants) in children and young people (Roberts et al. 2007) despite evidence for extensive comorbidity particularly among adolescents. In addition, information is lacking regarding the association between psychiatric disorder and substance use disorders. Few studies have been completed in South Africa on the association between psychopathology and substance use or substance use disorder, despite the problems experienced here with both psychiatric disorder and substance use, particularly among adolescents (Flisher et al. 2002; Taylor et al. 2003; Flisher et al. 2003).

This study examined the extent and nature of psychopathology and substance use among Grade 8 and Grade 11 students in Cape Town, South Africa, to determine the associations between psychopathology (specifically PTSD, depression and anxiety) and substance use (specifically tobacco, alcohol, cannabis and inhalants), and to establish the role of age, school grade, gender and racially classified social group (RCSG) in these associations.

METHODS

Study design and participants

The sample consisted of 939 Grade 8 and Grade 11 students, of whom 782 had sufficient data recorded to enable the selected analyses. The sample was randomly drawn from 2779 students selected from public (non-private) high schools in Cape Town (Flisher et al. 2003) in a multi-stage cluster sampling procedure. The latter involved selecting 39 schools, using a sampling frame of all high schools in Cape Town, stratified by four-digit postal (zip) codes, the first two digits of which define the geographical area which, in Cape Town is relatively homogeneous with respect to both social class and RCSG. The number of schools selected in each stratum was directly proportional to the number of students in that stratum, while the probability of a school being selected was directly proportional to the number of students in that school. In each

participating grade, two classes were randomly selected. The students in these classes were combined to form a single list from which forty students were randomly selected. To accommodate possible absentees, five additional students were selected, thus replacing a maximum of five absentees on the day.

Measurement tools

The instrument used was a self-administered questionnaire which elicited data regarding, demographic characteristics, substance use and psychopathology (PTSD, depression and anxiety). The demographic characteristics were school grade, gender, age (in years), and racially classified social group (RSCG). The RCSGs were Asian, White, Coloured and Black, as defined in the repealed Population Registration Act of 1950, with the category "Coloured" referring to mixed ancestry consisting of any combinations of Asian, European, African or other heritage. Substance use was defined as lifetime use of cigarettes, alcohol, cannabis and inhalants. Students were asked whether they had ever smoked a whole cigarette, ever had more than a few sips of alcohol, ever smoked cannabis alone or ever used inhalants such as glue, petrol or paint thinners. Test-retest reliability data were good with kappas and 95% confidence intervals of 0.85 (0.80-0.91) for ever having smoked a whole cigarette, 0.78 (0.71-0.85) for ever having had more than a few sips of alcohol and 0.80 (0.72-0.88) for ever having smoked cannabis alone (Flisher et al. 2003). Psychopathology was defined as the total scores obtained on the Harvard Trauma Questionnaire (modified to assess traumatic experiences in a local context), the Beck Depression Inventory, and the Zung Self-Rating Anxiety Scale (Ward et al. 2004). The questionnaire was available in English, Afrikaans and Xhosa, the major Cape Town languages. The English questionnaire was translated into Afrikaans and Xhosa and then back-translated by Afrikaans and Xhosa first language users respectively. The translation of the questionnaires was carefully scrutinized for reliability across the three languages, enabling all the students to answer the questions confidently in their preferred language.

Procedure

Ethical clearance was obtained from both the University of Cape Town Health Sciences Faculty Research Committee as well as from the Western Cape Education Department. Students were informed that they could refuse to answer questions with no risk of negative consequences to themselves or anyone else. Only members of the research team were present during the completion of the questionnaires. Confidentiality of the responses to the questions was preserved by

allowing the students to complete the questionnaires anonymously and under examination conditions. Once completed, each questionnaire was inserted into an envelope that was then sealed

Statistical analysis

The original sample of 939 students was found to have large swathes of missing and unreported data for 157 (16.7%) students, rendering statistical analyses of data for these students meaningless or inappropriate. These students were excluded from the study, resulting in a sample size of 782 students. Of the latter, the three Asian students were excluded because of their small number and their being present in Grade 8 only, while others were further excluded when their data relevant to the required analyses were found to be inadequate.

In analyzing the data, attempts were always made to optimize the sample size. However, missing data occurred across the sample, necessitating selected exclusions of students for the various statistical analyses, resulting in differing sample sizes for the different analyses.

Mean psychopathology scores (with 95% confidence intervals), and prevalence rates for lifetime use of cigarettes, alcohol, cannabis and inhalants (with 95% confidence intervals), were calculated and used to compare the Grade 8 and Grade 11 students (both within grades and across grades) in terms of gender, RCSG and age. Where the confidence intervals did not overlap, a statistically significant difference was concluded as existing between the selected groups ($p<0.05$). In cases where the confidence intervals overlapped to the extent that the percentage prevalence rate of one group was located within the confidence interval of the other group, the two groups were regarded as not statistically significant ($p>0.05$). In those cases where the confidence intervals overlapped, but not to the extent that the prevalence rate of one group was located within the confidence interval of the other group, the comparison was regarded as inconclusive.

Logistic regression, using survey design analyses, was performed to assess the association between psychopathology (PTSD, anxiety and depression total scores) and substances of use (cigarettes, alcohol, cannabis and inhalants). These analyses were adjusted for the sampling design with the data stratified according to the geographical location of the schools as defined by postal code, and weighted in terms of the number of students in each school and in each grade per school, and the number of students selected from each grade. The results of these analyses were expressed in terms of unadjusted odds ratios, 95% confidence intervals, and p-values. These regression analyses were then repeated,

taking into account the role of demographic factors in the associations, providing adjusted odds ratios, 95% confidence intervals and p-values. Substance use, through its component factors, was retained as the dependent variable throughout the analyses, while the components of psychopathology, and the sociodemographic factors, were the independent variables where required.

The results of the regression analyses were used to inform the selection of variables for the structural equation modeling (SEM) (Kline 1998). Gender and RCSG were selected to fit two separate multi-group models for the SEM. However, the RCSG model could not solve, resulting in a model stratified by gender only. For the males and females configural invariance and metric invariance (equal factor loadings), were achieved, thereby demonstrating that the calibration of the latent variables was comparable for males and females.

The data were analysed using STATA (Version 9) (STATA Release 9 2008) for descriptive statistics and multivariate analyses (in the form of regression modeling), taking into account the clustering of the schools. LISREL (Version 8.72) (Joreskog & Sorbom 1996) was used for the structural equation modeling.

RESULTS

The 157 students who were excluded from the sample were found to differ significantly (p=0.0001) from the 782 included students with respect to grade and RCSG. In particular, 78% of the excluded sample was in Grade 8 compared with 55.8% in the included group, 21.7% of the exclusions were in Grade 11 compared with 44.2% of the included students, 51.7% of the exclusions were male compared with 43.6% of the inclusions, 46.7% of the exclusions were female compared with 54.5% of the inclusions, 46.2% of the exclusions were Black compared with 20.9% of the inclusions, 7% of the exclusions were White compared with 25.4% of the inclusions, and 39.6% of the exclusions were Coloured compared with 50.3% of the inclusions.

As indicated in Table 1, there were more females than males in both Grade 8 and Grade 11. Coloured students were in the majority in both grades, reflecting the ethnic composition of the area from which the sample was selected. Females had significantly higher mean scores for all the measures of psychopathology compared with males. Barring depression in Grade 11, Black students had the highest mean psychopathology scores of all ethnic groups. No significant differences in psychopathology mean scores were identified among the selected age groups.

Table 2 lists the prevalence of lifetime substance use, stratified by grade, gender, ethnicity and age.

In the adjusted models, PTSD was significantly associated with cigarette, alcohol, cannabis and inhalant use, depression was significantly associated with alcohol, cannabis and inhalant use, and anxiety was significantly associated with cannabis use. The significant associations for PTSD and depression with alcohol and cannabis use, and between anxiety and cannabis use, and between depression and inhalant use, were moderated by grade (Table 3). In particular, Grade 8 students had a 1.8% increased risk of alcohol use with every one point increase in PTSD total score. The Grade 8 students had a 4.2% decreased risk of cannabis use with every one point increase in PTSD total score, while the Grade 11s had a 2.3% increased risk of cannabis use with every one point increase in the PTSD total score. Grade 8 students had a 5% increased risk of alcohol use, and an 8% increased risk of cannabis use, with every one point increase in the depression total score, while the Grade 11s had a 4.7% decreased risk of inhalant use with every one point increase in the depression total score. The associations between PTSD and alcohol use in Grade 11, between depression, alcohol and cannabis use in Grade 11, and between depression and inhalant use in Grade 8, were not statistically significant.

In the SEM structural model, though the Satorra-Bentler chi-squared value (88.04) was found to be significant (0.00003), its ratio with the related degrees of freedom (df = 41) provided evidence of adequate fit (Kline, 1998). The Global Goodness of Fit Statistics values obtained were above the generally-accepted threshold for reasonable fit, with the RMSEA value of 0.0547, and NFI=0.971, NNFI=0.978, PNFI=0.711; CFI=0.984; IFI=0.984; RFI=0.960. Thus, it can safely be concluded that the specified model provides a reasonable fit to the data.

In the males, weak evidence was found for an association between psychopathology and substance use (p=0.067) when adjusting for the effects of age. In females, there was also weak evidence for a statistically significant association between psychopathology and substance use (p=0.058) when adjusting for the effects of age. However, while neither of the effects for each gender was strongly statistically significant, there was slightly more evidence for an effect in the females than was found in the males. In addition, as illustrated in Figure 2, a statistically significant association (p=0.05) was found between age group and substance use in females, but not in males.

DISCUSSION

The results obtained are characterised by several major findings that have previously been limited or unknown in this population. These include firstly, that there is an association between psychopathology and lifetime substance use; secondly, that the association between psychopathology and substance use is more likely to occur between certain types of psychopathology and substances; thirdly, the association between psychopathology and substance use is influenced by demographic factors; and fourthly, that school grade in particular impacts on the association between psychopathology and substance use.

The specific associations that have been identified are between PTSD and all the selected substances of use (namely cigarettes, alcohol, cannabis and inhalants), between depression, alcohol, cannabis and inhalants, and between anxiety and cannabis. These findings reflect the trends in associations between psychopathology and substance use that have been illustrated elsewhere. For example, substance users have been found to be at greater risk of PTSD (Deykin & Buka 1997; Breslau et al. 1997), and have PTSD as the most common non-substance use diagnosis (Sonne et al. 1994). Furthermore, evidence has been provided for associations between PTSD and alcohol abuse (Breslau et al. 1997), between depression and general substance use (Hovens et al. 1994), between depression and specifically smoking (Anda et al. 1990; Glassman et al. 1990; Regier et al. 1990; Breslau et al. 1994) and alcohol use [Regier et al. 1990; Araujo & Monteiro, 1995; Rohde et al. 1996; Moscato et al. 1997; Dixit & Crum, 2000; Reinherz et al. 2000; Goodman et al. 2003), and between anxiety and both general substance use as well as specifically smoking, alcohol and cannabis use (Sonne et al. 1994;Hovens et al, 1994; Breslau et al. 1991; Rounsaville et al. 1991; Costello et al. 1999; Kushner et al. 1999; Johnson et al. 2000; McGee et al. 2000; Grant et al. 2000; Fernander et al. 2006). These results emphasize the specificity of associations between psychopathology and substance use, and have important implications for the planning of interventions geared at the prevention or treatment of comorbidity (Swendsen et al., 2010).

The results also provide evidence for the impact of demographic factors on the association between psychopathology and substance use. For example, age was found to influence cannabis use, and males were more likely to have used alcohol and cannabis compared with females. But this influence is not evident across all substances and psychopathology. Similarly, though the association between psychopathology and substance use appears stronger in females than males as indicated by the SEM, the influence of gender has not been clear. These results reflect trends in the literature. For example, Schwinn et al. (2010) have highlighted the paucity of studies that have examined the influence of gender on comorbidity, and emphasize the 'mixed results' that have been obtained from these studies. Racially classified social grouping (RCSG) was also significantly associated with some substances of use, with Black students being less likely to have used any of the selected substances while White students were more likely to have used alcohol and inhalants, as compared with Coloured students. These results concur with those of Wallace et al. (2003) who found that substance use was widespread among adolescents, and low specifically among Blacks compared with Native American, Hispanic or White adolescents. It must be noted that, in the South African context, RCSG has historically been defined almost exclusively in terms of skin colour and thus fundamentally has no intrinsic meaning. But, as a consequence of Apartheid policies, RCSG does reflect economic discrepancies, with the majority of the poorer South Africans being Black. However, in the current study, RCSG did not significantly influence the association between psychopathology and substance use. Class grade had the most significant impact on the association between psychopathology and substance use. In particular, Grade 8 students had an increased risk of alcohol use with increased PTSD and depression scores, and an increased risk of cannabis use with increase in depression scores. In contrast, Grade 11 students had a decreased risk of cannabis use and inhalant use with increase in anxiety and depression scores respectively.

There might be a tendency for the Grade 8 students who experience traumatic events to develop PTSD and use illicit (age-restricted) substances, and echo the findings of Breslau (Breslau et al. 1997) that PTSD increases the risk for first onset of major depression and alcohol abuse or dependence. However, in the Grade 11 students, it appears that increase in anxiety and depression scores decreases the risk of cannabis and inhalant use respectively. Thus, while PTSD and depression seem to be risk factors in illicit

substance use among the Grade 8 students, anxiety and depression appear to be protective factors in the Grade 11 students. It is possible that, in the Grade 11 students, the presence of anxiety and/or depression might limit the social interaction of the students, thereby limiting their exposure to illicit substance use.

The results obtained did not reflect some trends in associations that have been found elsewhere. For example, the literature demonstrates an almost undisputed association between depression and smoking. But this study found similar associations only in the absence of the effects of demographic factors. Considering that a previous local study (Fernander et al. 2006) had found an association between depression and smoking in females, a likely explanation for the absence of this and other associations in this study could involve a combination of methodological and conceptual factors that distinguish this group from others that have similarly been investigated elsewhere. The results obtained here might reflect a sampling bias introduced by the exclusions that were largely from Grade 8, male and Black; all demographic factors (namely grade, gender and RSCG) that have featured prominently in the associations between psychopathology and substance use. The results could also have been influenced by the conceptual framework of this study. For example, psychopathology was assessed in terms of a summed total score on a particular day. Substance use was defined as ever having used any of the selected substances, regardless of recency, frequency or amount. Neither of these definitions constitutes a definitive clinical diagnosis of psychopathology or substance use disorder, abuse or dependence, and these definitions provide no measure of severity of disorder or frequency of substance use. The elicited associations thus do not lend themselves to equivalent comparison with studies that have identified lifetime comorbidity of psychiatric or more severe substance use or disorders by other means.

However, despite these and the well-known limitations presented by self-administered questionnaires (such as, relying on the honesty of the respondents, missing data), the value of this study lies in its ability to provide comprehensive evidence for an association between psychopathology and substance use, and its concomitants, in a community sample where these details have previously been lacking. These findings, together with the fact that few similar studies have been conducted in this region, should inspire the need to conduct further and related research with a view to verifying and elaborating on the established associations.

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DECLARATION OF INTEREST

None

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TABLE 1

Psychopathology scores stratified by standard, gender, age and ethnicity (Mean scores and 95% CI)

Demographics	N (%)	PTSD	Anxiety	Depression
Grade 8				
Male	152 (43.4)	45.5 (42.9; 48.2)	30.5 (28.8; 32.2)	28.0 (26.4; 30.0)
Female	206 (54.7)	51.5 (49.3; 53.6)	34.0 (32.6; 35.3)	32.8 (31.3; 34.3)
Asian	3 (0.85)	53.3 (29.6; 77.0)	35.7 (23.4;48.0)	45.5 (18.8; 72.2)
Black	74 (19.5)	54.4 (51.0; 57.9)	37.9 (35.6; 40.3)	32.7 (29.8; 35.5)
Coloured	188 (53.4)	47.4 (45.0; 49.9)	30.6 (29.2; 32.0)	30.4 (28.5; 32.4)
White	91 (23.1)	48.1 (43.7; 52.4)	31.7 (30.1; 33.4)	29.9 (27.0; 32.8)
Age (years) <14	152 (41.1)	45.7 (43.6; 47.9)	31.1 (29.7; 32.4)	29.8 (28.0; 31.8)
14-<16	187 (51.1)	50.8 (47.7; 53.9)	32.6 (31.4; 33.7)	31.1 (29.6; 32.6)
16-<18	24 (6.8)	55.1 (47.5; 62.8)	38.3 (32.5; 44.2)	34.2 (27.1; 41.3)
18+	1 (0.3)	68.1 (38.0; 98.2)	55.2 (42.2; 68.3)	37.6 (24.3; 51.0)

Grade 11					
Male		171 (43.8)	51.8 (48.9; 54.6)	32.6 (31.3; 33.8)	31.7 (30.2; 33.0)
Female		237 (54.2)	60.7 (57.2; 64.1)	36.6 (35.0; 38.3)	37.7 (35.3; 39.7)
Black		91 (22.8)	63.5 (57.8; 69.1)	39.1 (36.4; 41.7)	35.7 (32.7; 38.6)
Coloured		212 (46.3)	58.1 (55.1; 61.2)	34.2 (32.9; 35.6)	36.7 (34.4; 39.0)
White		102 (28.4)	49.1 (45.4; 52.9)	32.7 (32.0; 33.5)	31.7 (29.4; 34.1)
Age (years)	14-<16	7 (2.0)	65.5 (50.7; 80.4)	36.4 (31.1; 41.7)	33.3 (25.3; 41.3)
	16-<18	290 (69)	55.0 (51.3; 58.6)	34.0 (33.0; 35.1)	34.6 (32.2; 37.0)
	18+	2 (0.3)	59.9 (56.1; 63.6)	37.1 (34.2; 40.0)	36.0 (33.6; 38.4)

TABLE 2
Lifetime substance use prevalence stratified by grade, gender, ethnicity and age (n; (%); 95% CIs)

Demographics	Cigarettes	Alcohol	Cannabis	Inhalants
Grade 8				
Male	66 (43.4) [34.4; 53.0]	60 (39.5) [30.2; 47.0]	7 (4.6) [2.1; 9.6]	6 (3.9) [1.6; 8.2]
Female	81 (39.3) [32.0; 48.7]	77 (37.40) [27.8; 45.1]	7 (3.4) [1.3; 7.3]	16 (7.8) [3.7; 15.8]
Asian	1 (34.8) [4.1; 87.0]	1 (34.8) [4.1; 87.0]	0	0
Black	9 (13.2) [6.9; 23.9]	13 (16.2) [8.7; 28.1]	2 (1.2) [0.12; 1.0]	0
Coloured	92 (49.1) [39.9; 58.3]	71 (36.8) [29.8; 44.5]	6 (3.9) [2.0; 7.6]	10 (5.2) [2.7; 9.7]

	White		44 (48.9) [34.8; 63.2]	52 (56.4) [42.1; 69.8]	6 (5.9) [2.1; 15.5]	12 (13.6) [7.9; 22.5]
	Age (years)	<14	54 (35.5) [27.2; 44.7]	50 (32.2) [24.5; 41.0]	4 (2.4) [0.8; 7.6]	9 (5.7) [2.7; 11.7]
		14-<16	88 (48.8) [41.6; 56.2]	81 (42.0) [31.8; 53.0]	10 (5.3) [2.6; 10.4]	13 (7.0) [3.3; 14.2]
		16-<18	7 (24.9) [8.8; 53.3]	9 (33.3) [16.0; 56.7]	0	0
		18+	1 (41.4) [3.8; 92.7]	0	0	0
Grade 11						
	Male		101 (59.1) [49.6; 66.0]	117 (68.4) [58.6; 77.5]	46 (26.9) [19.0; 36.2]	28 (16.3) [1.3; 7.6]
	Female		108 (45.6) [37.1; 54.1]	117 (49.4) [39.9; 56.7]	35 (14.8) [9.5; 19.8]	11 (4.6) [2.2; 10.1]
	Black		21 (21.8) [11.3; 37.9]	29 (32.0) [23.8; 41.5]	9 (9.2) [4.5; 17.9]	3 (3.6) [0.9; 13.0]
	Coloured		131 (62.9) [54.6; 70.4]	133 (62.8) [51.6; 72.7]	48 (23.2) [16.3; 31.8]	23 (13.0) [7.6; 21.3]

White		58 (56.8) [43.1; 69.5]	72 (70.0) [56.3; 80.8]	23 (21.4) [14.6; 30.4]	14 (15.2) [10.2; 21.9]
Age (years)	14-<16	1 (10.9) [1.7; 46.6]	3 (41.5) [10.9; 80.5]	1 (10.9) [1.7; 46.6]	1 (19.8) [2.6; 69.8]
	16-<18	161 (56.3) [49.8; 62.7]	178 (61.5) [52.1; 70.2]	53 (18.1) [13.4; 24.0]	30 (12.1) [7.4; 19.3]
	18+	52 (42.8) [29.4; 57.3]	55 (47.5) [38.1; 57.0]	27 (23.3) [14.7; 34.8]	9 (8.3) [4.0; 16.6]

TABLE 3

The association between psychopathology and substance use [a]

Psychopathology and demographic factors	Substance use							
	Cigarettes		Alcohol		Cannabis		Inhalants	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
PTSD	[1]1.010 [2](0.998;1.023) [3]0.101	1.016 (1.004;1.028) 0.010	1.005 (0.997;1.014) 0.208	[b]Gr. 8: 1.018 (1.000;1.037) 0.053 Gr. 11: 0.998 (0.977;1.019) 0.839	1.013 (0.995;1.031) 0.161	bGr. 8: 0.958 (0.920;0.998) 0.040 Gr. 11: 1.023 (1.003;1.043) 0.027	1.035 (1.012;1.058) 0.004	1.050 (1.019;1.081) 0.002
Depression	1.024 (1.004;1.046) 0.022	1.014 (0.992;1.035) 0.199	1.030 (1.010;1.050) 0.004	[b]Gr. 8: 1.050 (1.011;1.091) 0.014	1.022 (0.991;1.054) 0.156	[b]Gr. 8: 1.080 (1.007;1.159) 0.032	0.990 (0.956;1.026) 0.580	Gr. 8: 1.001 (0.948;1.057) 0.969

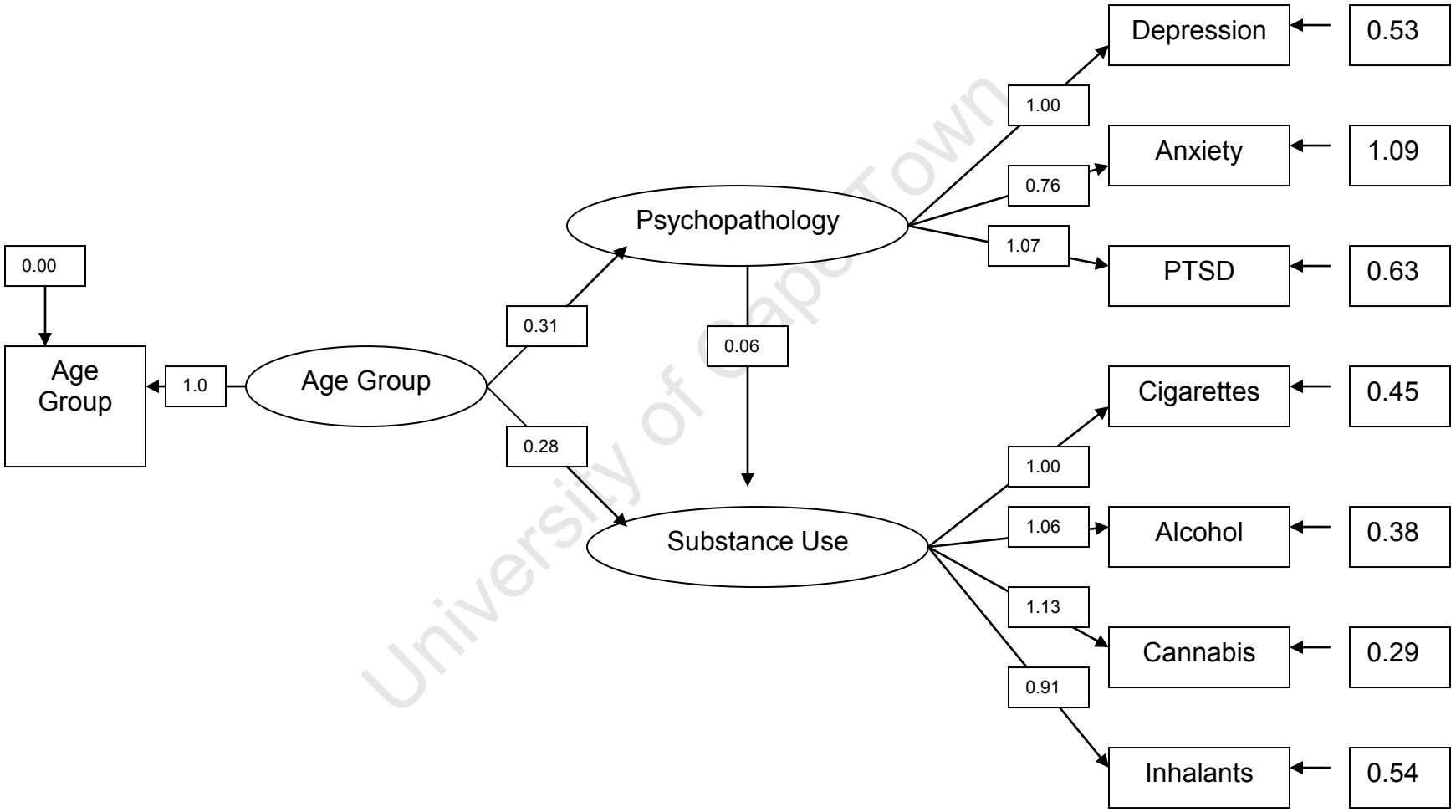
				Gr. 11: 1.011 (0.979;1.045) 0.487		Gr. 11: 0.999 (0.967;1.031) 0.934		Gr. 11: 0.953 (0.909;0.999) 0.044
Anxiety	0.966 (0.942;0.991) 0.009	0.986 (0.961;1.012) 0.274	0.967 (0.945;0.994) 0.007	0.981 (0.956;1.008) 0.164	0.965 (0.936;0.995) 0.023	[b]Gr. 8: 1.035 (0.963;1.112) 0.342 Gr. 11: 0.955 (0.919;0.993) 0.021	0.982 (0.946;1.020) 0.334	1.003 (0.954;1.054) 0.908

CI = Confidence Interval OR = Odds Ratio

[a] Models adjusted for grade, age, gender, ethnicity

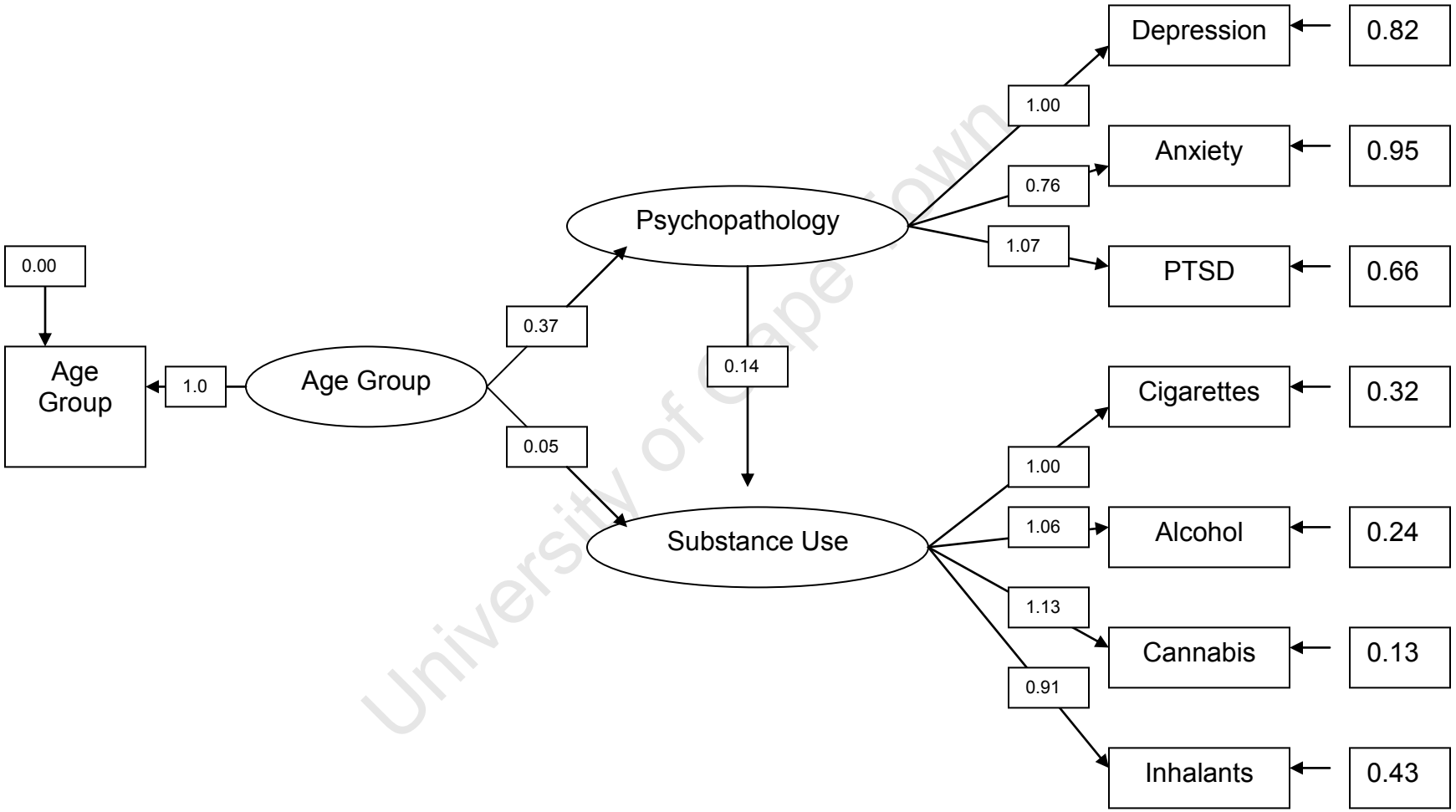
[b] Associations indicating statistical interactions

[1,2,3] OR, CI and p-values respectively



Chi Square = 88.04, df = 41, p-value = 0.0003, RMSEA = 0.055

Figure 1. Structural Equation Model: The association between psychopathology and substance use in males



Chi Square = 88.04, df = 41, p-value = 0.00003, RMSEA = 0.055

Figure 2. Structural Equation Model: The association between psychopathology and substance use in females

CHAPTER 4

The association between psychopathology and substance use: adolescent and young adult substance users in inpatient treatment in Cape Town, South Africa

The association between psychopathology and substance use: adolescent and young adult substance users in inpatient treatment in Cape Town, South Africa

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Running head: *Comorbidity in inpatient substance users in Cape Town*

Abstract

Introduction and Aims. Evidence suggests that comorbid psychopathology can negatively affect treatment outcomes in substance users. In South Africa, limited information is available regarding the prevalence, nature and contributing factors of the comorbid non-substance use psychopathology of substance users in treatment for their substance use. This study aimed to determine the frequency of occurrence and nature of comorbid non-substance use psychopathology, and its association with specific substance use, in adolescent and young adult substance users who received treatment for their substance use in Cape Town, South Africa. ***Design and Methods***. Between December 2008 and December 2009, male and female inpatient substance users (n=95; ages 17-30 years) were sampled consecutively in order of admission from three substance use treatment facilities in Cape Town. An interview schedule was administered to elicit patients'sociodemographic and substance use history details. The computer-assisted Diagnostic Interview Schedule DSM IV (C-DIS IV) was administered to screen patients for current psychiatric disorders. ***Results***. The sample was largely male, Coloured, Muslim and single. Cannabis (51.6%) and crystal methamphetamine (17.9%) were the most common first substances of use. Heroin (53.7%) and crystal methamphetamine (33.7%) were the most common substances for which treatment was sought (primary substances). The most common comorbid psychopathologies were anti-social personality disorder (ASPD 87.4%), conduct disorder (CD 67.4%), oppositional defiant disorder (33.7%), major depression (25.3%), specific phobia (15.8%) and post-traumatic stress disorder (PTSD 14.7%). Regression analyses found a marginally significant association between specific phobia and first use of cannabis, but overall indicated no statistically significant associations between psychopathology and substance use. ***Discussion and Conclusions***. The results demonstrated a high proportion of previously unidentified comorbid psychopathology in inpatient substance users. Further research is needed to investigate the prevalence and nature of such comorbid psychopathology in inpatient substance users, taking into account the context and heterogeneity of substance users in treatment.

Key words: comorbidity, psychopathology, substance use treatment.

Introduction

In psychiatry, the phenomenon where non-substance use psychopathology and problematic substance use coexist is a common form of comorbidity [1]. The comorbid conditions may co-exist simultaneously (concurrent), in tandem (sequential) or separately at any time in the patient's life (lifetime) [2]. Comorbidity is sometimes referred to as "dual diagnosis' or 'co-occurring disorders', and can involve the co-occurrence of two or more disorders. [3,4]. The comorbidity might involve pathology that meets the criteria for diagnosis of a disorder, or might refer to the presence of symptoms of a disorder [5]

Various suggestions have been proposed to explain relationships between comorbid psychopathology and substance. These include i) that the comorbidity might occur when people with psychiatric illness attempt to alleviate their discomfort by self-medicating with substances, leading to problematic use of the substances or to substance use-related disorders [2], ii) that the substance use could lead to mental illness [2], iii) that certain individuals might be genetically predisposed to either psychiatric illness and/or substance use resulting in comorbid conditions [2], iv) that in some cases, either condition could influence, or effect a change in, the course of the other [2], and v) that the substance use and psychopathology share a common neural substrate [4].

Community and hospital-based studies have provided evidence for an increased likelihood of comorbid psychiatric disorder in substance users [5], with a greater likelihood of such comorbidity as the severity of the substance use increases [6]. Psychological and psychiatric problems that have been associated with substance use include cognitive impairment, poor scholastic performance, personal and relationship problems [7], depression, anxiety [8] and PTSD [9]. Disruptive behaviour disorders like antisocial personality disorder

[10] and conduct disorder [11] have been found to be very common in patients who receive treatment for substance use [12].

However, the evidence for associations between specific forms of psychopathology and the use of specific substances has not been clear or consistent. For example, the review of community studies by Armstrong and Costello [6] indicated that, except for cannabis, associations between psychiatric disorders and the use of specific substances was not specific to either the psychiatric disorders or the substances of use. In the National Comorbidity Survey (NCS), anxiety disorders and conduct disorder/adult anti-social behaviour disorder were found to precede and predict later alcohol dependence, but such consistency in chronicity was not duplicated with the same certainty with regards to other mental disorders or substances of use [13].

In treatment populations, comorbidity is known to be characterised by heterogeneity [14]. For example, co-occurring substance use and psychopathology differ with respect to the types of substances and psychiatric problems, the temporality of the comorbid conditions [14], and the possible influence of sociodemographic factors such as age [15], gender or race/ethnicity in the associations [6].

Comorbid substance use and psychiatric disorder has also commonly been associated with poor treatment outcomes for either or both conditions, including increase in the use or abuse of substances and increased psychosocial impairment, compared with outcomes of treatment when either substance use or psychiatric disorder occur individually [16] [5]. The diagnosis of psychiatric comorbidity in substance users, and of substance use disorders in psychiatric patients, is thus an important component in the development of strategies for treatment [17].

More information is available on comorbid psychiatric disorders and substance use in adults than in children, adolescents and young adults [6] [18]. In South Africa, the prevalence of substance use is a cause for concern, with an increase in the use of substances such as crystal methamphetamine (locally known as 'tik') and diacetyl morphine (heroin) [19], and evidence for increased use of substances in general, and cannabis in particular, in adolescents and young adults [20]. Globally, substance use and psychiatric disorders are managed largely independently. Reasons for this include treatment facilities being historically specialised as either substance use treatment centres, or centres for the treatment of psychiatric disorders, with limited numbers of suitably-trained professionals to treat comorbidity [21]. The trend is similar in South Africa. As a result, patients with comorbid psychopathology and problematic substance use usually attend either a psychiatric or a substance use treatment facility depending on the problem deemed by the patient or his/her family as the one most urgently in need of attention.

In many substance use treatment centres comorbid psychopathology might be suspected in patients, but it is often not assessed or addressed. The reasons for this are usually a lack of expertise, capacity, time or opportunity at the treatment centres [21]. Consequently, if the substance use treatment results in the patient behaving more socially-appropriately, concurrent psychopathology will receive little attention unless the patient's behaviour becomes disruptive or dysfunctional. Since these behavioural problems are often accompanied by substance use [22], the cycle can be repeated endlessly. Individuals with comorbid psychopathology and substance use can thus repeatedly enter and exit either psychopathology and/or substance use treatment depending on which problem is regarded as the "most problematic'' at any one time.

The examination of comorbid psychopathology and substance use in both clinical and community populations of substance users is important particularly because these groups may

differ with respect to the nature of the comorbidity [6]. For example, morbidity might be more severe, and comorbidity rates might be higher, in clinical samples compared with community samples. Patients might be more likely to seek treatment for certain disorders (for example, disruptive behaviour disorders) than for others (for example, depression), resulting in clinical samples having a predominance of disorders that are more likely to precipitate admission to treatment [6]. Results from clinical samples might thus not be generalisable to community samples and, conversely, the information obtained from community samples might not apply to clinical populations. Examination of both community and clinical samples is, therefore, needed to ascertain the prevalence of comorbidity in general, and to determine the likelihood of associations between comorbid conditions.

As previously mentioned, research evidence indicates increased substance use amongst young people in South Africa [20][23]. Information from the South African Stress and Health (SASH) study provides evidence for high prevalence rates of mental disorders in particularly the urban areas of South Africa [22]. However, there has been only limited investigation of the occurrence and nature of comorbid psychiatric diagnoses in substance users in South Africa, and the factors that impact on this comorbidity, for both community [20] and treatment samples [23] of substance users.

As part of a series of studies on comorbidity in young people, this study aimed to determine the frequency and nature of non-substance psychopathology in adolescent and young adult substance users who were receiving inpatient treatment for their substance use, and to examine the association between psychopathology and substance use in these patients, adjusting for social and demographic factors.

Methods

Sample: Ninety-five inpatient substance users were sampled from three privately-funded inpatient substance use treatment centres in Cape Town, South Africa. The treatment centres were selected from the list of Cape Town substance use inpatient treatment centres affiliated to the South African Community Epidemiology Network on Drug Use (SACENDU) [23] for the surveillance of substance use trends across South Africa. The inpatient treatment centres that had the largest number of admissions over the previous six months were shortlisted as possible study sites to ensure obtaining the selected sample size within the study period. Since the Cape Town area is geographically still largely divided in terms of racially classified social groups (RCSGs, as defined by the Population Registration Act of 1950, and consisting of the categories White, Coloured, Black and Indian/Asian) and economic class, three clinic study sites were selected (from the shortlist of treatment centres) from three different suburbs of Cape Town, in an attempt to gain information from as broad a racial and economic spectrum of inpatients within the research period. These were i) a predominantly White upmarket residential-cum-commercial area, and followed a medical model of treatment ii) a middle-class residential area of largely White, Coloured and Indian communities, and followed a treatment modality that included homeopathy, spirituality and Ayurvedic medicine, and iii) an area which included largely Coloured and Black communities, brick homes, informal dwellings, smallholdings and farmland, and provided custodial care, and encouraged spirituality, accompanied by administration of vitamins, massage, periods in a sauna, motivational talks and group therapy.

Sampling of patients was completed over the period December 2008 to December 2009. The estimated required sample size for a precision of 0.05 and an anticipated proportion of 98% (the approximate proportion of patients that were found to be positive for psychopathology while sampling), was 45 and thus very small. As such, it was decided to aim

for a sample of 100 patients, thus more than doubling the estimated required sample size. A minimum sample size of 46 would also be required for logistic regression analyses with 6 predictor variables (excluding the constant), a precision of 0.05, 80% power, and a large effect (f^2=0.35 or model r^2=0.26), while a minimal sample size of 97 would be required for a medium anticipated effect (f^2=0.15, or model r^2=0.13). We assumed the latter effect being most likely in this study, given previous findings in the literature. A total of 95 adolescents (n=1) and young adults (n=94), constituting all admissions aged 30 years and younger, and admitted for inpatient treatment of their problematic substance use, had been sampled by the end of the data collection period. Instruments: An Interview Schedule was designed for the study to elicit demographic, social, substance use history and recent substance use information. The demographic and social information elicited included age, gender, racially classified social group (RCSG), religious denomination, highest educational level, referral source, marital status, living arrangements and employment status. The substance use information elicited included age of onset, the first substance of use (other than tobacco), the most frequently used substance, the substance for which treatment was sought, the frequency and quantity of substance use, and previous treatment for substance use. The most frequently used substance was invariably the substance for which treatment was sought and will alternatively be referred to in this paper as the primary substance of use. The computer-assisted Diagnostic Interview Schedule (DIS) for Diagnostic and Statistical Manual (DSM) IV (C-DIS IV) [24] was administered to screen for any current (12-month) psychiatric disorders. The C-DIS is a computerised version of the paper-and-pencil DIS-IV. The instrument was designed to allow administration by non-clinically experienced examiners who are trained to use the instrument, and does not need corroborating details from alternative sources, such as hospital records, to make diagnoses. The responses from interviewees are directly coded and captured, reducing possible error, and providing study data immediately via the diagnostic report using the SAS

computer programme. The C-DIS is considered to be more accurate than the pencil-and-paper version because it automatically counts symptoms for diagnostic criteria, checks dates to ensure accuracy of onset and remission of symptoms. The questions are designed to be specific, thus the responses to questions can be reliably recorded by a variety of interviewers. The C-DIS can be used in both treatment and community settings, has the option of being used in either a limited screening version or full version, with the screen version providing information about the presence or absence of a disorder without details regarding the symptoms, course or severity of the disorder. The C-DIS can be self-administered with the proviso of training for the respondent. The instrument also allows the interviewer to skip certain diagnostic modules, thus tailoring the interview to the diagnoses of interest.

Instructions for use of the C-DIS [24] suggest that full versions of the instrument be used to assess disorders with early onset (such as attention deficit hyperactivity disorder, separation anxiety, oppositional disorder and conduct disorder) since these disorders might be risk factors for disorders of later onset. However, it is also recommended that full and screened versions for making diagnoses not be combined in interviews. Thus, to ensure parity in the mode of administration throughout the study, it was elected to use the screened version of the instrument for all interviews to minimize the duration of the interviews, and to include all the C-DIS modules in the interviews.

It was felt that the study would not be compromised with use of the screened version of the C-DIS with respect to early onset diagnoses because the study sample consisted largely of young adults. All the interviews were conducted by a trained DIS interviewer (primary author). Procedure: Admitted patients who were aged 30 years and under were considered for selection in the sample after completing the detoxification programme (a period ranging from one to two weeks, as determined by the treatment centre managers) offered at each clinic. This was done to ensure that patients selected for interviewing had largely overcome the

discomfort and agitation associated with withdrawal from substance use, and were more amenable to interviewing. This delay also allowed for the symptoms of substance-induced psychiatric symptoms to be minimized, where present. Each identified potential study subject was approached to obtain written informed consent for participating in the study. The one patient under the age of 18 completed assent forms, and written parental consent was obtained before interviewing this patient. All interviews were conducted by the primary author, at the clinics, and in private, with only the interviewer and patient present. Each interview was completed in one session, with the duration of each session approximating 90 to 120 minutes. The study was approved by the Research Ethics Committee of the University of Cape Town (REC REF: 340/2007).

Data analyses

The data were analysed using STATA Version 10 [25]. Percentages were estimated for demographic factors, substance use, and psychiatric diagnoses. The demographic factors selected for analyses in this study were: age, gender, racially classified social grouping (RCSG), religious denomination (none, Christian, Muslim, Jewish, other), highest educational level (none, primary, secondary, tertiary), marital status (never married or other), employment (employed, unemployed or student), and living arrangements (alone, with immediate family). Substance use data were recorded in terms of the first substance of use (other than tobacco), the age at which the first substance of use was initiated, and the most frequently used substance (which was always the substance for which treatment was sought, listed in the tables as primary substance of use).

Bivariate associations [to compare the distribution of patients across the clinics sociodemographically (Table 1), by substance use (Table 2), and by current psychopathology (Table 3)] were assessed using Fisher's Exact tests in those cases where the cell sizes were less than or equal to 5, and chi-squared tests where the cell sizes were greater than 5. The

percentage of psychopathology and first and primary substances of use (Table 4), and the percentage of first and primary substance use with respect to the most commonly-occurring forms of psychopathology (Table 5) were calculated. Bivariate associations between psychopathology and substance use were calculated using Fisher's Exact and chi-squared analyses (Tables 6 and 7). Multiple logistic regression analyses (Table 8) were conducted to determine associations between type of psychiatric disorder (selected from the most commonly-occurring psychiatric diagnoses) and a) the first substances of use, and b) the most frequently used (primary) substances. First substance of use was coded as either cannabis, crystal methamphetamine, or other, based on the most common substances first used; most common primary substance of use was coded as crystal methamphetamine , heroin or other, based on the most common substances for which patients were admitted for treatment. For these, odds ratios and 95% confidence intervals were calculated, unadjusted and adjusted for the treatment centres, and sociodemographic factors including age, gender, religious denomination, racially classified social group and treatment centre. In all the relevant analyses, substance use (in the form of first and primary substances of use) was the dependent variable, and the sociodemographic characteristics and psychopathology diagnoses were the independent variables. Forced statistical modelling was used for the logistic regression. The independent variables were not formally tested for multicollinearity and singularity since the statistical programme (STATA 10)[25] used for the analyses automatically tests for tolerance, and excludes variables which have insufficient tolerance. Statistical significance was indicated by $p<0.05$ while p-values between 0.05 and 0.10 were regarded as reflecting marginal effects.

Results

Table 1 shows the demographic characteristics of the sample at the three treatment centres(clinics). The total sample consisted of 95 inpatients [ages 17-30 years, with a mean

age of 23 years (SD = 2.9)]. The sample consisted predominantly of males (89.5%), individuals of Coloured origin (88.4%), and Muslim religious denomination (68.4%). Eighty-six percent of the patients had some secondary school education, 77.9% had never been married, 91.6% lived with immediate family, and 61.1% had entered treatment on their own volition. More than half the sample (54.7%) was unemployed, while nearly a third had fulltime employment, at the time of entering treatment. The proportions of patients at the three clinics differed with respect to two demographic variables - religious denomination ($p < 0.001$), with Clinics 2 and 3 having 90% and 75% Muslim patients respectively, while Clinic 1 had 88.2% Christian patients, and RCSG ($p=0.066$), with Clinics 2 and 3 having more than 90% Coloured patients while 17.7% of the patients at Clinic 1 were White.

A total of 51.6% of the sample had commenced substance use between the ages of 10 and 14 years (Table 2) while 85.3% (n=81) had started using substances by age 17 years, with a mean age of substance use onset of 14.7 years (SD=2.4). The most common first substances of use were cannabis (51.6%) and crystal methamphetamine (tik) (17.9%). The most common substances for which treatment was sought (i.e. primary substances of use) were heroin (53.7%) and crystal methamphetamine (33.7%). The large majority of patients used substances every day (90.5%), and used as much as they could obtain (58.9%) or afford to buy (38.9%). All except two of the patients smoked cigarettes every day, did not count how many cigarettes they smoked, and did not regard their cigarette smoking as a problem (not listed in Table 2). There was a statistically significant difference in the proportion of patients at the three clinics with respect to the primary substance of use. Heroin was the primary substance of use in more than 60% of the patients at Clinics 2 and 3, compared with 11.8% at Clinic 1. At Clinic 1, more than 40% of the patients had crystal methamphetamine as their primary substance of use compared with 26.7% and 35.4% at Clinics 2 and 3 respectively. Forty-four percent of the patients were in substance use

treatment for the first time at the time of the study. Of those who had had previous treatment for their substance use (n=53), 68% (n=36) had been between the ages of 15 and 20 years when they had their first treatment. However, the proportion of patients at each clinic was marginally different with respect to their previous history of substance use treatment (p=0.081), with the majority of patients at Clinic 1 (64.7%) being in substance use treatment for the first time.

Table 3 lists the proportions of patients at each of the clinics with respect to their diagnosis of current psychopathology. In the study all the C-DIS IV modules were administered, but only the most common psychiatric diagnoses are listed in Table 3. In total, 95.8% of patients had some form of psychopathology; only three patients had no non-substance use psychiatric diagnosis. Some patients had more than one current psychiatric disorder. Sixty patients (63.2%) had at least two non-substance use psychopathology diagnoses, and 27 patients (28.4%) had at least three non-substance use psychopathology diagnoses. Of the 92 patients with psychopathology, only four patients had previously been diagnosed with a non-substance use psychiatric disorder (Table 3). There was no statistically significant difference in the proportions of patients at each clinic who had never previously been diagnosed with a psychiatric disorder. The most common current psychiatric diagnoses were substance dependence (91.6%), anti-social personality disorder (ASPD) (87.4%), conduct disorder (CD) (67.4%), oppositional defiant disorder (33.7%) and major depression (25.3%). The proportion of patients differed significantly at the three clinics with respect to mania (p=0.007), with one patient at Clinic 2 having had a manic episode in the last 12 months compared with six and five patients at Clinics 1 and 3 respectively. The numbers of patients diagnosed with substance dependence differed significantly across the treatment centres (p=0.007), with Clinics 2 and 3 having more than 95% of patients dependent on substances compared with 70.6% of patients with substance dependence at Clinic 1. The

Clinics also differed marginally with respect to generalised anxiety disorder (p=0.059) and post-traumatic stress disorder (PTSD) (p=0.065) although the numbers of patients with these diagnoses were generally relatively small.

Table 4 presents the frequency of psychopathology by first substance of use and primary substance of use. There was no statistically significant difference in the proportions of any psychopathology by either first substance of use or by primary substance of use.

Table 5 presents the percentage of patients with the most common first and primary substances of use in terms of the most commonly-occurring non-substance use psychopathology. These results indicate that a statistically significant proportion of those who were positive for conduct disorder had started out using cannabis (p=0.048) compared with those who were not positive for conduct disorder. The proportion of patients who had anti-social personality disorder and had used cannabis as their first substance was marginally higher than the proportion of patients who were positive for the other commonly-occurring disorders and used cannabis as their first substance of use. The difference in the proportions of the other psychopathologies by substance use were not statistically significant.

Tables 6 and 7 list the percentage of the most common first and primary substances of use by the most common psychopathology, and the percentage of the most common psychopathology by the most common first and primary substances of use respectively. These tables thus essentially list the same frequency of occurrences in terms of row and column totals. Significantly more patients (p=0.049) who were found to be positive for conduct disorder, compared with those who were not diagnosed with conduct disorder, had used cannabis as their first substance. Marginally more patients (p=0.0654) who were found to be positive for antisocial personality disorder, compared with those who were not positive for antisocial personality disorder, had their substance use debut with cannabis.

Table 8 documents the results of the regression analyses which were conducted to determine associations between different forms of non-substance use psychopathology and different forms of first substance used and primary substance use, listing odds ratios, 95% confidence intervals and p-values for these associations. Odds ratios are presented both unadjusted and adjusted for age, gender, religion, racially classified social group, and treatment centre (clinic).

The marginal unadjusted association (p=0.061) found between anti-social personality disorder and cannabis as the first substance of use on bivariate comparisons (Table 8) was lost on adjustment for age, gender, religion, treatment centre and racially classified social group (p=0.117).

Similarly, the apparent association between conduct disorder and cannabis as the first substance of use which was statistically significant (p=0.031) before adjustment for age, gender, education, treatment centre and RCSG, became statistically not significant after adjustment (p=0.103).

The unadjusted odds ratio for the association between specific phobia and cannabis as the first substance of use was not statistically significant before adjustment (p=0.479) but approached statistical significance on adjustment (OR=4.74; 95% CI 0.99-22.66, p=0.051).

The unadjusted odds ratio for the association between oppositional defiant disorder and crystal methamphetamine as the primary substance of use was marginally significant (p=0.087) but became not statistically significant on adjustment for age, gender, treatment centre and racially classified social group.

Discussion

This study aimed to determine the frequency and nature of non-substance use psychopathology in young adult substance users in inpatient treatment for their substance use, and to identify demographic, social and substance use factors that influenced the association between psychopathology and substance use.

The results obtained indicate a large proportion of inpatient substance users who had not previously been diagnosed with a psychiatric disorder (95.8%) (Table 3). A large number of patients was diagnosed with a current (12-month) non-substance psychiatric disorder in this study (n=92; 96.8%), demonstrating a high percentage of comorbid psychopathology in these inpatients in Cape Town, with a percentage that exceeds the prevalence of these psychiatric diagnoses reported for the general adult community but using a different instrument, namely the Composite International Diagnostic Interview (CIDI) which also provides DSM IV diagnoses [22].

The high percentage of previously-undiagnosed psychopathology in these inpatient substance users, despite many of the patients having been in treatment for their problematic substance use previously, suggests a need for substance users to be assessed for co-occurring psychopathology as part of the rehabilitation from either the substance use or psychopathology. It might also be necessary to recognize the demographic and social heterogeneity of these patients, and to tailor their treatment according to their individual needs.

It is, however, likely that the study sample was vulnerable to Berkson's Bias [26] in that there would be an increased likelihood of patients seeking treatment for their substance use problems because they experienced a co-existing non-substance use psychiatric disorder. The presence of disruptive behavior disorders (noted by the high prevalence of diagnoses

such as anti-social personality disorder, conduct disorder and oppositional defiant disorder) could also have played a role in treatment-seeking by causing social conflict in the lives of the substance users [7], precipitating admission for substance use treatment. It is also possible that the percentage of psychopathology in this substance use treatment group differed from that in community substance users because of differences in the severity of the extant conditions in the two groups [6]. In other words, substance users in the community might experience symptoms related to the same psychiatric diagnoses as those of patients in this study, but these psychiatric symptoms might be less severe and not yet meet the criteria for diagnoses and hence might not yet play a role in treatment-seeking behavior.

While there is debate on whether substance use (in the form of problematic substance use, or abuse or dependence) may be regarded as a dysfunctional or antisocial behaviour, constituting part of a psychiatric disorder, or a psychiatric disorder itself [8], there is little doubt about the predominance of disruptive behavior disorders in clinical samples of substance users compared with the prevalence of other non-substance use psychopathology [7] (as was found in this study), and the role that disruptive behaviour disorders might play in treatment-seeking.

The presence of a comorbid disruptive behavior disorder might also be more likely to precipitate treatment- seeking for substance use problems than would a co-occurring anxiety disorder [6], possibly accounting for the low proportions, or absence, in the present study, of those comorbid psychiatric diagnoses (for example, depression [8] anxiety [7] and posttraumatic stress disorder [6]) that have commonly been associated with substance use, abuse or dependence in the community [7; 8] and in patients who receive treatment for their substance use [5].

The proportions of patients with the most common psychiatric diagnoses did not show statistically significant differences by either the first or primary substances of use (Table 4). However, a significantly greater proportion of patients who were diagnosed with conduct disorder had also initiated their substance use with cannabis (59.4%) (Table 6) compared with the proportion of patients in whom conduct disorder was absent (p=0.049). Similarly, a marginally larger proportion of patients with antisocial personality disorder had cannabis as their first substance of use (55.4%) (Table 6), compared with those patients in whom antisocial personality disorder was absent (p=0.065). It is thus possible that cannabis was indeed a notable first substance of use in those who were diagnosed with conduct disorder or antisocial personality disorder. Further multivariate investigation of the association between psychopathology and substance use (Table 8) indicated a (marginally) statistically significant association only between specific phobia and cannabis as the first substance of use (OR=4,74 95%CI 0.99-22.68; p=0.051). It is, however, important that the marginal results obtained in this study be interpreted with caution.

There might be other factors that also play a role in the nature, prevalence and associated substance use of psychopathology amongst inpatient substance users. For example, when examining the psychiatric symptoms of patients in the National Treatment Outcome Research Study, Marsden et al. [7], found that the relationship between psychiatric symptoms and substance use was not a direct relationship but rather a relationship that was conditional on the types of substance use. For example, these authors reported that depressive symptoms were less likely or less severe in opiate users in treatment, than in users of stimulants who were in treatment. They also found that, in substance users who receive treatment, the frequency and severity of psychiatric symptoms were predicted by poor physical health, previous psychiatric treatment, gender, and personal relationships characterized by high levels of conflict. It is thus possible that factors such as these, of which physical health,

previous psychiatric treatment and personal relationships were not assessed in relation to comorbidity in the present study, contributed to the findings of the present study by influencing psychiatric symptoms and disorders, and, indirectly, the association between psychopathology and substance use.

The distribution of the Western Cape province (of which Cape Town is the capital city) treatment population during the study period, in terms of racially classified social grouping, indicates that Coloured patients who presented for substance use treatment constituted 54% of the treatment population, with Whites, Blacks and Indians consisting of 18%, 27% and 1% respectively [27]. The study sample, with comparative RCSG figures of 88.4% Coloured, 4.2% White, and 7.4% Indian, thus reflects the population preponderance of Coloured substance use patients relative to White and Indian patients. The complete absence of Black patients from this sample is, however, surprising, particularly considering the close proximity to Clinic 3 of a largely Black informal settlement. This finding could possibly be a result of a combination of factors that involved financial constraints and/or the nature of the treatment offered at the treatment centres selected for sampling.

The sample contained few females. However, the proportion of males (90%) to females in the sample, appears to be consistent with the gender distribution of the substance using population that sought treatment, from which the sample was drawn [27], and with samples of similar studies [28, 29]. On examining possible reasons for the uneven gender distribution of substance use inpatients, Green et al. [30] found that in females, a comorbid psychiatric diagnosis predicted a failure of treatment initiation, while in males a low educational level predicted a failure of treatment initiation. It is possible that comorbid psychopathology might have played a role in the treatment initiation of some females, but this association was beyond the design of the present study, as was the role of low educational level in potential male substance use inpatients in treatment initiation.

However, the paucity of females in this study sample could also be indicative of females possibly facing more obstacles to entering inpatient treatment [for example, social stigma and treatment beliefs [30], or financial constraints [31] compared with males.

Further investigations could be geared at identifying and minimising the obstacles that females face with regards to attending inpatient treatment facilities. Based on the findings of Green et al. [32], it might thus be useful to emphasise assessment of females for psychiatric disorder prior to suggesting inpatient admission. Such assessment, coupled with treatment for psychiatric disorder and counselling, might aid admission of females where this is deemed appropriate and potentially beneficial. Similar support for males with low educational levels might also prove helpful in aiding initiation of treatment for substance use.

The high percentage of cigarette smoking amongst this group of substance users in treatment might be cause for concern. Only two patients in the sample did not smoke cigarettes. The other patients smoked cigarettes every day, did not count the number of cigarettes they smoked, did not regard cigarettes as another substance of use, and viewed their cigarette smoking as more socially acceptable and with a smaller impact on their lives than their use of other substances. There is thus the possibility that cigarette smokers who receive treatment for use of other substances could potentially face a future of compromised health as a result of their cigarette smoking, irrespective of whether or not they attain abstinence from their other substance use.

It is notable that few of the patients were in treatment for problem-drinking of alcohol when alcohol is still the most common substance of abuse for which treatment is sought in the area [27]. The preponderance of Muslim patients in this sample could have accounted for this result since alcohol consumption is forbidden in Islam and is considered a social taboo in Muslim communities, even among users of other substances. However, alcohol generally

appears to be an unlikely substance of use for which treatment is sought in young people, particularly when there are other (usually illicit) substances of use available [33]. The most likely reason for the small number of patients in treatment for alcohol use in this sample might thus be that patients in treatment for alcohol use were usually older [27] and thus not eligible for selection in the study.

The present study did not elicit information regarding the mode of substance use. Hence information on intravenous versus other drug administration is absent. Injecting substances like heroin is known to be associated with increased Severity of Dependence scores compared with smoking heroin [34], while increased severity of dependence on substances has been associated with increased risk of psychopathology [13]. Thus, in the absence of information regarding mode of drug administration, its relevance for associations between substance use, substance use severity and psychopathology cannot be commented on. However, smoking appears to be the most common means of non-alcohol substance administration in this community [27] so it would be appropriate to assume that, where relevant, substances in this sample were smoked rather than injected.

It is important that the implications of these study findings also be considered in light of the small sample size and its role in limiting the study power. There is the possibility that the multiple comparisons could have produced differences between groups that might be chance findings, while, with the relatively small sample size, real differences between groups might have been missed.

In addition, the lack of a representative sample precludes generalisability of the results beyond the study sample, while the cross-sectional design of the study limits inferences regarding temporality, causality, and gateway pathways to comorbid substance use and psychopathology, even in those cases where statistically significant associations

emerged. Further investigations in the form of longitudinal studies that i) examine the risk for substance use in individuals diagnosed with psychiatric disorder, and ii) examine the risk for psychiatric disorder in substance users, are needed to provide information regarding temporal associations between the psychopathology and substance use. In addition, further investigations of both treatment and community samples might provide additional insights, particularly as regards differences in comorbid non-substance use psychopathology.

The use of the C-DIS to diagnose psychiatric and substance use disorders in this population could have placed limitations on this study. Testing the validity of the DIS has been a complicated and difficult task because of the absence of suitable benchmarks against which to measure the instrument [24]. The reliability of the computer-assisted version of the DIS compared with the pencil-and-paper version of the instrument has also not been tested, although the DIS reflects 79%-96% agreement with diagnoses assisted by clinical judgement [35]. In addition, the instrument has not been standardized for use with the South African population.

The screening version of the C-DIS [24] might also have influenced the results by limiting information about the duration and impairment of psychiatric disorders, and about the sequence or temporality of non-substance use and substance use disorders. Furthermore, use of the screen version for disorders with early onset (such as attention deficit disorder, separation anxiety, oppositional defiant disorder and conduct disorder) might have compromised the percentage of these disorders that could be identified, as well as the percentage of the disorders they preempt [such as antisocial personality disorder being regarded as the adult version ($\geq$ 18 years) of conduct disorder (< 18 years)]. Lastly, errors with respect to the diagnoses of the earlier and later disorders could have occurred because of the manner in which the C-DIS codes assessment of the diagnostic criteria for these disorders [24]. However, the DIS is one of few available recognized diagnostic instruments that are

regarded as sufficiently reliable for use by lay interviewers [35], that shows high concordance with clinically-derived diagnoses [35], and provides the opportunity to screen for current diagnoses when the interviewing time is limited [24].

This study has highlighted that psychopathology is common in substance using young people who received inpatient treatment for their substance use. The study has illustrated the need for psychiatric assessment of comorbid psychopathology in substance users who receive treatment for their substance use in Cape Town, South Africa, with the suggestion that integrated service models be developed for the treatment of mental illness and substance use.

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Table 1. *Demographic characteristics of the sample in the three treatment centres (n; %)*

Demographic variable	Clinics				
	Clinic 1	Clinic 2	Clinic 3	Total	p-value
	n =17	n = 30	n = 48	n = 95	
Mean Age	21.7	23.2	23.4	23.0	
SD	3.5	3.0	2.6	2.9	0.111†
Gender Male	16 (94.1)	24 (80.0)	45 (93.8)	85 (89.5)	0.151††
Racially Classified Social Group					
White	3 (17.7)	1 (3.3)	0	4 (4.2)	
Coloured	13 (76.5)	27 (90.0)	44 (91.7)	84 (88.4)	
Indian	1 (5.9)	2 (6.7)	4 (8.3)	7 (7.4)	0.066††
Religion					

Muslim	2 (11.8)	27 (90.0)	36 (75.0)	65 (68.4)	
Christian	15 (88.2)	3 (10.0)	11 (22.9)	29 (30.5)	
None	0	0	1 (1.1)		<0.001††
Highest educational level					
Primary school	1 (5.9)	0	2 (4.2)	3 (3.2)	
Secondary school	16 (94.1)	24 (80.0)	42 (87.5)	82 (86.3)	
Tertiary	0	6 (20.0)	4 (8.3)	10 (10.5)	0.176††
Referral source					
Self	10 (58.8)	18 (60.0)	30 (62.5)	58 (61.1)	
Family	3 (17.6)	11 (36.7)	13 (27.1)	27 (28.4)	
Other	4 (23.5)	1 (3.3)	5 (10.4)	10 (10.5)	0.250††
Marital status					
Never married	15 (88.2)	22 (73.3)	37 (77.1)	74 (77.9)	
Other	2 (11.8)	8 (25.7)	11 (22.9)	21 (22.1)	0.488††
Living arrangements					

Live alone	0	0	2 (4.2)	2 (2.1)	
Live with immediate family	16 (94.1)	29 (96.7)	42 (87.5)	87 (91.6)	
Other	1 (5.9)	1 (3.3)	4 (8.3)	6 (6.3)	0.819[††]
Employment status					
Unemployed	7 (41.2)	18 (60.0)	27 (56.3)	52 (54.7)	
Casually employed	1 (5.9)	2 (6.7)	4 (8.3)	7 (7.4)	
Permanently employed	7 (41.2)	7 (23.3)	17 (35.4)	31 (32.6)	
Other	2 (11.8)	3 (10.0)	0	5 (5.3)	0.186[††]
Usual employment					
Professional	0	0	1 (2.1)	1 (1.1)	
Skilled	6 (35.3)	10 (33.3)	18 (37.5)	34 (35.8)	
Unskilled	4 (23.5)	10 (33.3)	16 (33.3)	30 (31.6)	
None/student/scholar	7 (41.2)	8 (26.7)	8 (16.7)	23 (24.2)	
Other	0	2 (6.7)	5 (10.4)	7 (7.4)	0.635[††]

[†]Comparisons between clinics based on Kruskal-Wallis testing for age, and on chi-squared tesing for other sociodemographic variables

[††] Fisher's Exact testing for expected frequencies <5

Table 2. *Distribution of substance use and related variables at the three treatment centres (n; %)*

Substance use variable	Clinics				
	Clinic 1	Clinic 2	Clinic 3	Total	p-value
	n = 17	n = 30	n = 48	n = 95	
Age of first substance use (years)					
10 – 14	13 (76.5)	13 (43.3)	23 (47.9)	49 (51.6)	
15 – 17	3 (17.6)	11 (36.7)	18 (37.5)	32 (33.7)	
18 – 20	0	5 (16.7)	7 (14.6)	12 (12.6)	
21 – 24	1 (5.9)	1 (3.3)	0	2 (2.1)	

Mean (SD)	13.6 (2.4)	15.1 (2.6)	14.8 (2.3)	14.7 (2.4)	0.127†
First substance of use					
Alcohol	4 (23.5)	0	3 (6.3)	7 (7.4)	
Cannabis	8 (47.1)	16 (53.3)	25 (52.1)	49 (51.6)	
Ecstasy	0	5 (16.7)	4 (8.3)	9 (9.5)	
Heroin	1 (5.9)	2 (6.7)	3 (6.3)	6 (6.3)	
Methaqualone (mandrax)	0	2 (6.7)	0	2 (2.1)	
Crystal methamphetamine (tik)	4 (23.5)	3 (10.0)	10 (20.8)	17 (17.9)	
Multiple	0	2 (6.7)	3 (6.3)	5 (5.3)	0.163††
Primary substance of use					
Alcohol	3 (17.6)	0	0	3 (3.2)	
Cannabis	4 (23.5)	0	1 (2.1)	5 (5.3)	
Heroin	2 (11.8)	20 (66.7)	29 (60.4)	51 (53.7)	
Crystal methamphetamine (tik)	7 (41.2)	8 (26.7)	17 (35.4)	32 (33.7)	
Methaqualone (mandrax)	0	1 (3.3)	0	1 (1.1)	
Multiple	1 (5.9)	0	1 (2.1)	2 (2.1)	<0.001††
Frequency of use of primary substance					

Daily	15 (88.2)	28 (93.3)	43 (89.6)	86 (90.5)	
Few times a week	1 (5.9)	2 (6.7)	3 (6.3)	6 (6.3)	
Sometimes	1 (5.9)	0	2 (4.2)	3 (3.2)	0.844††
Intensity/Volume of primary substance use					
As much as I can obtain	11 (64.7)	14 (46.7)	31 (64.6)	56 (58.9)	
As much as I can afford to buy	6 (35.3)	15 (50.0)	16 (33.3)	37 (38.9)	
Other	0	1 (3.3)	1 (2.1)	2 (2.1)	0.509††
Previous treatment for substance use					
None	11 (64.7)	12 (40.0)	19 (39.6)	42 (44.2)	
Once in past year	3 (17.6)	2 (6.7)	8 (16.7)	13 (13.7)	
More than once in past year	0	5 (16.7)	12 (25.0)	17 (17.9)	
More than a year ago	3 (17.6)	11 (36.7)	9 (18.8)	23 (24.2)	0.081††
Age of first treatment for substance use (yrs)	n=6	n=18	n=29	n=53	
10 – 14	1 (16.7)	2 (11.1)	0	3 (5.7)	
15 – 17	0	4 (22.2)	7 (24.1)	11 (20.8)	
18 – 20	5 (83.3)	7 (38.9)	13 (44.8)	25 (47.2)	
	0	3 (16.7)	9 (31.0)	12 (22.6)	

21 – 24	0	2 (11.1)	0	2 (3.8)	0.139††
>24	17.5 (3.3)	18.9 (3.9)	19.3 (2.6)	19 (3.1)	0.454†
Mean (SD)					

†Comparisons between clinics based on Kruskal-Wallis testing for age, and on chi-squared testing for other sociodemographic variables

†† Fisher's Exact testing for expected frequencies <5

Table 3. *Distribution of psychopathology at the three treatment centres (n; %)*

	Clinics				
	Clinic 1	Clinic 2	Clinic 3	Total	p-value[††]
Psychopathology	n = 17	n = 30	n = 48	n = 95	
No previous diagnosis of psychopathology	15 (88.2)	29 (96.7)	47 (97.9)	91 (95.8)	0.298
Generalised anxiety disorder	3 (17.6)	1 (3.3)	1 (2.1)	5 (5.3)	0.059
Post-traumatic stress disorder (PTSD)	3 (17.6)	5 (16.7)	6 (12.5)	14 (14.7)	0.065
Depression	6 (35.3)	9 (30.0)	9 (18.8)	24 (25.3)	0.291
Mania	6 (35.3)	1 (3.3)	5 (10.4)	12 (12.6)	0.007
Schizophrenia	0	2 (6.7)	0	2 (2.1)	0.128
Obsessive Compulsive Disorder (OCD)	2 (11.8)	1 (3.3)	1 (2.1)	4 (4.2)	0.298
Eating disorder	0	2 (6.7)	2 (4.2)	4 (4.2)	0.656
Separation anxiety	1 (5.9)	2 (6.7)	2 (4.2)	5 (5.3)	0.848
Oppositional defiant disorder	7 (41.2)	10 (33.3)	15 (31.1)	32 (33.7)	0.771
Conduct disorder	10 (58.8)	18 (60.0)	36 (75.0)	64 (67.4)	0.263

Antisocial personality disorder	14 (82.4)	26 (86.7)	43 (89.6)	83 (87.4)	0.657
Pain disorder	3 (17.7)	4 (13.3)	3 (6.3)	10 (10.5)	0.330
Specific phobia	4 (23.5)	5 (16.7)	6 (12.5)	15 (15.8)	0.565
Substance dependence	12 (70.6)	29 (96.7)	46 (95.8)	87 (91.6)	0.007
Substance abuse	4 (23.5)	5 (16.7)	6 (12.5)	15 (15.8)	0.606

[††] Fisher's Exact testing for expected frequencies <5

Table 4. *Frequency of psychopathology by substance use*

	Psychopathology (n; row%)				
Substances of use	Conduct Disorder	Oppositional Defiant Disorder	Major Depression	Anti-Social Personality Disorder	Total n=95 (column%)
First substance of use					
Alcohol	4 (57.1)	2 (28.6)	4 (57.1)	6 (85.7)	7 (7.4)
Cannabis	38 (77.6)	20 (40.8)	14 (28.6)	46 (93.9)	49 (51.6)
Ecstasy	3 (33.3)	0	1 (11.1)	7 (77.8)	9 (9.5)
Heroin	3 (50.0)	2 (33.3)	2 (33.3)	4 (66.7)	6 (6.3)
Methaqualone (mandrax)	2 (100.0)	1 (50.0)	0	2 (100.0)	2 (2.1)
Crystal methamphetamine (tik)	11 (64.7)	4 (23.5)	2 (11.8)	14 (82.4)	17 (17.9)
p-value[†]	0.130	0.136	0.297	0.194	
Most common primary substance of use					
Heroin	19 (37.2)	9 (17.6)	8 (15.7)	29 (56.9)	51 (53.7)

Crystal methamphetamine	15 (46.9)	10 (31.3)	3 (9.4)	16 (50.0)	32 (33.7)
p-value[†]	0.352	0.199	0.117	0.366	

[†] Fisher's Exact testing for expected frequencies <5

Table 5. *Frequency of most common first and primary substances of use by most common psychopathology diagnoses*

	First substance of use				Most common primary substance of use			
Psychopathology	Cannabis	p-value†	Crystal Methamphetamine	p-value†	Heroin	p-value†	Crystal Methamphetamine	p-value†
Conduct disorder	38 (59.3)	0.048	11 (17.2)	0.782	19 (29.7)	0.170	15 (23.4)	0.592
Anti-social personality disorder	46 (55.4)	0.065	14 (16.9)	0.445	29 (34.9)	1.000	16 (19.3)	0.271
Major depression	14 (58.3)	0.486	2 (8.3)	0.223	8 (33.3)	1.000	3 (12.5)	0.385
Oppositional defiant disorder	20 (62.5)	0.192	4 (12.5)	0.405	9 (28.1)	0.371	10 (31.1)	0.111

†Chi-squared testing when expected frequencies ≥5 and Fisher's Exact testing when expected frequencies <5

Table 6. *Prevalence of most common substance use by most common psychopathology**

	First substance of use n (%)				Primary substance of use n (%)			
Most common psychopathology (n)	Cannabis (Total = 49)	p	Crystal Methamphetamine (Total = 17)	p	Heroin (Total = 33)	p	Crystal Methamphetamine (Total = 20)	p
Conduct disorder								
Present: 64	38 (59.4)	0.049	11 (17.2)	0.796	19 (29.7)	0.209	15 (23.4)	0.587
Absent: 31	11 (35.5)		6 (19.4)		14 (45.2)		5 (16.1)	
Oppositional defiant disorder								
Present: 32	20 (62.5)	0.193	4 (12.5)	0.405	9 (28.1)	0.461	10 (50.0)	0.141
Absent: 63	29 (46.0)		13 (20.6)		24 (38.1)		10 (15.9)	
Major depression								
Present: 24	14 (58.3)	0,596	2 (8.3)	0.223	8 (57.1)	0.867	3 (21.4)	0.385
Absent: 71	35 (49.3)		15 (21.1)		25 (35.2)		17 (23.9)	
Anti-social personality disorder								

Present: 83	46 (55.4)	0.064	14 (16.9)	0.445	29 (34.9)	1.000	16 (34.8)	0.271
Absent: 12	3 (25.0)		3 (25.0)		4 (33.3)		4 (33.3)	

*Chi squared tests were used to calculate p-values when cell sizes were >5 and Fisher's Exact was used when cell sizes were <5

Table 7. *Prevalence of psychopathology by most common substances of use**

Substance use	Psychopathology n (%)							
Most common first substance of use	Conduct disorder Total=64	p	Oppositional defiant disorder Total=32	p	Major depression Total=24	p	Anti-social personality disorder Total=83	p
Cannabis								
Present: 49	38 (77.6)	0.049	20 (40.8)	0.193	14 (28.6)	0.596	46 (93.9)	0.065
Absent: 46	26 (56.5)		12 (26.1)		10 (21.7)		37 (80.4)	
Crystal methamphetamine								
Present: 17	11 (64.7)	0.796	4 (23.5)	0.405	2 (11.8)	0.223	14 (82.4)	0.445
Absent: 78	53 (67.9)		28 (35.9)		22 (28.2)		69 (88.5)	
Most common primary substance of use								
Heroin								
Present: 33	19 (57.6)	0.209	9 (27.3)	0.461	8 (24.2)	0.867	29 (87.9)	1.000
Absent: 62	45 (72.6)		23 (37.1)		16 (25.8)		54 (87.1)	

Crystal methamphetamine								
Present: 20	15 (75.0)	0.581	10 (50.0)	0.141	3 (15.0)	0.385	16 (80.0)	0.271
Absent: 75	49 (65.3)		22 (29.3)		21 (28.0)		67 (89.3)	

*Chi-squared tests were used to calculate p-values for cell sizes >5 and Fisher's Exact was used for cell sizes < 5

Table 8. *Association between psychopathology and substance use (OR, 95% CI and p-value)*[†]

		First substance of use				Most common primary substance of use			
		Cannabis		Crystal methamphetamine		Heroin		Crystal methamphetamine	
Psychopathology		Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Anti-social personality	OR	3.730	3.228	0.609	0.644	1.074	1.496	0.478	0.424
	95%CI	0.942-14.773	0.745-13.975	0.146-2.537	0.136-3.047	0.298-3.872	0.326-6.857	0.128-1.785	0.100-1.800
	p-value	0.061	0.117	0.495	0.579	0.913	0.604	0.272	0.245
Conduct disorder		2.657	2.256	0.865	0.722	0.513	0.413	1.592	1.895
		1.092-6.464	0.847-6.006	0.287-2.605	0.213-2.443	0.211-1.246	0.139-1.229	0.520-4.870	0.553-6.493
		0.031	0.103	0.796	0.600	0.140	0.112	0.415	0.309
Oppositional defiant		1.954	1.920	0.549	0.503	0.636	0.670	2.409	2.192
		0.818-4.666	0.749-4.917	0.163-1.847	0.139-1.824	0.253-1.601	0.232-1.939	0.879-6.599	0.752-6.385
		0.131	0.174	0.333	0.296	0.336	0.460	0.087	0.150

PTSD	0.929	1.571	0.313	0.334	2.115	2.207	0.251	0.245
	0.299-2.888	0.388-6.363	0.038-2.568	0.030-3.753	0.672-6.659	0.482-10.116	0.031-2.045	0.025-2.385
	0.898	0.527	0.279	0.375	0.200	0.308	0.197	0.226
Major depression	1.440	1.669	0.339	0.586	0.920	1.014	0.454	0.569
	0.565-3.670	0.537-5.183	0.072-1.608	0.111-3.083	0.346-2.448	0.296-3.467	0.120-1.710	0.131-2.479
	0.445	0.376	0.173	0.528	0.867	0.983	0.243	0.453
Specific phobia	1.500	4.739	0.286	0.417	1.309	1.665	0.926	1.098
	0.488-4.607	0.990-22.677	0.035-2.337	0.045-3.857	0.422-4.060	0.382-7.249	0.235-3.660	0.230-5.237
	0.479	0.051	0.243	0.441	0.641	0.497	0.913	0.906
Pain disorder	1.144	1.077	1.022	1.609	0.675	0.677	1.478	1.812
	0.324-4.040	0.276-4.199	0.200-5.221	0.269-9.634	0.166-2.737	0.124-3.699	0.354-6.174	0.354-9.263
	0.834	0.915	0.979	0.602	0.582	0.652	0.592	0.475

[†]Adjusted for age, gender, racially classified social group, religion and treatment centre

INTERVIEW SCHEDULE FOR TREATMENT CENTRE STUDY

Treatment Centre……. | | | |

Patient/Subject number……... | | | |

Folder/File number…….. **DATE……**

Patient/Subject name……...
Address……
Telephone numbers i)…… ii)…… iii)……

I would like to start by asking you a few questions about yourself, your home-life, and your past. I would like you to answer each question as honestly and openly as you can. If any question makes you feel uncomfortable, please feel free to tell me. No-one, other than I will know that the information you give me has come from you. I will, however, need to inform the treatment centre staff of things that might be harmful to yourself or someone else.

A. DEMOGRAPHIC FACTORS

AI. Kind of patient

1. Inpatient
2. Outpatient
3. Daypatient
4. Other Specify…….

A2. Home language

1. English
2. Afrikaans
3. Xhosa
4. Other Specify……...

A3. Age

Date of birth**…….**
Actual age……years

1. 14-16 years
2. 17-19 years
3. 20-24 years
4. 25-29 years

A4. Gender

1. Male
2. Female

A5. Racial classification

1. Black
2. Coloured
3. Indian
4. White
5. Other Specify……...

A6: Religious denomination

1. None
2. Christian
3. Muslim
4. Jewish
5. Other Specify……

A7. Highest educational level

Highest standard passed/diploma/degree……

1. None
2. Primary school
3. High school
4. Tertiary Specify……

A8. Referral source

1. Self
2. Family
3. Friend
4. Doctor/other professional
5. Employer
6. Correctional services
7. Other Specify…….

Now I want to ask you a few questions about your home-life and work situation.

B. SOCIAL FACTORS

B1. Current marital status

1. Never married
2. Married with children
3. Married, no children
4. Divorced
5. Separated
6. Widowed Comments……..

B2. Living arrangements

1. Live alone
2. Live with immediate family
3. Live with extended family

4. Live with non-relatives
5. Other Specify……..

B3. Employment status

1. Employed (permanent)
2. Casual
3. Unemployed
4. Part-time/Student/Scholar
5. On leave of absence
6. Other Specify/Comments…….

B4. Nature of usual employment

1. None/Student/Scholar
2. Unskilled
3. Skilled
4. Managerial
5. Professional Specify……...

I would now like to ask you a few questions about your being here and your use of substances. Please remember that the information you give me will be treated confidentially. Please feel free to tell me if any question makes you feel uncomfortable.

C. HISTORY OF SUBSTANCE USE

C1. Age of first use

Actual age of first use……years

1. < 10 years
2. 10-14 years
3. 15-17 years
4. 18-20 years
5. 21-24 years
6. > 24 years

C2. First substance of use

Actual first substance of use……..

1. Cigarettes/Tobacco
2. Alcohol
3. Cannabis
4. Methamphetamine (Tik)
5. Other Specify……...

Comments……..

C3. Substance currently consumed most frequently

1. Cigarettes/Tobacco
2. Alcohol

3. Cannabis
4. Methamphetamine (Tik)
5. Heroin
6. Cocaine
7. Other Specify……...

Comments……..

C4. Frequency of use

1. Daily
2. Few times a week Specify……..
3. Weekends only
4. Sometimes Specify……..
5. Other Specify……...

C5. Intensity of use

Actual amount consumed at any one time…….

C6. What other substances do you use currently (in descending frequency)?

Specify other substances of use

1. Tobacco
2. Alcohol
3. Cannabis
4. Methamphetamine
5. Other Specify……..

Comments……..

C7. How often do you use each of these substances?

	1. Tobacco	2. Alcohol	3. Cannabis	4. Tik	5.Other
1.Daily					
2.Few times/wk					
3.Weekends only					
4.Seldom/Sometimes					
5. Never					

Specify other…….

C8. Previous treatment for substance use

Have you ever received treatment for your substance use?

1. None/Never
2. Once in past year Specify details……
3. More than once in past year Specify details……
4. More than a year ago Specify details……

Comments……..

C9. Actual age of first Rx for substance use problem……

1. < 10 years
2. 10-14 years

3. 15-17 years
4. 18-20 years
5. 21-24 years
6. > 24 years

C10. What was the nature of your substance use treatment in the past?

1. Inpatient Specify details where, when, how long……
2. Outpatient Specify details where, when, how long……
3. Daypatient Specify details where, when, how long……
4. Other Specify details where, when, how long……

Comments……
……
……

C11. EXPECTATIONS

What do you expect from the treatment you will be receiving/have received at this visit?
……
……
……
Specify nature of current Rx if known……...

I will now ask you a few questions relating to other treatment that you might have received in the past.

D: HISTORY OF PSYCHIATRIC PROBLEMS

D1. Have you ever been diagnosed with a psychiatric problem?

1. Yes
2. No

If no, that will be the end of this part of our session. I will now ask you a few questions relating to your general health and other treatment you might have received in the past. (Proceed to DIS)

D2. If yes, what was the diagnosis for your psychiatric problem(s)?

1.
2.
3.
4.

D3. Who made the diagnosis of your psychiatric problem made?

1.
2.
3.
4.

D4. Where was this diagnosis made?
1.
2.
3.
4.

D5. How old were you when you were first diagnosed with a psychiatric problem?
Actual age of first psychiatric diagnosis…….

1. < 10 years
2. 10-14 years
3. 15-17 years
4. 18-20 years
5. 21-24 years
6. > 24 years

D6. Did you ever receive treatment for a psychiatric problem?

1. Yes
2. **No**

D7. If YES, how long ago did you receive treatment the first time?
Specify actual date of first treatment…….
1. In the last month
2. In the last year
3. More than a year ago
4. More than 2 years ago

D8. Actual age of first Rx for psychiatric problem…….

1. < 10 years
2. 10-14 years
3. 15-17 years
4. 18-20 years
5. 21-24 years
6. > 24 years

D9. Where did you receive treatment for your psychiatric problem the first time?
Specify where……
1.
2.
3.

D10. What treatment did you receive the first time?
Specify……..
1.
2.

3.

D11. How many times have you received treatment for that first psychiatric problem?
Specify exactly how many times…….
1.
2.
3.
4.

D12. When was the last time that you received treatment for a psychiatric problem?
Specify date of last treatment……
1. In the last month
2. In the last year
3. More than a year ago
4. More than 2 years ago

D13. Was the last treatment you received for the same psychiatric problem or for a different psychiatric problem?

1. Same
2. Different Specify……

D14. What treatment did you receive the last time?
Specify……
1.
2.
3.
4.

D15. Where were you last treated for your psychiatric problem?
Specify where……..
1.
2.
3.
4.

That will be the end of this part of our discussion. I will now ask you a few more questions relating to your health and substance use. Some questions will have been asked before, but I will need to ask them again, so just bear with me and try to answer each question as accurately as possible. Don't worry if you cannot remember what you answered when I first asked you the question. (Proceed to DIS)

CHAPTER 5

Comorbid psychopathology, substance use and treatment outcomes: a follow-up of inpatient substance users in Cape Town, South Africa

Comorbid psychopathology, substance use and treatment outcomes: a follow-up of inpatient substance users in Cape Town, South Africa

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ABSTRACT

Comorbid psychopathology in substance users is thought to be associated with poor substance use treatment outcomes. This study followed up 95 substance users after inpatient treatment for substance use. Males, and patients who were single, were more likely to complete treatment. Females were more likely than males to relapse, or not complete treatment. No statistically significant associations were found between comorbid psychopathology, substances of use, and treatment outcomes. Primary users of crystal methamphetamine were marginally more likely than primary users of other substances not to complete treatment (OR=0.291; p=0.062). Major depression was marginally associated with decreased odds of relapse (OR=0.346; p=0.076). Further investigation is needed to explore the factors that influence treatment completion and relapse in female inpatients.

KEYWORDS comorbid psychopathology, substance use treatment, inpatients

INTRODUCTION

Comorbid psychopathology appears to occur in the majority (70% – 80%) of substance users in treatment (Kaminer, Connor and Curry, 2007). Evidence seems to indicate that the presence of comorbid psychopathology could play a role in i) increasing patients' risk of dropout from substance use treatment and relapse (Compton et al., 2003; Kaminer, Connor and Curry, 2007), ii) increasing the risk of increased frequency and intensity of substance use after treatment for substance use (Brooner, King, Kidorf, Schmidt (Jr), & Bigelow, 1997), and iii) exacerbating psychopathology symptoms after treatment (Brooner, King, Kidorf, Schmidt (Jr), & Bigelow, 1997; Armstrong & Costello, 2002; Schuckit, 2006). For example, relapse after substance use treatment has been associated with pre-treatment depression (Mc Carthy et al., 2005; Greig et al., 2006) and externalising disorders (Tomlinson et al., 2004), with comorbid substance users being more likely than substance use-only individuals to resume substance use treatment subsequent to discharge (Tomlinson et al., 2004).

The developmental pathway to adulthood is often characterised by factors that have been identified as possible risks for substance use. For example, adolescents in treatment for problematic substance use have commonly been found to have a history of behavioural problems such as aggressiveness, impulsivity, poor frustration tolerance, to have experienced problems at school (such as learning disabilities, attention deficit), psychiatric disorders (such as oppositional defiant disorder), or family problems (such as abuse or neglect) (Riggs, 2003). These factors could adversely affect intellectual and psychosocial development, with the possibility of lifelong difficulties for the individuals involved. Evidence has indicated that when psychiatric problems and substance use co-occur, there is an increased risk of poorer psychosocial outcomes than when substance use occurs alone (Greig et al., 2006; Tomlinson et al., 2004). Early identification of risk factors for substance use thus provide opportunities for earlier intervention and management of the individuals involved to increase their chances of improved future development.

Yet, even though evidence indicates that comorbid psychopathology might influence substance use treatment outcomes (Compton et al., 2003; Kaminer, Connor and Curry, 2007), and,

while the effectiveness of substance use treatment has not been demonstrated unequivocally (Singh et al., 2008), relatively few studies have examined associations between psychiatric disorder and outcome from substance use treatment (Chi and Weissner, 2008; Lubman et al., 2007) among adolescents and young adults (Lubman et al., 2007). Hence, information regarding the impact of psychiatric disorder on the outcomes of substance use treatment, particularly in adolescents and young adults, is sparse (Chi and Wessner, 2008).

Globally (including in South Africa), understanding of how comorbid psychopathology and substance use is treated, and what the substance use treatment outcomes in patients with comorbidity are, and how these are managed, remains limited (Lichtenstein et al., 2010). The limited reporting of treatment outcomes in substance-using inpatients with comorbid psychopathology might be a consequence of general difficulties experienced with the follow-up of substance using patients (Desmond et al., 1995). These include the cost associated with follow-up (Kleschinsky et al., 2009), and difficulties encountered in engaging or retaining substance users in treatment research (McHugo, Drake, Brunette et al., 2006) or locating substance use patients after treatment (Desmond et al., 1995).

In addition, psychiatric and substance use treatment facilities are commonly separate facilities (McHugo, Drake, Brunette et al., 2006), and this appears to be the case in South Africa as well. Problematic substance users with comorbid psychopathology might thus be referred for substance use treatment, where they might not be assessed or treated for comorbid psychopathology (Lichtenstein et al., 2010), possibly because the treatment emphasis would be on the substance use as the primary problem. Thus, while substance use in patients referred for psychiatric disorders is likely to be addressed within a psychiatric treatment facility, substance use treatment institutions frequently do not have the capacity to assess or treat comorbid psychopathology (Riggs, 2003).

This study examined the post-substance use treatment status of adolescent and young adult substance users, sampled from three substance use treatment centres in Cape Town between December 2008 and December 2009, on average six months after they had been discharged from an

inpatient substance use treatment programme. The study aimed to examine the association between comorbidity identified on admission for substance use treatment, and post-treatment status as defined by relapse, and treatment completion.

METHODS

Sample

At baseline (December 2008 to December 2009), 95 substance users aged 17 to 30 years (Mean 23 SD 2.9) were sampled consecutively in order of admission for inpatient substance use treatment at three privately-funded substance use treatment centres in Cape Town, South Africa.

Each patient was followed up on average six months after discharge from the baseline inpatient treatment programme. Nine patients could not be located for a follow-up interview, even after several attempts to contact them. These nine patients were considered officially lost to follow-up, resulting in a follow-up sample of 86 patients.

Study sites

Three inpatient treatment centres (sometimes referred to as clinics in the study) in Cape Town, South Africa, were selected from the South African Community Epidemiology Network on Drug Use (SACENDU) (Pluddemann et al., 2009; 2010) list of treatment centres that are regularly monitored as part of a programme that tracks substance use trends in the country.

One clinic (Clinic 1) was the dedicated chemical dependency unit in a private hospital, located in an upmarket and predominantly White [racially classified social group (RCSG) as defined by the population Registration Act of 1950, and including, White, Coloured, Indian and Black] residential-cum-commercial suburb of Cape Town, and offered a 21-day substance use treatment programme based on a medical model, and largely admitting patients with medical insurance. The second clinic (Clinic 2) was a house in a middle-class residential suburb that had a mix of White,

Coloured and Indian residents. The treatment at this clinic was an eclectic mix of psychology, spirituality and Asian medicine, offered in an environment where Muslim principles predominated, with a duration of 28 days and the possibility of patients' having extended treatment either as daypatients, outpatients or inpatients. The third clinic (Clinic 3) was a large house on a farm/smallholding in an underdeveloped and largely Coloured residential area, bordering on an informal settlement of makeshift shacks that housed a mix of Coloured and Black residents. This treatment centre offered custodial care in a Muslim environment, coupled with motivational talks, group therapy and the administration of vitamins and massages. The duration of the inpatient programme was 28 days, with patients having the option of extending their stay indefinitely as either inpatients or daypatients, and of remaining resident at the treatment centre while being employed elsewhere. The inpatient treatment programme at all three treatment centres included a 7-day detoxification period, and had abstinence as a prerequisite for inpatient admission, and maintenance of abstinence as the primary treatment goal.

Instruments

At baseline, an interview schedule, designed for the study, was administered to elicit sociodemographic (Table 1a) and substance use information (Table 1b). The sociodemographic factors that were assessed included age, gender, racially classified social group (RCSG), religious denomination, marital status, highest educational level, employment status and referral sources. Substance use information included the first substance(s) used (other than cigarettes), age of onset of substance use, the substance(s) for which inpatient treatment was sought (also referred to as the primary substance of use), and history of substance use treatment.

The interview schedule was followed by administration of the computer-assisted Diagnostic Interview Schedule for Diagnostic and Statistical Manual (DSM) IV (C-DIS IV) (Robins, Cottler, Bucholz, Compton, North & Rourke, 2002), by a trained C-DIS IV interviewer (the primary author), to screen for current (12-month) psychopathology. The C-DIS is a computerised version of the pencil-and-paper DIS, and was designed for use by trained lay interviewers to make psychiatric diagnoses

that match the capabilities of the pencil-and-paper DIS. The C-DIS, however, has greater flexibility than the pencil-and-paper version in that it is possible to administer the C-DIS in Full mode (the Full version mimics the complete pencil-and-paper version), in Screen mode (the Screen version allows current diagnoses to be made in a shorter time than the duration of the Full version). It is also possible to exclude DIS diagnostic modules that might not be of interest to a particular study. The DIS was designed for use with treatment and community populations, and has 'reasonably satisfactory' reliability with clinical diagnoses, with an overall agreement of 90% with diagnoses based on clinical judgement for most diagnoses (Helzer et al., 1985:665).

In this study, all the diagnostic modules of the DIS were administered at baseline, and all the modules were administered using the Screen version. The decision to administer all the DIS diagnostic modules in Screen mode was made to reduce the duration of the baseline interviews. The reasons for electing to economise on the duration of interviews included being able to complete all the interviews within the projected timeline of the project, and to minimise the burden on patients in terms of attention and time. All the baseline DIS interviews followed the instrument recommendation of not combining Full and Screen versions of the instrument in one interview (Robins et al., 2002).

Follow-up information was obtained by administering a follow-up questionnaire designed specifically for the study. The follow-up questionnaire elicited information about patient's completion or non-completion of the inpatient programme, and whether the patient had returned to treatment or, when electing to and being allowed to (as offered at Clinics 2 and 3), continued to remain in treatment after discharge from the initial inpatient programme. Substance use-related questions referred to whether the patient had relapsed with respect to substance use at any time during or after completion of the inpatient programme, whether or not the patient was using substances on the day of the follow-up interview, and what substances, if any, had been used after treatment discharge.

Procedure

The baseline interviews were conducted in private at the treatment centres, with only the patient and interviewer present. All the interviews were conducted by the same trained interviewer (primary author) and had a duration of approximately 90-120 minutes.

Admitted patients were identified for selection on admission, and interviewed after completing the detoxification period to decrease the likelihood of substance-use induced symptoms of psychopathology. No admitted eligible patients that met the study inclusion criteria of being aged 30 years or younger, refused study participation or were excluded from selection.

All study participants completed informed consent forms at baseline for both the baseline and follow-up interviews, and granted permission for their possible DIS diagnoses to be shared with their professional treatment managers if requested For the one patient who was aged 17, an assent form was completed by the patient, and written informed consent was obtained from a parent. The informed consent forms also contained contact details for patients' parent(s) or guardian whom patients consented to being contacted in their absence, particularly since patients had their mobile telephones confiscated while in treatment and were usually unable to provide reliable future mobile telephone contact details.

Patients were followed up after they had been discharged from the inpatient programme. The reasons for discharge from the programme were completion of the programme, premature discharge for any reason (for example, bringing substances such as cannabis, methamphetamine onto the treatment centre premises, or using substances such as these while at the treatment facility), or absconding from the programme for any reason before its completion. All patients were followed up in the year after their discharge from the inpatient programme. Follow-up of patients was initiated from 5 weeks after discharge. However, because it was not always possible to locate the patients for follow-up interviews immediately, these interviews were conducted as soon as the patients were available for the interviews. This resulted in a range in the time interval from discharge to successful

patient follow-up (5 weeks to 9 months; Mode = 3 months), with, a mean of six months elapsing after discharge from the inpatient treatment.

Some follow-up patients were resident at the clinic where they had completed the inpatient programme. In these cases the patients had usually elected to continue treatment because they felt they needed more assistance with their substance use-related problems, or to remain within the therapeutic environment because they did not feel sufficiently equipped to cope without the support of the clinic staff and fellow patients. These patients paid a rental for their stay, funded by family, or themselves if they were employed outside the clinic during this time. Some patients had moved in with family (usually their parents) after discharge. Others did not feel comfortable to move in with family, or had been rejected by their families on discharge.

On follow-up, patients were interviewed (by the same interviewer, and in all cases, the primary author) in person if they were still in treatment or resident at the treatment centre, or telephonically (via landline or mobile telephones) if they lived elsewhere. In cases where the patient was repeatedly inaccessible by telephone and could not be located for an interview, the interviewer consulted the director of the clinic (for 10 cases) or the patient's parent or guardian (two cases) personally or by telephone to obtain the required information where possible. In cases where the clinic director or a parent were interviewed, the questions asked were restricted to whether it was known if the patient had completed the inpatient programme (also obtainable from clinic records), whether it was known if the patient had relapsed since discharge, and whether it was known if the patient was back in a treatment programme. The interviewees answered these questions to the best of their knowledge. Where follow-up information was obtained from a parent, guardian or clinic director, abstinence was assumed where there was no known use of substances other than cigarettes. Details about the patients were kept to the minimum three questions (answering Yes or No with respect to treatment completion, relapse and treatment resumption) so as not to breach patient confidentiality, while still obtaining the most important required follow-up information for the study.

The study was approved by the Research Ethics Committee of the Health Sciences Faculty, University of Cape Town (REC REF: 340/2007).

Operational definitions

Relapse was defined as ever having used any substances, other than cigarettes, since the baseline interview, irrespective of whether or not the treatment programme had been completed in its entirety. Completion of treatment was defined as remaining in the programme for which the patient was admitted until the conclusion of the programme.

DATA ANALYSES

The data were analysed using STATA Version 10 (2007).

At baseline (Tables 1, 2 and 3): The demographic factors recorded for analysis were age, gender, racially-classified social group (RCSG), religious denomination (none, Christian, Muslim, Jewish, other), highest educational level (none, primary, secondary, tertiary), marital status [(never married (single), partnered/married], employment (employed, unemployed, student), and living arrangements (alone, with immediate family, other). The psychopathology variables consisted of the most common current (12 months) DIS psychiatric diagnoses (namely, antisocial personality disorder, conduct disorder, oppositional defiant disorder, major depression, post-traumatic stress disorder and specific phobia). Substance use was recorded in terms of substance use history (substance use initiation age, previous treatment for substance use), the first substance of use (other than tobacco), and the substance use for which treatment was sought (coincided with the most frequently used substance, and referred to as primary substance of use).

At follow-up: The baseline sociodemographic factors considered for the follow-up analyses were gender, RCSG, religious denomination and marital status. The psychopathology variables were

the most common DIS psychiatric diagnoses identified at baseline. The treatment outcome factors were treatment completion, relapse and back/still in treatment (Table 5). In all analyses, where relevant, the independent variables were the sociodemographic and psychopathology variables, while the dependent variables were the treatment outcome variables.

Percentages of patients were calculated at follow-up and compared with prevalence at baseline in terms of the selected sociodemographic variables (Table 4). Bivariate analyses were completed using Chi squared tests when cell sizes were five or larger, and Fisher's Exact tests when cell sizes were smaller than five to i) compare the distribution of sociodemographic, psychopathology and substances variables, by treatment outcomes (Table 5), ii) to compare the distribution of sociodemographic, psychopathology and substance use variables by loss to follow-up status, and iii) to compare the the distribution of sociodemographic, psychopathology and substance use variables by whether the patients were interviewed personally or by proxy. Multivariate logistic regression analyses were used in two distinct models to determine associations between baseline psychopathology, first substance of use and primary substance of use, respectively, and treatment outcome variables [completion of treatment (Table 6), relapse (Table 7)], adjusting for baseline factors (namely, age, gender, RCSG, religion and treatment centre/clinic). Separate multivariate analyses were conducted to determine associations between each of the most common forms of psychopathology and treatment outcomes, adjusting for age, gender, RCSG, religion, and treatment centre/clinic, and including primary substance of use as independent variables in the regression predicting outcomes (Tables 6 and 7), as well as previous substance use treatment. Additional bivariate analyses were completed to examine the association between time elapsed, between baseline and follow-up, and treatment outcomes. The follow-up (outcome) variables were dichotomous (Yes/No), making logistic regression analyses appropriate, and forced modelling was used for the regression analyses. Baseline sociodemographic, psychopathology and first and primary substance use variables were tested for multicollinearity, with STATA automatically excluding any variables with insufficient tolerance from the analyses. Odds ratios, 95% confidence intervals, and p-values were

calculated for these associations. Statistical significance was assumed if $p \leq 0.05$ while marginal a p-value between 0.05 and 0.10 was regarded as marginal.

RESULTS

Tables 1, 2 and 3 present the distribution of the sample at baseline in terms of sociodemographic, substance use and psychopathology factors. The baseline sample was predominantly male (89.5%), Coloured (88.4%), Muslim (68.4%) and with some secondary school education (86.3%). A large proportion of the baseline sample had never been married (77.9%) and lived with their immediate family (91.6%). The first substance of use was cannabis in more than half of the baseline sample (51.6%), and crystal methamphetamine was the first substance of use in 17.9% of the sample. Heroin was the substance for which treatment was sought in 53.7% of the sample, while 33.7% of the sample sought treatment for use of crystal methamphetamine.

Table 4 lists the numbers of patients sampled at baseline and the percentage reached for follow-up with respect to selected demographic factors. This table indicates that 86 patients were followed up (90.5%), with an approximate attrition of 10% at a mean of six months after discharge from inpatient treatment, and the characteristics of patients in the follow-up sample reflecting the characteristics of the baseline sample (Table 1). The follow-up sample was thus also largely male (89.4%), Coloured (89.3%), Muslim (93.8%) and single (87.8%). All the White, Indian, and partnered or married patients were located for interviews at follow-up. Bivariate analyses indicated that there were no statistically significant differences, in terms of sociodemographic, psychopathology and substance use factors between those who were lost to follow-up and those patients who were located for follow-up. However, those who were located for follow-up were marginally more likely (n=3; 3.4%) to have been diagnosed with current (12-month) generalised anxiety disorder (p=0.069), compared with those who were lost to follow-up (n=2; 22%). The cell sizes for these analyses were, however, very small. Patients lost to follow-up were also marginally more likely to have used crystal

methamphetamine as their primary substance of use (n=5; 55%; p=0.092) than were those patients who were located for follow-up (n=27; 31%).

Table 5 presents the percentage of patients who completed treatment or who had relapsed, in terms of the sociodemographic factors, psychopathology and substance use details examined. In this table, 70 patients (64 males and 6 females) had completed the inpatient treatment programme, 46 (38 males and 8 females) had relapsed by the time the follow-up interview was conducted.

In addition, at follow-up, 38 patients (32 males and 6 females) were found to have resumed treatment for their substance use.

The proportions of patients who completed the inpatient programme differed statistically significantly by marital status (p=0.002), while the proportion of patients who relapsed differed marginally by gender (0.097). It appeared that females (80.0%) in this sample were more likely than males (50%) to relapse, while single patients (92.3%) were more likely than married or partnered patients (47.6%) to complete their treatment. There was no statistically significant difference in the proportions of patients who completed treatment compared with those who did not, or relapsed compared with those who did not, in terms of the other factors examined (Table 5).

Tables 6 and 7 present the results of multivariate logistic regression analyses between psychopathology (independent variable) and treatment completion, and relapse (dependent variables) respectively, after discharge from treatment, adjusted for age, gender, religion, RCSG, first, and primary, substance use, treatment centre (clinics in Tables 1, 2 and 3) and previous substance use treatment.

Table 6 shows no statistically significant associations between comorbid psychopathology at baseline, and completion of the inpatient treatment programme. There was a marginal association (p=0.062) between crystal methamphetamine as the primary substance of use, and treatment completion. Thus primary users of crystal methamphetamine appeared to be 71% more likely than primary users of other substances to drop out of the inpatient treatment programme.

Table 7 indicates that there were largely no statistically significant associations between psychopathology or substance use, and relapse. However, there was a marginal association between having crystal methamphetamine as the first substance of use and relapse (p=0.080). Those patients who used crystal methamphetamine as their first substance of use had 67% decreased likelihood of relapsing compared with those patients who had cannabis as their first substance of use. Thus first users of crystal methamphetamine were less likely than first users of cannabis to relapse.

On adjustment for sociodemographic and substance use factors (Table 7), there was a marginal association between current (12-month) major depression and relapse (p=0.076), with patients diagnosed with current depression appearing to have a 65% decreased odds of relapse compared with those who were not diagnosed with depression (Table 7). These results thus indicate that, on adjustment for both sociodemographic and substance use factors, patients diagnosed with current (12-month) major depression had decreased odds of relapse, and, on further analyses, that these patients also had increased odds of resuming treatment after discharge.

In addition, no statistically significant associations were found between time elapsed to follow-up and treatment outcomes (relapse and treatment resumption). Similarly, bivariate analyses indicated no statistically significant associations between previous substance use treatment and treatment outcomes, and the association between psychopathology and treatment outcomes was not altered when previous treatment for substance use was added to the completed models.

DISCUSSION

The primary objectives of this study were to determine whether patients, who had been in inpatient substance use treatment, had completed the inpatient treatment programme, or had relapsed, and whether these outcomes were associated with psychopathology or substance use factors identified at baseline. No statistically significant associations were found between comorbid psychopathology, controlled for substance use and sociodemographic variables, and the treatment outcome factors.

Overall, this study had a low attrition rate in the five-week to nine-month period after inpatient treatment for substance use. This could be the result of the relatively short follow-up period (mean 6 months), and patients in the sample having retained some form of contact with their treatment managers or fellow inpatients. The finding that patients who were lost to follow-up were more likely to have been diagnosed with generalised anxiety disorder, and more likely to have had primary use of heroin or crystal methamphetamine might be an indication of lost patients with generalised anxiety disorder and/or primary use of crystal methamphetamine having moved from their baseline places of residence, or that their anxiety disorder might have made them less likely to want to continue participation in the study. These reasons for loss to follow-up, however, are speculative since reasons for the loss to follow-up were not specifically investigated.

Treatment completers were largely single and male, possibly reflecting the increased time available to these patients to complete the treatment due to reduced domestic responsibilities compared with married or female substance users. For example, Grella (2003) found that, compared with males, prospective female patients for substance use treatment were more likely to require assistance related to family needs and trauma while, in a study of females who were pregnant or entered residential treatment for substance use with their children, treatment completion was associated with having completed high school, having no arrests in the six months preceding admission, and having friends who were less deviant (Knight et al., 2001). A recent review of the literature regarding treatment entry, retention and outcome in women (Greenfield et al., 2007) indicated that gender differences played a role in treatment entry, with males being more likely to enter treatment, but that gender was not a statistically significant predictor of treatment retention, thus echoing the findings of the present study. Similarly, recent studies with adolescents and young adults have indicated that fixed client factors such as age, gender and ethnicity were not significantly associated with completion of treatment (Schroder et al., 2009). Instead, it was found that retention in treatment was more likely to be a function of so-called dynamic patient factors such as patients' experiences in the treatment process, the degree to which patients are motivated to attend treatment, and their expectations about the treatment offered. It is thus possible that unmeasured factors [for

example, patients' readiness to change their behaviour (Saban et al., 2001), patients' experience of the treatment programme and their relationship with treatment staff (Schroder et al., 2009)] were operative in dropout from treatment, relapse, and possibly resumption of treatment in the present study. It has also been suggested that gender might moderate the relationship between comorbid psychopathology in substance users and treatment outcome (Compton et al., 2003), but this was not assessed in this study.

There was a marginal association between primary use of crystal methamphetamine and treatment completion (p=0.062) (Table 6), with crystal methamphetamine users being 71% less likely to complete treatment (OR=0.291) than were primary users of substances other than crystal methamphetamine. Methamphetamine is the primary substance of use in 47% of all individuals (and 51% of individuals under 20 years of age) who present for treatment in the Western Cape area of South Africa (including Cape Town) (Pluddemann, et al., 2010). It might, thus, be useful for further investigations to examine the suggestion that crystal methamphetamine might play a role in non-completion of inpatient treatment.

Initiating substance use with of crystal methamphetamine was marginally (p=0.080) and inversely (OR=0.331; CI 0.096-1.143) associated with relapse, suggesting that users of crystal methamphetamine as a first substance might be less likely than first users of other substances, such as cannabis, to relapse. Evidence indicates that initiation of substance use appears to be a function of factors such as environmental and economic stressors (Brook et al., 2006), while choice of debut substance is subject to availability and affordability (Anderson, 2006). However, initiating crystal methamphetamine use specifically has been found to be associated with factors such as age, ethnicity, earlier criminal behaviour and sensation-seeking in substance users in treatment for their substance use (Brecht et al., 2007). It might thus be of value to investigate further the association between crystal methamphetamine (versus other substances) as a first substance of use, and treatment outcomes such as relapse, particularly since comparable information on the Cape Town inpatient substance using population is currently not available.

Overall, no clear-cut statistically significant associations were found between comorbid psychopathology and treatment outcome. The results of the current study also indicated that patients diagnosed with current (12-month) depression were less likely than those who were not diagnosed with depression to relapse. These findings of continued engagement in substance use treatment amongst patients who were depressed, even if they did not relapse, might reflect the recognition by these patients of a need for some assistance, but associating the need with problems relating to substance use rather than a psychiatric disorder. Thus, since the study sample had largely previously undiagnosed psychiatric disorders, it is possible that the affected patients were unaware of their mental health status and its possible role in either their discomfort or their substance use or need for substance use. In addition, Miller et al. (1999), in examining substance users in private outpatient treatment for their substance use, had previously found that post-treatment factors such as a lack of peer support groups and continuing care, played a larger role in the prediction of relapse than did pre-treatment factors such as lifetime depression. It is possible that parts of the sample for the present study lacked such continuing care and support, and that the absence of continued support accounted for, for example, relapse in the female patients.

The results of this study, however, need to be considered in light of possible study limitations imposed by the study design, sample size, and diagnostic instrument.

The sample was a consecutively-selected clinical sample obtained from three purposively selected treatment centres in Cape Town, South Africa. The sample was not selected from a representative sample of inpatient treatment centres, and was not selected randomly. The sample was thus not representative of Cape Town substance users in inpatient treatment for their substance use even though it reflected the broader population trends for the geographical area with respect to some demographic factors (such as gender and RCSG). As such, the results obtained are not generalisable beyond the selected sample, and comparisons with the results of similar studies have to be made with caution. It is also possible that the sample size might have limited the study power, and the kinds of statistical analyses that could be performed, with the baseline sample size being slightly smaller than the anticipated minimal sample size and subsequent attrition on follow-up. However, it is also likely

that the finding that nearly all the inpatients had a psychiatric disorder reduced the gradient for looking at associations between psychiatric disorder and treatment outcomes. If the exceedingly large proportion of patients of patients with psychiatric disorder had been anticipated, a larger sample size could have been estimated, but the large proportion of patients with psychiatric disorder in this sample was unexpected based on the literature (Kaminer et al., 2007).

Considering that substance use and psychopathology treatment facilities are usually separated (Kaminer, Connor &Curry, 2007), it is possible that patients with more severe psychopathology had not been represented in this sample of patients in treatment for substance use if patients with more severe psychopathology were more likely to be in psychiatric institutions. Severity of comorbid psychopathology was not assessed in the sampled patients because using the C-DIS in screen mode assesses presence or absence of a diagnosis, and does not indicate severity of diagnoses (Robins et al., 2002). Thus if the psychopathology in the sample was of varying severity or possibly less severe than in patients who receive treatment for psychiatric disorder, and the degree of psychopathology severity influenced treatment outcomes, it is possible that omission of a psychopathology severity factor could have influenced the associations between psychopathology and treatment outcome in the present study.

The frequency with which comorbid psychopathology occurred in this sample could also have been influenced by use of the C-DIS IV since this instrument had not been standardised for use with the sample. Generally, validation studies of the DIS have proven difficult, because of the lack of an absolute standard that covers the full range of the DSM diagnoses with which to compare it (Robins et al., 1981). Furthermore, though the DIS has been found to have satisfactory concordance with diagnoses based on clinical judgement (Helzer et al., 1985) this comparison assumes clinical judgement to be the appropriate yardstick against which to measure the skills of lay interviewers (Robins et al., 1981). The C-DIS also elicited patient information via self-reports, the reliability of which was not verified from other sources. Thus, if patients over- or under-reported information relevant to the study, the results of the study could have been affected.

Furthermore, the variability in the time period between baseline and follow-up interviews could have influenced the findings related to outcome. For example, patients who had their follow-up interview after a few weeks might have had different outcomes with regards to relapse or treatment resumption compared with patients who had their follow-up interviews several months after the baseline interviews.

In addition, resumption of substance use treatment (after discharge from the initial inpatient substance use treatment programme) was considered as a treatment outcome measure since comorbid psychiatric disorder has been found to be associated with increased rates of re-entry into substance use treatment (Arendt et al., 2007). However, this treatment outcome measure proved to be problematic in the present study when it was found that some patients elected to continue their inpatient substance use treatment programme after discharge, irrespective of their substance use status at the time. Thus some patients who had resumed substance use treatment after discharge might have been abstinent, or might have elected to resume treatment because of relapse or the effects of a psychiatric disorder. Since the reasons for resumption of treatment were not elicited in the study, it would be inappropriate to assume that resumption of treatment in this study necessarily reflects a negative treatment outcome.

Generally, the sample for this study did not constitute an homogeneous group. Patients had used different substances (both individual and multiple substances), possibly in differing amounts and with differing frequencies, presumably had differing social supports, differing psychosocial developments, and differing patterns of severity of psychiatric disorder and/or substance use. It is possible that, with the limited information collected at follow-up, some unmeasured sources of heterogeneity in the sample might have contributed to confounding, resulting in a lack of significant associations between comorbid psychopathology and treatment outcomes. It is also possible that information obtained via proxy (clinic directors or parents/guardians) might have differed from information obtained from the patients themselves, providing further sources of confounding.

To identify associations between psychiatric disorder and substance use treatment outcome, it might thus be necessary for the heterogeneity of substance users to be considered. Furthermore, it

might be advantageous for patient heterogeneity to be considered in attempts to improve the efficacy of substance use treatment by, for example, having the treatment tailored to suit the needs of individuals. One suggestion has been to provide primary care in substance use treatment facilities as a cost-effective means of accommodating treatment for comorbidity, compared with fully integrating psychiatric and substance use treatment services (McKay 2005). In the longer term, this approach might result in improved compliance with inpatient and follow-up treatment in these patients since both (or all) comorbid conditions could be stabilized and monitored.

In conclusion, similar future studies might examine treatment outcomes in a cohort of comorbid substance use patients versus patients with only a substance use disorder. Future studies of the treatment outcomes of substance use inpatients might also have to consider assessment of patient factors that include severity of comorbid psychopathology, patients' readiness to change their behaviour (Saban et al., 1999), coping skills, reasons for extending or resuming substance use treatment after discharge, and psychosocial functioning (Ciraulo et al., 2003), while treatment programmes might have to be supplemented with practices that ensure continuity of care after treatment discharge (Schaefer et al., 2008).

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TABLE 1 Demographic characteristics of the sample in the three treatment centres (n; %)

Demographic variable	Clinic 1	Clinic 2	Clinic 3	Total
	n =17	n = 30	n = 48	n = 95
Mean Age	21.7	23.2	23.4	23.0
SD	3.5	3.0	2.6	2.9
Gender Male	16 (94.1)	24 (80.0)	45 (93.8)	85 (89.5)
RCSG				
White	3 (17.7)	1 (3.3)	0	4 (4.2)
Coloured	13 (76.5)	27 (90.0)	44 (91.7)	84 (88.4)
Indian	1 (5.9)	2 (6.7)	4 (8.3)	7 (7.4)
Religion				
Muslim	2 (11.8)	27 (90.0)	36 (75.0)	65 (68.4)

Christian	15 (88.2)	3 (10.0)	11 (22.9)	29 (30.5)
Highest educational level				
Primary school	1 (5.9)	0	2 (4.2)	3 (3.2)
Secondary school	16 (94.1)	24 (80.0)	42 (87.5)	82 (86.3)
Tertiary	0	6 (20.0)	4 (8.3)	10 (10.5)
Referral source				
Self	10 (58.8)	18 (60.0)	30 (62.5)	58 (61.1)
Family	3 (17.6)	11 (36.7)	13 (27.1)	27 (28.4)
Other	4 (23.5)	1 (3.3)	5 (10.4)	10 (10.5)
Marital status				
Never married	15 (88.2)	22 (73.3)	37 (77.1)	74 (77.9)
Other	2 (11.8)	8 (25.7)	11 (22.9)	21 (22.1)
Living arrangements				
Live alone	0	0	2 (4.2)	2 (2.1)
Live with immediate family	16 (94.1)	29 (96.7)	42 (87.5)	87 (91.6)

Other	1 (5.9)	1 (3.3)	4 (8.3)	6 (6.3)
Employment status				
Unemployed	7 (41.2)	18 (60.0)	27 (56.3)	52 (54.7)
Casually employed	1 (5.9)	2 (6.7)	4 (8.3)	7 (7.4)
Permanently employed	7 (41.2)	7 (23.3)	17 (35.4)	31 (32.6)
Usual employment				
Professional	0	0	1 (2.1)	1 (1.1)
Skilled	6 (35.3)	10 (33.3)	18 (37.5)	34 (35.8)
Unskilled	4 (23.5)	10 (33.3)	16 (33.3)	30 (31.6)
None/student/scholar	7 (41.2)	8 (26.7)	8 (16.7)	23 (24.2)

TABLE 2 Frequency of substance use at baseline (n; %)

Substance use variable	Clinic 1	Clinic 2	Clinic 3	Total
	n = 17	n = 30	n = 48	n = 95
Age of first illicit substance use (years)				
10 – 14	13 (76.5)	13 (43.3)	23 (47.9)	49 (51.6)
15 – 17	3 (17.6)	11 (36.7)	18 (37.5)	32 (33.7)
18 – 20	0	5 (16.7)	7 (14.6)	12 (12.6)
21 – 24	1 (5.9)	1 (3.3)	0	2 (2.1)
Mean (SD)	13.6 (2.4)	15.1 (2.6)	14.8 (2.3)	14.7 (2.4)
First illicit substance of use				
Alcohol	4 (23.5)	0	3 (6.3)	7 (7.4)

Cannabis	8 (47.1)	16 (53.3)	25 (52.1)	49 (51.6)
Ecstasy	0	5 (16.7)	4 (8.3)	9 (9.5)
Heroin	1 (5.9)	2 (6.7)	3 (6.3)	6 (6.3)
Methaqualone (mandrax)	0	2 (6.7)	0	2 (2.1)
Crystal methamphetamine (tik)	4 (23.5)	3 (10.0)	10 (20.8)	17 (17.9)
Multiple	0	2 (6.7)	3 (6.3)	5 (5.3)
Primary substance of use				
Alcohol	3 (17.6)	0	0	3 (3.2)
Cannabis	4 (23.5)	0	1 (2.1)	5 (5.3)
Heroin	2 (11.8)	20 (66.7)	29 (60.4)	51 (53.7)
Crystal methamphetamine (tik)	7 (41.2)	8 (26.7)	17 (35.4)	32 (33.7)
Methaqualone (mandrax)	0	1 (3.3)	0	1 (1.1)
Multiple	1 (5.9)	0	1 (2.1)	2 (2.1)
Frequency of use				
Daily	15 (88.2)	28 (93.3)	43 (89.6)	86 (90.5)
Few times a week	1 (5.9)	2 (6.7)	3 (6.3)	6 (6.3)
Intensity/Volume of use				
As much as I can obtain	11 (64.7)	14 (46.7)	31 (64.6)	56 (58.9)

As much as I can afford to buy	6 (35.3)	15 (50.0)	16 (33.3)	37 (38.9)
Previous treatment for substance use				
None	11 (64.7)	12 (40.0)	19 (39.6)	42 (44.2)
Once in past year	3 (17.6)	2 (6.7)	8 (16.7)	13 (13.7)
More than once in past year	0	5 (16.7)	12 (25.0)	17 (17.9)
More than a year ago	3 (17.6)	11 (36.7)	9 (18.8)	23 (24.2)
Age of first treatment for substance use (yrs)	n=6	n=18	n=29	n=53
10 – 14	1 (16.7)	2 (11.1)	0	3 (5.7)
15 – 17	0	4 (22.2)	7 (24.1)	11 (20.8)
18 – 20	5 (83.3)	7 (38.9)	13 (44.8)	25 (47.2)
21 – 24	0	3 (16.7)	9 (31.0)	12 (22.6)
>24	0	2 (11.1)	0	2 (3.8)
Mean (SD)	17.5 (3.3)	18.9 (3.9)	19.3 (2.6)	19 (3.1)

TABLE 3 Prevalence of psychopathology at baseline (n; %)

	Clinic 1	Clinic 2	Clinic 3	Total
Psychopathology	n = 17	n = 30	n = 48	n = 95
No previous diagnosis of psychopathology	15 (88.2)	29 (96.7)	47 (97.9)	91 (95.8)
Generalised anxiety disorder	3 (17.6)	1 (3.3)	1 (2.1)	5 (5.3)
Post-traumatic stress disorder (PTSD)	3 (17.6)	5 (16.7)	6 (12.5)	14 (14.7)
Depression	6 (35.3)	9 (30.0)	9 (18.8)	24 (25.3)
Mania	6 (35.3)	1 (3.3)	5 (10.4)	12 (12.6)
Schizophrenia	0	2 (6.7)	0	2 (2.1)
Obsessive Compulsive Disorder (OCD)	2 (11.8)	1 (3.3)	1 (2.1)	4 (4.2)

Eating disorder	0	2 (6.7)	2 (4.2)	4 (4.2)
Separation anxiety	1 (5.9)	2 (6.7)	2 (4.2)	5 (5.3)
Oppositional defiant disorder	7 (41.2)	10 (33.3)	15 (31.1)	32 (33.7)
Conduct disorder (CD)	10 (58.8)	18 (60.0)	36 (75.0)	64 (67.4)
Antisocial personality disorder (ASPD)	14 (82.4)	26 (86.7)	43 (89.6)	83 (87.4)
Pain disorder	3 (17.7)	4 (13.3)	3 (6.3)	10 (10.5)
Specific phobia	4 (23.5)	5 (16.7)	6 (12.5)	15 (15.8)
Substance dependence	12 (70.6)	29 (96.7)	46 (95.8)	87 (91.6)
Substance abuse	4 (23.5)	5 (16.7)	6 (12.5)	15 (15.8)

TABLE 4 Percentage retention at follow-up by demographic characteristics

Demographic factors	Baseline (n)	Follow-up (n; % of baseline)	Lost to follow-up (n; % of baseline)
Total	95	86 (90.5)	9 (9.5)
Males	85	76 (89.4)	9 (10.6)
RCSG			
Coloured	84	75 (89.3)	9 (10.7)
White	7	7 (100)	0
Indian/Asian	4	4 (100)	0
Religion			
Muslim	65	61 (93.8)	4 (6.2)
Christian	29	24 (82.8)	5 (17.2)
Marital status			

Never married	74	65 (87.8)	7 (10.4)

Table 5 Frequency of treatment outcome by demographics, most common psychopathology, first substances of use, and primary substances of use [n, (%), p-value]

Demographic, psychopathology and substance use factors		Completed Treatment Yes n (% of baseline) p-value	Relapsed Yes n (% of follow-up) p-value	Back/Still in Treatment Yes n (% of follow-up) p-value
	n at follow-up (% of baseline total n=95)	n=70	n=86	n=86
Age				
Mean(SD)		23.0 (3.1) 0.428	22.8 (3.0) 0.488	23.2 (2.8) 0.723
Gender				
Male	76 (80)	64 (75.3)	38 (50.0)	32 (42.1)
Female	10 (10.5)	6 (60.0) 0.220	8 (80.0) 0.097	6 (60.0) 0.326
RCSG				
Coloured	75 (78.9)	62 (73.8)	39 (52.0)	35 (46.7)
White/Indian	11 (10.5)	8 (72.7) 0.660	7 (63.6) 0.410	3 (27.3) 0.333

Religious denomination				
Muslim	61(64.2)	49 (75.4)	33 (54.0)	29 (47.5)
Christian	24 (25.3)	21 (72.4)	13 (54.2)	9 (37.5)
		0.255	1.000	0.477
Marital Status				
Never married	65 (63.2)	60 (81.1)	36 (55.4)	30 (46.2)
Other	21(22.1)	10 (47.6)	10 (47.6)	8 (38.0)
		0.002	1.000	1.000
Psychopathology	n at baseline			
Anti-social personality disorder	83	61 (73.5)	41 (49.4)	31 (41.9)
		0.725	0.748	0.355
Conduct disorder	64	47 (73.4)	32 (50.0)	23 (35.9)
		1.000	1.000	0.168
Oppositional defiant disorder	32	23 (71.9)	17 (53.1)	12 (37.5)
		1.000	0.368	1.000
Major Depression	24	19 (79.2)	9 (37.5)	12 (50.0)
		0.772	0.218	0.322
PTSD	14	10 (71.4)	7(58.3)	6 (50.0)
		1.000	0.765	0.758
Specific phobia			8 (57.1)	4 (28.6)
			1.000	0.248

	15	12 (80.0) 0.727		
First substance of use				
Cannabis	49	36 (73.5)	27 (55.1)	20 (40.8)
Crystal methamphetamine	17	11 (64.7)	5 (29.4)	6 (35.3)
Other	29	23 (79.3)	12 (41.3)	12 (41.3)
		0.887	0.244	0.876
Primary substance of use Heroin	51	23 (45.1)	20 (62.5)	18 (56.3)
Crystal methamphetamine	32	12 (37.5)	7 (41.2)	7 (41.2)
		0.108	0.148	0.213

TABLE 6 Association, using logistic regression analyses, between psychopathology and treatment completion (OR, 95% CI, p-value)

	Rx Completion (Yes) n=70								
	Unadjusted			Adjusted[†]			Adjusted[††]		
Psychopathology	OR	95% CI	p	OR	95% CI	p	OR	95%CI	p
ASPD	1.118	0.272-4.598	0.878	1.361	0.266-6.956	0.711	1.225	0.230-6.531	0.812
Conduct disorder	0.918	0.310-2.725	0.878	0.967	0.291-3.209	0.956	1.014	0.282-3.641	0.984
Oppositional defiant	0.867	0.302-2.489	0.790	0.796	0.261-2.425	0.688	0.738	0.227-2.392	0.612
Major depression	1.500	0.442-5.092	0.516	1.672	0.422-6.622	0.464	2.273	0.512-10.093	0.280
PTSD	0.895	0.217-3.681	0.878	1.855	0.276-12.470	0.525	1.640	0.228-11.777	0.623
Specific phobia	2.000	0.408-9.799	0.393	2.757	0.416-18.271	0.293	2.953	0.445-19.608	0.262

Primary substance use						
Heroin	0.500	0.181-1.380	0.181	0.705	0.233-2.127	0.534
Crystal methamphetamine	0.467	0.147-1.481	0.196	0.291	0.080-1.065	0.062
First substance of use						
Cannabis	1.200	0.441-3.267	0.721	1.493	0.477-4.672	0.491
Crystal methamphetamine	0.800	0.224-2.856	0.731	0.841	0.205-3.454	0.810

[†]Adjusted for age, gender, RCSG, religion and treatment centre

[††] Adjusted for age, gender, RCSG, religion, first substance of use, most frequently used (primary) substance and treatment centre

TABLE 7 Association, using logistic regression analyses, between psychopathology and relapse (OR, 95% CI, p-value)

	Relapse (Yes) n=86								
	Unadjusted			Adjusted[†]			Adjusted[††]		
Psychopathology	OR	95% CI	p	OR	95% CI	p	OR	95%CI	p
ASPD	1.739	0.505-5.985	0.380	2.293	0.600-8.767	0.225	2.071	0.530-8.104	0.295
CD	1.101	0.442-2.740	0.837	1.425	0.523-3.880	0.489	1.299	0.453-3.723	0.626
Oppositional defiant	1.545	0.618-3.865	0.352	1.717	0.656-4.495	0.271	1.629	0.601-4.414	0.337
Major depression	0.505	0.189-1.352	0.174	0.420	0.136-1.296	0.131	0.346	0.107-1.120	0.076
PTSD	1.256	0.365-4.320	0.717	0.806	0.173-3.760	0.784	0.662	0.136-3.221	0.610
Specific phobia	1.193	0.376-3.787	0.765	1.066	0.291-3.908	0.923	0.873	0.224-3.400	0.845
Primary substance use									
Heroin	1.795	0.735-4.383	0.199	1.430	0.537-3.804	0.474			
Crystal methamphetamine	0.538	0.183-1.581	0.260	0.551	0.177-1.717	0.304			

First substance of use						
Cannabis	1.571	0.669-3.690	0.300	2.108	0.797-5.576	0.133
Crystal methamphetamine	0.366	0.113-1.181	0.093	0.331	0.096-1.143	0.080

[†]Adjusted for age, gender, RCSG, religion and treatment centre

[††] Adjusted for age, gender, RCSG, religion, first substance of use, most frequently used (primary) substance and treatment centre

FOLLOW-UP QUESTIONNAIRE FOR TREATMENT CENTRE STUDY

Treatment Centre……. | | | |

Patient/Subject number……... | | | |

Folder/File number…….. **Date……**

Time lapse since baseline interview (weeks)…….

Patient/Subject name……...
Address…….
Telephone numbers i)**……** ii)**……**iii**)……...**

You will/might remember that I interviewed you a little while ago. At that time I mentioned that I will speak with you again. So now I would like to ask you a few short questions.

A. TREATMENT

A1. Where was treatment received since we last spoke?

1. Horizon Halfway House
2. Claro Clinic
3. Other Specify……..

A2. What kind(s) of treatment did you receive?

1. Medication Specify……..
2. Group psychotherapy
3. Individual psychotherapy
4. Alternative treatments (eg massage, reiki etc) Specify……..
5. Other Specify……..

A3. Do you feel that the treatment you received was what you expected?

1. No
2. Yes
3. Didn't have expectations about Rx
4. Don't know

A4. Do you have any suggestions about how your treatment could have been improved/altered?

1. No
2. Yes

A5. If YES, what changes/improvements would you suggest?

……
……
……

B. CURRENT STATUS

B1. How would you describe how you are now compared with when we last spoke?

1. Better
2. Worse
3. Same
4. Not sure

Comments……
……
……

B2. Are you using any substance(s) now?

1. No
2. Yes
3. Not sure

Comments……
……
……

If NO, then that is the end of this interview. Many thanks for your time. I wish you well and hope you don't mind if I contact you again in the future.

B3. If YES, what are you currently using?

1. Tobacco
2. Alcohol
3. Cannabis
4. Methamphetamine
5. Heroin
6. Cocaine
7. Other Specify……...

B4. What would you say your main current substance of use is?

1. Tobacco
2. Alcohol
3. Cannabis
4. Methamphetamine
5. Heroin
6. Cocaine
7. Other Specify……...

B5. Is your current main substance of use different from what it was when we last spoke?
1. No
2. Yes
3. Not sure

Comments……
……
……

B6. How often do you use this substance?
1. Daily
2. Few times per week
3. Weekends only
4. Seldom/Sometimes
5. Never

Comments……
……
……

B7. How much of this substance do you consume at any one time?
Actual amount……

Thanks very much for your time and cooperation. I would like to contact you again some time in the future, if that will be alright with you. Meanwhile, all the best.

CHAPTER 6

The association between substance use and common mental disorders in young adults: results from the South African Stress and Health (SASH) Survey

The association between substance use and common mental disorders in young adults: results from the South African Stress and Health (SASH) Survey

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ABSTRACT

Although substance use is commonly associated with mental disorders, limited data on this association is available from low and middle income countries such as South Africa. The South African Stress and Health (SASH) study is a nationally-representative random cross-sectional survey of South African households, and forms part of a World Health Organisation (WHO) World Mental Health (WMH) initiative to standardise information on the global burden of mental illness and its correlates. In this study, data from a subset (n=1766; aged 18 to 30 years) of the SASH sample of 4351 individuals were analysed. The aims of the study were i) to determine patterns of substance use in young adults, ii) to identify trends of common psychiatric disorders in relation to use of specific substances, and iii) to determine whether specific psychiatric disorders were associated with use of specific substances in the South African population. The Composite International Diagnostic Interview Version 3 (CIDI 3.0) was used to elicit basic demographic details and information regarding mental illness and substance use. Multiple regression analyses, adjusted for age and gender, were used to identify associations between mental disorders and substance use. Results indicated significant associations between substance use and mood and anxiety disorders, with a particularly strong relationship between cannabis use and mental disorder. The data here are consistent with those from previous studies, and reinforce the argument that comorbid substance use and mental disorders constitute a major public health burden

Key words: SASH comorbidity mental disorders substance use

1. Introduction

Debilitating mental illness often places a burden on society (Teeson et al., 2009). Mental illness can result in reduced economic productivity in affected individuals (Chatterji et al., 2009), and can influence the quality of life for individuals and their families as a result of the disabling effects of the mental illness (Kessler et al., 2009). Mental illness can also increase the load on service providers who treat the affected individuals (Kessler et al., 1997). Similarly, problematic substance use poses a challenge to society because of its effects on the psychosocial functioning, productivity and general health of the affected individuals (Glassner-Edwards et al., 2010; Goldstein and Bukstein, 2009). It has been argued that individuals who suffer from mental illnesses are more likely to be or become dependent on substances than are individuals who do not have mental disorders (Kessler et al., 1997). Conversely, individuals who abuse substances appear to be more likely to develop or suffer from mental illnesses than are those who do not abuse substances (Buckley, 2007). Thus, when mental illness and problematic substance use or abuse co-occur (commonly described as comorbidity), the resulting problems are often compounded and more complex than when either mental illness or problematic substance use occurs individually (de Graaf et al., 2004), increasing the challenges posed to the management and treatment of the affected individuals (Kessler et al., 1997)

Globally, many studies have examined comorbid psychopathology and substance use. However, more details on comorbidity are generally available for older individuals, and less regarding children, adolescents and young adults (Goldstein and Bukstein, 2009). Furthermore, most of these studies have examined samples in treatment for either substance use or psychiatric disorders (Armstrong and Costello, 2002) resulting in less published information on comorbidity in communities.

Armstrong and Costello (2002) described six important reasons for examining comorbid psychopathology and substance use in representative community samples. The reasons for this are based primarily on inherent differences between clinical and community samples and the consequent inappropriateness of extrapolating information from clinic-based studies to communities. Firstly, since individuals with more than one disorder are more likely to seek treatment for either disorder than are individuals with only one disorder, clinical samples are more likely than community samples to contain comorbid individuals. Secondly, the nature of some disorders might be more likely to precipitate treatment seeking. Hence, for example, a disruptive behaviour disorder (such as conduct or antisocial personality disorder) that co-occurs with substance use might be more likely to elicit treatment seeking than would an internalising disorder (such as depression), resulting in clinical samples possibly having a higher percentage of comorbid disruptive behaviour disorders than is commonly prevalent in communities. Thirdly, community and clinical samples might differ with respect to the severity of occurring symptoms. Fourthly, community and clinical samples might differ with respect to the temporality of comorbidity. Fifthly, clinic and community samples might differ with respect to the risk factors for comorbid psychopathology and substance use. These differences can usually be assessed for diseases where most cases are treated. However, since not all comorbid substance users receive treatment, it would be inappropriate to assume that risk factors for comorbidity are the same in both treatment and community samples. Lastly, substance use treatment samples might reflect a different patient economic profile compared with community samples by containing mainly individuals who have access to finances for treatment, and thus excluding those individuals who might need treatment but cannot afford it.

In South Africa, as in other developing countries, information regarding comorbid psychopathology and substance use, its consequences, and the implications for society, is limited by a paucity of published studies (Sharan et al., 2009; Saban and Flisher, 2010). Evidence has indicated that sociodemographic factors can play a significant role in comorbidity and its effects (Hovens et al., 1994; Brook et al., 1995; Riggs et al., 1995; Rohde et al., 1996; Deykin & Buka, 1997; Escobedo et al., 1998; Costello et al., 1999; McGee et al., 2000; Shrier et al., 2003). Findings from non-South

African studies have included evidence for associations between conduct disorder and substance use within specific developmental stages (Grilo et al., 1995; Ferdinand, Blum and Verhulst, 2001), and differing associations between psychopathology and substance use in males and females (Brooner et al., 1997; Deyken and Buka, 1997). While some findings included evidence for associations between depression and smoking (Escobedo et al., 1998; Ferguson et al., 1996; Kendler et al., 1993), between depression and alcohol use (Araujo and Monteiro, 1995), and between psychopathology in general and cannabis use (McGee et al., 2000), other findings have not indicated definitive associations between psychopathology and substance use (Boyle et al., 1992; Costello et al., 1999; Degenhardt et al., 2001). For example, Boyle et al. (1992) found associations between conduct disorder and cannabis use, but not between conduct disorder and use of tobacco or alcohol, while Costello et al. (1999) found no evidence for associations between anxiety and substance use. Though these findings play a significant role in the understanding of associations between psychopathology and substance use, their generalisability to the South African population cannot be assumed. In particular, these studies had not always used similar psychopathology assessment tools, had often examined differing substances of use with differing instruments, and subscribed to differing conceptual frameworks, suggesting that over-arching conclusions about the nature of comorbid psychopathology and substance use be drawn with caution.

The World Health Organisation (WHO) World Mental Health (WMH) initiative was embarked upon to provide standardised information on the global burden of mental disorders and its correlates in 28 countries. The South African Stress and Health (SASH) survey, initiated in 1999 and commenced in 2002, represents the South African arm of the WHO WMH initiative. The SASH survey is significant in that it is a nationally representative survey of selected mental disorders in South Africa and in Africa (Stein et al., 2009; Herman et al., 2009). One of the primary aims of the SASH survey was to address a recognised gap in knowledge regarding the prevalence and severity of selected mental disorders in South Africa, in a manner that was comparable with similar data from other parts of the world.

The current study focussed on the nature of associated psychopathology and substance use in a previously unexamined sample of young South African adults aged 18 to 30 years. The study advances knowledge about comorbidity in general, and particularly in South Africa, by using a nationally representative community sample.

The aim of the study was threefold. Firstly, the prevalence of substance use was calculated with respect to selected demographic factors (namely, age, gender, racially classified social group, highest educational level, marital status, employment status, income and urbanicity) to determine substance use patterns in young adults. Secondly, the prevalence of psychopathology (namely mood and anxiety disorders) amongst younger users of various selected substances was calculated, to determine percentage of psychopathology in relation to specific substances of use. Thirdly, and finally, the current study calculated associations between selected lifetime and 12-month psychopathology (namely mood and anxiety disorders) and substance use, adjusted for age and gender to determine whether specific psychopathology was associated with use of specific substances of use in young South African adults.

2. Methods

The SASH study was a nationally representative mental health survey that was conducted between January 2002 and June 2004 (Williams et al., 2004). The study protocol was approved by the Institutional Review Board of the University of Stellenbosch. All sampled individuals provided written informed consent for participation in the study.

2.1. Sample

The SASH study randomly sampled adult males and females, aged 18 years and older, from all the South African racially classified social groups (RCSGs). RCSGs are defined according to the Population Registration Act of 1950 that classified citizens largely in terms of skin colour. These

RCSGs were selected because they still reflect ongoing social disparities in South Africa (Kon and Lackan, 2008). The RCSGs were Asian/Indian, White, Coloured and Black, with Coloured referring to individuals of mixed origins including Asian, European, African or any other heritage. A three-stage probability sample design was used. The primary stage stratified by census enumerator areas (EA). A probability sample of households (that excluded prisons, hospitals and military barracks) and hostel quarters (single-sex migrant labour accommodation) was then selected from each EA. One adult was randomly selected from each household to be included in the sample. Of these, questionnaires were adequately completed for 98.1% of the interviewed individuals, resulting in a final sample size of 4351 study participants aged 18 years and older. The present study extracted data regarding those individuals who were aged 18 to 30 years (inclusive), with the aim of addressing comorbid psychopathology and substance use in young adults. This resulted in a sub-sample size of 1766.

2.2. Instruments

The mental health of each selected individual was assessed using the lay-administered World Mental Health (WMH) Composite International Diagnostic Interview Version 3 (CIDI 3.0) (Kessler & Ustun, 2004), providing both Diagnostic and Statistical Manual-Version IV (DSM IV) and International Classification of Diseases-Version 10 (ICD-10) psychiatric diagnoses for lifetime and last 12-months. Since the CIDI had not previously been used in a South African population sample, parallel validation interviews were conducted by a clinician who was blind to the CIDI diagnoses, on 100 study participants (Williams et al., 2004). Some CIDI questions were modified, and additional questions were included, to suit the South African context. The interview questions were translated from English into six of the 11 official languages in South Africa, to enable respondents to communicate in their mother tongue.

2.3. Procedure

Interviewers were trained to use the CIDI and become fieldworkers, operating in conjunction with fieldwork supervisors to identify and select potential subjects. The scheduled face-to-face interview

was completed by the fieldworker, usually at the home of the participant, after informed consent had been obtained from the subject. Interviews were conducted in seven of the 11 official languages of South Africa, namely English, Afrikaans, isiXhosa, isiZulu, seSotho, Northern Sotho and seTswana. The duration of interviews averaged three hours. In the event of an interview not being completed in one sitting, a second interview was scheduled and conducted.

2.4. Measures

The pencil-and paper version of the CIDI was administered to all study participants. It elicited lifetime and 12-month occurrence for major depression (MD), panic disorder, social phobia, agoraphobia, generalised anxiety disorder (GAD), intermittent explosive disorder (IED), suicidality, substance use and post-traumatic stress disorder (PTSD), while personality disorders and psychoses were screened for. Anxiety disorders included panic disorder, generalised anxiety disorder (GAD) with hierarchy, social phobia, agoraphobia, and PTSD. A summary category was created for 'any anxiety disorder or mood disorder'. Diagnoses of mood (namely, major depression) and anxiety disorders were selected for analyses in the present study (Tables 2, 3 and 4), thus excluding intermittent explosive disorder, suicidality and those disorders that were screened for (personality disorders and psychoses).

Basic sociodemographic information was elicited, including both time-fixed (age, gender and RCSG) and time-varying factors (highest educational level, marital status, employment, income and urbanicity). Income was defined as the participant's personal earnings from employment in the past 12 months, before taxes, and excluded income from investments or pensions. Participants also answered questions regarding their own substance use, including use of tobacco, alcohol, cannabis, extra-medical drugs (including non-medical use of sedatives, tranquilisers, stimulants, analgesics, or any other psychoactive over-the-counter compounds) and any other drugs (including cocaine, LSD, heroin, opium or glue). Tobacco smokers were defined as those who reported having smoked more than 100 cigarettes in their lifetime. Alcohol use was defined as ever having had a drink of alcohol. In cases where the latter question was unanswered and/or missing, participants who had recorded an age

at which they had had their first drink, were also defined as having used alcohol. Cannabis users, users of other drugs, and users of extra medical drugs were defined as those who answered 'yes' to ever having used those drugs.

2.5. Data analyses

Data were analysed using Stata Version 11.0 (2007). All reported analyses took into account the survey design based on person-level weights, and incorporated sample selection, non-response and post-stratification factors. All statistical tests were two-sided at α=0.05.

Descriptive statistics were generated, providing mean age, and proportions for categorical data. The prevalence of the demographic and socioeconomic variables was examined and stratified, and presented by substance use categories (tobacco, alcohol, cannabis, other drugs, extra-medical drugs). Differences between the proportions were tested with the chi-squared test, and p-values reported to compare demographic and socioeconomic characteristics by substance use. The prevalence and 95% confidence intervals of lifetime and 12-month DSM-IV disorders were stratified by substance use and again p-values from chi-squared tests for proportions were reported, with prevalence of comorbidity reported for specific forms of psychopathology in relation to specific substances of use. To look at the associations between DSM-IV disorders (both lifetime and 12-month) and substance use, regression analyses were conducted, calculating prevalence odds ratios with p-values and 95% confidence intervals, including adjustment for age (as a continuous variable) and gender.

3. Results

The study sample consisted of 1766 males and females. These study participants comprised a subset of the SASH survey sample (n=4351), and consisted of all the SASH survey participants aged 18 to 30 years (Mean age 23.6 years; 95% CI 23.4-23.8).

Table 1 summarises the prevalence of substance use in terms of the selected demographic factors. This table indicates that 27.4% of the sample had smoked 100 or more cigarettes in their

lifetime, 38.7% had ever used alcohol, 10.7% had ever used cannabis, 2.7% had used other substances such as cocaine, heroin, opium, glue, LSD or peyote, and 20.6% had used sedatives, tranquilisers, stimulants or analgesics for non-medical use (extra-medical drugs). Significantly more males than females smoked cigarettes ($p<0.001$) and significantly fewer Blacks smoked cigarettes compared with the other RCSGs ($p<0.001$). Smokers were also more likely to be employed ($p<0.001$) and to live in urban environments ($p=0.006$).

A larger proportion of males used alcohol compared with females ($p<0.001$), and a significantly smaller proportion of Indians/Asians used alcohol compared with the other RCSGs ($p<0.001$). Significantly more alcohol users were employed ($p<0.001$), and lived in urban environments ($p=0.003$).

The proportion of cannabis users differed statistically significantly by gender ($p<0.001$), RCSG ($p<0.001$), highest educational level ($p=0.020$), employment status ($p=0.003$) and urbanicity ($p<0.001$). Significantly more males than females used cannabis ($p<0.001$). A larger proportion of Whites had ever used cannabis compared with the other RCSGs. The highest proportions of cannabis users were reported for those who had no formal education (21.6%) and those who had tertiary education (16.8%), suggesting a bimodal distribution. A significantly larger proportion of cannabis users was unemployed and lived in rural environments.

A larger proportion of males had ever used drugs such as cocaine, heroin, opium, glue, LSD, and/or peyote) ($p<0.001$) while the proportion of Blacks who used these substances was significantly smaller than the proportions of other RCSGs who used these substances ($p=0.004$). A significantly larger proportion of extra-medical substance users lived in urban environments ($p=0.010$) compared with the proportion who lived in rural environments.

Table 2 lists the prevalence odds ratios of mental disorders by substance of use. In the total sample, the odds of any lifetime anxiety disorder were 14.7, and 19.7 for any lifetime anxiety or mood disorder. The odds of any 12-month anxiety or mood disorder were 10.3 while for the total sample, the odds of having any 12-month anxiety disorder was 7.1. The prevalence odds ratios of lifetime

anxiety disorders in the sample was lowest for panic disorder (0.7) and highest for agoraphobia(11.1), while the prevalence odds of 12-month anxiety disorders was lowest for PTSD (0.3) and highest for agoraphobia (5.1). The prevalence odds were 8.6 for lifetime major depression and 4.3 for 12-month major depression.

Compared with non-tobacco users, tobacco users had a significantly higher likelihood of lifetime social phobia (OR=5.1; p=0.011), and major depression (OR=12.1; p=0.027), and had significantly higher prevalence odds of 12-month generalised anxiety disorder (OR=1.6; p=0.005), major depression (OR=7.0; p=0.037) and any anxiety or mood disorder (OR=14.7; p=0.004). Alcohol users differed significantly from non-alcohol users with respect to the prevalence of lifetime social phobia, PTSD, major depression and any anxiety or mood disorder; and alcohol users differed significantly from non-alcohol users with respect to the prevalence of 12-month PTSD, major depression and any anxiety or mood disorder. Those who had ever used cannabis differed significantly from those who had never used cannabis with respect to the prevalence of lifetime social phobia, PTSD, major depression, and 12-month generalised anxiety disorder, PTSD, major depression and any anxiety or mood disorder. Users of other drugs differed significantly from non-users with respect to the prevalence of lifetime PTSD, major depression and any anxiety or mood disorder, and to 12-month major depression and any anxiety or mood disorder. The proportion of individuals who had ever used extra-medical substances differed significantly from that of non-users of extra-medical drugs with respect to the prevalence of lifetime panic disorder, major depression and any anxiety or mood disorder, and 12-month panic disorder.

Table 3 presents associations between any anxiety or mood disorders and substance use in general. Most of these associations were significant after adjustments were made for age and gender (Table 4). It is evident from Tables 3 and 4 that the odds of comorbid psychopathology are increased in the presence of substance use compared with the odds of psychopathology in the absence of substance use. For example, the odds of having any lifetime anxiety or mood disorder was 1.4 with use of tobacco and extra-medical substance use, 1.6 with use of alcohol or cannabis, and 3.2 with use of other substances. The equivalent odds on adjustment for age and gender were 2.2 and 1.5 for

tobacco and extra-medical substance use respectively ,2.1 and 2.2 for alcohol and cannabis use, and 4.0 for other substance use. Similarly, the odds of a 12-month mood or anxiety disorder, on adjustment for age and gender, were 1.4 for extra-medical substance use, 2.4 for alcohol use, 3.8 for tobacco use, and 4.1 and 4.7 for cannabis and other substance use respectively.

On adjustment for age and gender, there was approximately a twofold increased likelihood of lifetime psychopathology, and a threefold increased likelihood of 12-month psychopathology in tobacco users versus non-tobacco users. Tobacco users had a six- to sevenfold increased likelihood of 12-month panic or generalised anxiety disorder over non-tobacco users, and a 5-fold increased likelihood of 12-month major depression. The increased likelihood of lifetime and 12-month PTSD in alcohol, cannabis and other drug users, the increased likelihood of 12-month major depression in cannabis and other drug users, and the increased likelihood of lifetime and 12-month panic disorder in extra-medical users were significant.

It is also notable that, on adjustment for age and gender, lifetime generalised anxiety disorder (GAD) was not significantly associated with any of the substances of use examined, while lifetime agoraphobia, panic disorder, PTSD and social phobia were associated with only some of the selected substances of use. Similarly, with regards to 12-month disorders, the specific disorders were significantly associated with certain, and not all, the selected substances of use. Both lifetime and 12-month major depression were significantly associated with all (barring one) the selected substances of use.

Overall comorbidity rates in the SASH sample were as follows (percentages adjusted for survey weighting with 95% CIs): For any lifetime substance use and any DSM IV disorder 21.3% (CI 18.8-23.9); For any lifetime substance use disorder and any anxiety or depression disorder 4.0% (CI 2.6-6.1); For any 12-month substance use and any DSM IV disorder 11.5% (CI 9.2-14.2); For any 12-month substance use disorder and any anxiety or depression disorder 1.6% (CI 1.0-2.7).

4. Discussion

The main findings of the study were that, in young adults 1) substance users were more likely than non-substance users to be male, White, employed and living in urban environments, 2) lifetime and 12-month anxiety or mood disorder was more likely to occur in substance users than in non-users of substances, and 3) strengths of association between psychopathology and substances of use were higher in relation to specific psychopathology (for example PTSD) and specific substances of use (for example, cannabis and alcohol) .

Overall, the results obtained concur with previous findings that males were more likely than females to smoke (McGee et al., 2000), and to have been regular users of alcohol (Steinhausen & Metzke, 2003) and other drugs. These results possibly reflect the stereotypical norms of male socialisation with regards to cigarette smoking and use of alcohol. However, recent evidence suggests that, as traditional gender roles start to equalise, prevalence of female substance use might approach that of males, with potentially similar consequences regarding substance-related morbidity (Seedat et al., 2009).

Employed individuals were more likely to use substances, possibly reflecting greater access to disposable income to purchase substances, compared with unemployed individuals. However, substance users did not differ significantly from non-substance users with respect to income, thus suggesting that factors other than economic resources and linked to employment status, such as access to particular social networks, may also be operative.

Blacks were the least likely of the RCSGs to smoke cigarettes suggesting that maybe there was a protective factor(s) against cigarette smoking among the Blacks in this sample, or a potentially increased rate of cigarette smoking in the non-Black population, or a link between being Black and being unemployed. Similarly, individuals of Indian or Asian origin were the least likely to use alcohol, cannabis or any substances other than cigarettes. These findings concur with that of studies reported by Rodriguez et al. (1999) that, for example, found associations between unemployment and substance abuse, but also demonstrated differences between population groups in terms of the impact

that factors such as gender, marital status, employment status, job satisfaction and educational level had on health and wellbeing. Other reports from the SASH study showed that there were marked racial differences on all indicators of economic status including education, income, employment, and ownership of material resources (Jackson et al., 2010). The latter authors suggested that it might be important to distinguish between minority status and racial-ethnic groups when assessing the impact of sociodemographic factors on the mental health of individuals in South Africa.

Substance users in the SASH sample were more likely than non-substance users to have had lifetime or 12-month anxiety disorders or major depression, irrespective of the choice of substance use (Table 2). In addition, the results in the current study indicated some statistically significant associations between psychopathology and substance use, irrespective of the substances of use (Table 4). These findings echo those of several earlier studies reviewed by Saban and Flisher (2010) that have indicated increased risk of psychiatric disorder with substance use (Saban & Flisher, 2010). The trends in this younger adult sample are also similar to those in the National Comorbidity Survey-Replication (NCS-R), with the prevalence of the anxiety disorders exceeding that of the mood disorders (Kessler et al., 2005). Further, the results similarly concur with the findings of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (Grant et al., 2004) with the odds ratios of associated specific lifetime and 12-month psychiatric diagnoses and substance use largely exceeding 1.0.

More specifically, the results indicated that illicit substances such as cannabis had a manifold increased risk of psychopathology with adjustment for age and gender. The Australian National Survey of Mental Health and Well-being (NSMHWB) reported similar findings in relation to adult anxiety disorders (OR=1.2, 2.8 and 2.6 for cannabis use, abuse and dependence respectively) (Degenhardt et al., 2001). It is thus important that the risks of psychopathology with cannabis use be emphasised, particularly in communities where exposure to cannabis use is high. It is also important that the factors that place individuals at risk of cannabis use are identified and addressed, both to protect against cannabis use, and to decrease the risk of associated psychopathology.

The results indicated relatively high increased odds of lifetime and 12-month PTSD, particularly when PTSD was comorbid with alcohol or cannabis. Earlier studies with substance-using inpatients and war veterans also provided evidence for a strong association between PTSD and substance use and related disorders (Triffleman et al., 1995; McFall et al., 1991). However, these studies have cautioned that the associations be considered with particular reference to the role of trauma in more general family or social dysfunction. Thus, it might be necessary to identify the factors that predispose individuals with PTSD diagnoses to substance use, and particularly alcohol and cannabis use, and to identify the factors that increase the risk of PTSD in substance users (Cacciola et al., 2009).

The limitations of the SASH study should, however, be recognised when interpreting these results. For example, firstly, the SASH sample excluded individuals who were in prison, hospital or mental institutions, or who lived on military bases. Thus psychiatric disorders or substance use pertinent to these categories of individuals, would have been underestimated or excluded from the sample. These include, for example, antisocial personality disorders and available substances of use in the prison population, psychiatric or substance use diagnoses that might have precipitated admission in hospital or mental institution patients, and PTSD that might have been more prevalent in soldiers than in the non-military community. Secondly, the SASH survey assumed equal chance of representation of mentally ill and healthy subjects in the sample, even though individuals with psychopathology are known to be less likely than those without psychopathology to be willing participants in surveys, particularly when those surveys relate to mental illness (Tomlinson et al., 2009, citing Kessler, Wittchen and Abelson, 1998). These are factors that might have skewed the prevalence of psychopathology in favour of mentally-healthy individuals, and provided an under-estimate of substance use. Thirdly, the SASH data excluded certain psychiatric diagnoses such as bipolar disorder, oppositional defiant disorder, conduct disorder, attention deficit hyperactivity disorder, obsessive compulsive disorder, specific phobia and separation anxiety disorder, thus limiting the associations between psychopathology and substance use that could be examined. Fourthly, the cross-sectional nature of the sample did not permit identification of causative factors in the

associations, or the temporal order of co-occurring psychopathology and substance use. Fifthly, the SASH data relied on self-reports. The reliability of the information obtained might thus have been compromised if, for example, use of substances was under- or over-reported, particularly since this information was not verified with biomarkers. Lastly, the statistical analyses for this study involved multiple comparisons between variables, suggesting that the statistically significant results might have been chance findings and, thus, subject to error. This error could have benefitted from adjustment using a method such as the Dunn-Bonferroni correction. However, the Dunn-Bonferroni correction was not applied in the study since an inherent limitation of the method is to increase the probability of false negative results, thus reducing statistical power in the study.

In conclusion, the results obtained have highlighted the prevalence of substance use in young adults, with particular reference to sociodemographic factors and the most commonly-occurring psychiatric diagnoses, and have provided compelling evidence for an association between psychopathology and substance use.

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Contributors

All the authors participated in the development of the study and/or the preparation of the manuscript. All the authors have approved the final manuscript. Authors DJS and DW were the PIs

for the SASH study, author AS was responsible for drafting the manuscript, authors DJS, NM, LL and DW were involved with revisions of the manuscript, and author AG was responsible for the data analyses. Alan Flisher sadly passed away before completion of the final draft of the manuscript.

Conflict of interest

None

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Table 1

Prevalence of substance use by demographics [%, (95% CI), chi-squared p-value].

		Tobacco		Alcohol		Cannabis		Other substances[a]		Extra-medical substances[b]	
		100+ cigarettes (%)	p-value	Ever (%)	p-value	Ever (%)	p-value	Ever (%)	p-value	Ever (%)	p-value
Total sample		27.4 (24.9-30.1)		38.7 (35.5-41.9)		10.7 (9.0-12.8)		2.7 (1.8-4.0)		20.6 (17.5-24.1)	
Age	Mean (95% CI) 23.6 (23.4-23.8)									20.6 (17.5-24.1)	
Gender	Males	44.9 (40.2-49.8)	<0.001	54.0 (49.8-58.1)	<0.001	17.7 (14.5-21.6)	<0.001	4.2 (2.5-7.0)	0.001	21.4 (17.2-26.4)	0.497
	Females	9.8 (7.5-12.6)		22.7 (19.4-26.4)		3.6 (2.5-5.2)		1.1 (0.6-1.9)		19.8 (16.7-23.4)	
RCSG	Black	23.7 (21.2-26.3)	<0.001	34.0 (30.5-37.7)	<0.001	9.3 (7.5-11.4)	<0.001	2.1 (1.3-3.4)	0.004	21.2 (18.2-14.5)	0.416
	White	47.7 (39.4-56.2)		67.4 (57.2-76.2)		25.4 (19.7-32.0)		6.7 (3.3-13.4)		13.8 (6.8-26.2)	
	Coloured	44.0 (30.1-58.9)		59.3 (46.9-70.6)		11.2 (4.4-25.8)		5.1 (2.6-9.5)		25.6 (11.4-48.0)	
	Indian/Asian	32.0 (21.9-44.2)		26.1 (19.1-34.6)		6.5 (3.9-10.6)		0		13.4 (5.6-28.7)	
Education	None	40.8 (21.9-62.8)	0.152	55.9 (34.5-75.3)	0.574	21.6 (5.6-56.4)	0.020	0	0.094	11.6 (4.0-29.4)	0.482
	Grade 1-7	35.8 (28.3-44.2)		37.7 (29.7-46.5)		11.9 (7.0-19.4)		2.0 (0.6-6.8)		19.7 (12.3-29.9)	
	Grade 8-11	26.9 (23.2-31.0)		38.2 (33.8-42.8)		10.4 (7.9-13.6)		3.5 (1.9-6.5)		18.8 (14.7-23.6)	
	Matric	25.1 (20.7-30.0)		37.9 (33.3-41.8)		7.6 (5.3-10.7)		1.1 (0.5-2.7)		21.3 (16.5-27.1)	
	Matric +	29.5 (23.0-37.1)		40.3 (33.1-48.1)		16.8 (12.4-22.5)		4.3 (2.4-7.8)		24.3 (18.2-31.6)	
Marital status	Not married	25.9 (23.0-29.1)	0.073	38.8 (34.5-42.8)	0.684	10.0 (8.0-12.5)	0.289	2.7 (1.7-4.2)	0.978	19.8 (16.6-23.4)	0.241
	Married	31.9 (26.6-37.7)		37.3 (31.4-43.5)		12.8 (8.8-18.2)		2.6 (1.3-5.4)		23.1 (17.7-29.6)	
Employment	Employed	40.9 (33.8-48.4)	<0.001	56.1 (49.6-62.4)	<0.001	16.9 (12.5-22.4)	0.003	4.1 (2.4-7.1)	0.120	25.9 (19.3-33.9)	0.061
	Unemployed	23.9 (21.2-26.8)		33.8 (30.3-37.5)		9.1 (7.1-11.5)		2.3 (1.4-3.8)		19.2 (16.1-22.8)	
Income [c]	Zero	23.2 (19.3-32.1)	0.912	39.9 (31.9-48.5)	0.715	12.3 (7.7-19.2)	0.167	3.7 (1.2-11.2)	0.401	19.4 (13.5-27.2)	0.404
	Low	26.6 (31.7-32.1)		36.1 (31.7-40.6)		8.4 (6.0-11.7)		3.3 (1.7-6.6)		21.6 (17.6-26.3)	
	Low-average	28.5 (23.2-34.6)		42.5 (35.6-49.6)		7.3 (4.5-11.7)		0.6 (0.1-4.4)		15.8 (11.1-22.1)	
	High-average	28.7 (23.2-34.9)		37.6 (31.1-44.6)		12.4 (8.7-17.4)		3.5 (1.6-7.8)		20.5 (15.4-26.8)	
	High	28.2 (22.4-34.8)		38.3 (31.4-45.8)		13.0 (9.3-17.9)		1.8 (0.7-4.4)		23.1 (17.7-29.6)	
Urbanicity	Rural	22.3 (17.9-27.4)	0.006	31.8 (26.5-37.7)	0.003	13.6 (11.0-16.8)	<0.001	1.7 (0.8-3.6)	0.133	15.8 (12.3-20.1)	0.010
	Urban	30.8 (27.9-33.8)		42.7 (38.9-46.6)		6.2 (4.7-8.2)		3.3 (2.2-5.2)		23.8 (19.5-28.7)	

[a] cocaine, heroin, opium, glue, LSD, peyote

[b] non-medical use of sedatives, tranquilisers, stimulants, analgesics

[c] personal earnings from employment in the past 12 months, before taxes, excluding pensions and investments

Table 2

Prevalence of anxiety and mood disorders by substance use [%, (95% CI), chi-squared p-value].

		TOTAL	Tobacco Use		Alcohol Use		Cannabis		Other substances[a]		Extra-medical substances[b]	
		Prevalence (95% CI)	100+ cigarettes % (CI)	p-value	Ever % (CI)	p-value	Ever % (CI)	p-value	Ever % (CI)	p-value	Ever % (CI)	p-value
Lifetime DSM-IV Disorders												
Anxiety Disorders	Panic Disorder	0.7 (0.3-1.3)	1.1 (0.4-2.8)	0.211	1.0 (0.4-2.3)	0.287	0.8 (0.1-5.8)	0.815	1.8 (0.2-12.1)	0.321	2.2 (1.0-5.1)	<0.001
	GAD with hierarchy	1.1 (0.7-1.7)	1.7 (0.9-3.5)	0.102	1.3 (0.6-2.5)	0.485	2.4 (0.9-6.4)	0.080	1.9 (0.3-13.3)	0.536	1.7 (0.7-4.0)	0.189
	Social Phobia	2.8 (2.0-4.1)	5.1 (2.7-9.6)	0.011	4.4 (2.4-8.1)	0.044	5.9 (2.7-12.5)	0.021	5.8 (0.8-33.4)	0.438	4.1 (2.0-8.3)	0.120
	Agoraphobia	11.1 (9.2-13.4)	10.0 (6.8-14.5)	0.498	12.2 (9.1-16.1)	0.387	8.8 (5.5-13.7)	0.276	4.0 (0.9-16.5)	0.142	10.8 (8.1-14.3)	0.816
	PTSD	4.5 (1.0-2.2)	2.1 (1.0-4.4)	0.230	2.6 (1.5-4.5)	0.004	5.1 (2.0-12.2)	0.003	10.6 (3.9-26.1)	<0.001	1.3 (0.4-3.6)	0.758
	Any anxiety disorder	14.7 (12.5-17.2)	16.4 (11.8-22.2)	0.388	17.7 (13.5-22.9)	0.063	17.7 (10.9-27.4)	0.405	24.1 (9.9-48.1)	0.219	16.4 (12.7-20.9)	0.312
Mood Disorders	Major Depression	8.6 (7.1-10.3)	12.1 (8.4-17.1)	0.027	11.8 (9.0-15.5)	0.001	15.4 (10.1-22.7)	0.003	27.2 (10.8-53.6)	0.009	12.8 (9.1-17.7)	0.010
Any anxiety or mood disorder		19.7 (17.3-22.3)	23.3 (18.0-29.8)	0.092	24.1 (19.7-19.1)	0.007	26.8 (19.4-35.8)	0.054	42.5 (21.0-67.3)	0.021	24.4 (19.8-19.6)	0.027
12-month DSM-IV Disorders												
Anxiety Disorders	Panic Disorder	0.5 (0.2-1.1)	1.1 (0.4-2.8)	0.068	0.7 (0.3-1.9)	0.415	0.8 (0.1-5.8)	0.594	1.8 (0.2-12.1)	0.199	2.2 (1.0-5.1)	<0.001
	GAD with hierarchy	0.7 (0.4-1.3)	1.6 (0.8-3.4)	0.005	1.2 (0.6-2.5)	0.062	2.4 (0.9-6.4)	0.007	1.9 (0.3-13.3)	0.295	0.9 (0.3-2.8)	0.691
	Social Phobia	1.9 (1.3-2.8)	2.9 (1.2-6.5)	0.192	2.7 (1.3-5.3)	0.189	4.3 (1.6-10.5)	0.042	4.8 (0.5-35.8)	0.361	3.3 (1.5-7.1)	0.067
	Agoraphobia	5.1 (3.9-6.6)	4.9 (2.9-8.2)	0.872	4.9 (3.1-7.9)	0.898	5.0 (2.5-9.8)	0.958	0	-	4.1 (2.8-6.0)	0.259
	PTSD	0.3 (0.2-0.7)	5.4 (0.2-1.9)	0.296	0.6 (0.2-1.6)	0.030	1.4 (0.4-4.9)	0.006	1.9 (0.3-12.8)	0.055	0	-
	Any anxiety disorder	7.1 (5.5-9.0)	8.8 (5.8-13.2)	0.102	8.1 (5.3-12.3)	0.340	10.1 (5.5-17.9)	0.181	10.4 (2.5-34.3)	0.532	8.1 (5.3-12.1)	0.384
Mood Disorders	Major Depression	4.3 (3.3-5.6)	7.0 (4.4-10.9)	0.037	6.1 (4.3-8.7)	0.012	11.0 (6.9-17.2)	<0.001	21.0 (7.2-47.5)	0.002	6.7 (4.2-40.7)	0.059
Any anxiety or mood disorder		10.3 (8.5-12.5)	14.7 (10.7-19.8)	0.004	12.9 (9.9-16.8)	0.019	19.6 (13.3-27.7)	0.001	26.6 (10.5-52.6)	0.025	12.9 (9.6-17.2)	0.086

[a] cocaine, heroin, opium, glue, LSD, peyote

[b] non-medical use of sedatives, tranquilisers, stimulants, analgesics

Table 3

Crude associations between anxiety and mood disorders, and substance use, using regression analyses [OR, (95% CI), p-value].

		Tobacco Use		Alcohol Use		Cannabis		Other substances[a]		Extra-medical substances[b]	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Lifetime DSM-IV Disorders											
Anxiety Disorders	Panic Disorder	2.5 (0.6-8.4)	0.223	2.1 (0.5-8.3)	0.298	1.3 (0.2-11.0)	0.815	2.8 (0.3-25.1)	0.342	9.3 (2.4-35.5)	0.001
	GAD with hierarchy	2.2 (0.8-5.8)	0.110	1.4 (0.6-3.4)	0.487	2.7 (0.8-8.9)	0.093	1.9 (0.2-15.6)	0.543	1.9 (0.7-5.2)	0.196
	Social Phobia	2.7 (1.2-5.8)	0.014	2.5 (1.0-6.0)	0.050	2.5 (1.1-5.4)	0.025	2.2 (0.3-16.5)	0.449	1.7 (0.9-3.2)	0.124
	Agoraphobia	0.9 (0.5-1.4)	0.499	1.2 (0.8-1.8)	0.388	0.7 (0.4-1.3)	0.278	0.3 (0.1-1.6)	0.162	1.0 (0.7-1.4)	0.816
	PTSD	1.8 (0.7-4.6)	0.236	3.8 (1.5-9.7)	0.007	5.2 (1.6-16.8)	0.006	9.8 (2.9-32.5)	<0.001	0.8 (0.2-2.8)	0.758
	Any anxiety disorder	1.2 (0.8-1.8)	0.388	1.5 (1.0-2.2)	0.064	1.3 (0.7-2.3)	0.406	1.9 (0.7-5.3)	0.226	1.2 (0.9-1.6)	0.312
Mood Disorders	Major Depression	1.8 (1.1-2.9)	0.029	1.9 (1.3-2.8)	0.001	2.2 (1.3-3.6)	0.003	4.3 (1.3-13.7)	0.016	1.8 (1.2-2.9)	0.011
Any anxiety or mood disorder		1.4 (0.9-1.9)	0.092	1.6 (1.1-2.1)	0.008	1.6 (1.0-2.5)	0.056	3.2 (1.1-8.7)	0.028	1.4 (1.0-1.9)	0.027
12-month DSM-IV Disorders											
Anxiety Disorders	Panic Disorder	4.1 (0.8-20.8)	0.091	1.9 (0.4-9.2)	0.423	1.8 (0.2-16.1)	0.599	3.8 (0.4-35.7)	0.232	49.5 (9.4-259.4)	<0.001
	GAD with hierarchy	4.5 (1.4-13.8)	0.010	2.9 (0.9-9.0)	0.074	4.9 (1.4-17.3)	0.015	2.9 (0.3-24.8)	0.318	1.3 (0.3-5.2)	0.691
	Social Phobia	1.9 (0.7-5.0)	0.199	1.9 (0.7-5.0)	0.196	2.7 (1.0-7.4)	0.050	2.7 (0.3-26.6)	0.381	2.2 (0.9-5.0)	0.073
	Agoraphobia	1.0 (0.6-1.6)	0.872	1.0 (0.5-1.8)	0.898	1.0 (0.6-2.1)	0.958	-	-	0.8 (0.5-1.2)	0.260
	PTSD	2.3 (0.5-11.3)	0.309	4.6 (1.0-20.7)	0.047	7.2 (1.4-36.3)	0.017	6.8 (0.7-64.5)	0.096	-	-
	Any anxiety disorder	1.4 (0.9-2.2)	0.104	1.3 (0.7-2.3)	0.341	1.6 (0.8-3.1)	0.184	1.6 (0.4-6.4)	0.535	1.2 (0.8-1.9)	0.385
Mood Disorders	Major Depression	2.2 (1.1-4.6)	0.034	2.0 (1.2-3.5)	0.013	3.4 (1.9-6.4)	<0.001	6.7 (1.7-25.6)	0.007	1.9 (1.0-3.8)	0.063
Any anxiety or mood disorder		1.8 (1.2-2.7)	0.004	1.6 (1.1-2.3)	0.019	2.4 (1.4-4.0)	0.001	3.3 (1.1-9.8)	0.033	1.9 (1.0-2.0)	0.087

[a] cocaine, heroin, opium, glue, LSD, peyote

[b] non-medical use of sedatives, tranquilisers, stimulants, analgesics

Table 4

Adjusted associations between anxiety and mood disorders, and substance use using regression analyses. [†] [OR, (95% CI), p-value]

		Tobacco Use		Alcohol Use		Cannabis		Other substances[a]		Extra-medical substances[b]	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Lifetime DSM-IV Disorders											
Anxiety Disorders	Panic Disorder	3.1 (0.7-13.7)	0.129	2.5 (0.8-7.8)	0.0124	1.4 (0.2-11.3)	0.731	3.1 (0.3-33.5)	0.349	9.5 (2.5-36.5)	0.001
	GAD with hierarchy	3.0 (1.0-9.4)	0.061	1.5 (0.6-3.8)	0.373	3.2 (0.9-12.2)	0.082	2.0 (0.2-17.6)	0.516	1.87 (0.7-5.1)	0.214
	Social Phobia	3.9 (1.5-10.1)	0.006	3.0 (1.1-7.9)	0.030	2.9 (1.1-7.5)	0.025	2.3 (0.3-21.6)	0.460	1.7 (0.9-3.4)	0.113
	Agoraphobia	1.2 (0.8-2.1)	0.390	1.6 (1.0-2.5)	0.044	1.0 (0.6-1.8)	0.997	0.4 (0.1-2.0)	0.266	1.0 (0.7-1.4)	0.966
	PTSD	2.7 (0.8-9.1)	0.119	5.2 (2.0-13.4)	0.001	8.1 (2.3-29.2)	0.002	12.5 (3.9-40.6)	<0.001	0.8 (0.2-2.8)	0.712
	Any anxiety disorder	1.8 (1.1-2.9)	0.011	2.0 (1.3-3.2)	0.004	1.7 (0.9-3.3)	0.087	2.4 (0.8-6.8)	0.108	1.2 (0.9-1.7)	0.247
Mood Disorders	Major Depression	3.0 (1.7-5.4)	<0.001	2.7 (1.8-3.9)	<0.001	3.1 (1.8-5.5)	<0.001	5.6 (17-18.1)	0.005	1.8 (1.2-2.0)	0.011
Any anxiety or mood disorder		2.2 (1.4-3.2)	<0.001	2.1 (1.5-3.1)	<0.001	2.2 (1.3-3.6)	0.003	4.0 (1.5-11.1)	0.008	1.5 (1.1-2.0)	0.020
12-month DSM-IV Disorders											
Anxiety Disorders	Panic Disorder	6.9 (1.5-31.7)	0.014	2.3 (0.6-8.5)	0.215	2.1 (0.3-16.3)	0.471	4.3 (0.4-52.8)	0.247	50.5 (9.5-268.4)	<0.001
	GAD with hierarchy	6.2 (1.5-25.7)	0.012	3.1 (0.9-10.3)	0.065	5.5 (1.2-25.4)	0.028	2.9 (0.3-27.6)	0.356	1.3 (0.3-5.1)	0.723
	Social Phobia	3.5 (1.0-12.9)	0.059	2.7 (0.9-8.0)	0.066	4.4 (1.5-13.0)	0.009	3.7 (0.3-42.6)	0.296	2.2 (1.0-5.1)	0.063
	Agoraphobia	1.9 (1.1-3.1)	0.016	1.5 (0.7-3.0)	0.289	1.7 (0.7-3.8)	0.216	-	-	0.8 (0.5-1.3)	0.356
	PTSD	3.1 (0.4-24.2)	0.276	5.9 (1.3-27.6)	0.025	10.4 (1.5-70.1)	0.017	7.5 (0.7-75.2)	0.086	-	-
	Any anxiety disorder	2.9 (1.8-4.6)	<0.001	2.0 (1.0-3.8)	0.043	2.6 (1.2-5.6)	0.012	2.2 (0.5-9.9)	0.284	1.3 (0.8-2.0)	0.302
Mood Disorders	Major Depression	4.7 (2.2-10.0)	<0.001	3.0 (1.7-5.4)	<0.001	6.3 (3.0-13.2)	<0.001	10.2 (2.8-37.0)	0.001	1.9 (1.0-3.8)	0.060
Any anxiety or mood disorder		3.8 (2.5-5.8)	<0.001	2.4 (1.5-3.7)	<0.001	4.1 (2.3-7.4)	<0.001	4.7 (1.6-14.4)	0.006	1.4 (1.0-2.1)	0.058

[†] Adjusted for age and gender

[a] cocaine, heroin, opium, glue, LSD, peyote

[b] non-medical use of sedatives, tranquilisers, stimulants, analgesics

CHAPTER 7

Discussion

CHAPTER 7

Discussion

Introduction

The aims of this thesis were i) to examine the association between psychopathology and substance use in adolescents and young adults, ii) to identify the role of demographic and social factors in comorbidity, and iii) to examine the role of sociodemographic factors and comorbid psychopathology in outcomes from substance use inpatient treatment. The objectives were i) to quantify the occurrence of psychopathology, substance use and comorbidity in adolescents and young adults, ii) to identify associations, and measure the strengths of association, between specific forms of psychopathology and the use of specific substances of use, and iii) to identify sociodemographic factors and/or psychopathology that influence substance use inpatient treatment outcomes. The thesis has produced five manuscripts, two of which have been published, and three that are currently in journal review.

This chapter will provide a synopsis of the thesis, highlighting the salient features of comorbidity research and the principal findings of the conducted studies. Specific reference will be made to the aims and objectives of the thesis, and to how the conducted studies addressed knowledge gaps. To avoid repeating contents from the manuscripts in earlier chapters, in its discussion of strengths and limitations, this chapter will concentrate on discussing the strengths and limitations of the thesis as a whole, with reference to the relevant thesis studies when deemed necessary or appropriate. The chapter will conclude with suggestions for continued and future research into comorbid psychopathology and substance use.

Critical issues in comorbid psychopathology and substance use and related research

This thesis has confirmed the burden of mental illness and substance use and the contribution of these to the global burden of diseases (Hoelzer, 2009), highlighting this among adolescents and young adults in Cape Town (in the high schools study), and in South Africa (in the SASH survey). In this respect, mental illness and substance use have been identified as accounting for significant loss of quality life (Desjarlais, 1995), due to their disabling effects on the individuals involved. Mental illness and problematic substance use have been associated with suffering, economic loss, victimisation and discrimination associated with access to housing, employment, treatment and familial support (Kakuma et al., 2010). Problematic use of substances has been associated with sexually risky behaviour (Pahl et al., 2010), sexually transmitted infections such as HIV (Myer et al., 2009b), and scholastic under-achievement and school dropout (Myer et al., 2009a).

The thesis has confirmed the view that comorbid mental illness and substance use is a common co-occurrence (Volkow, 2001), with significant associated social and cost burden (Clark et al., 2009), and has highlighted the increased recent (1986 onwards) interest in epidemiological comorbidity research, particularly with respect to children and adolescents or young adults (Angold, Costello and Erkanli, 1999). In the introductory and literature review chapters, various patterns of associated psychopathology and substance use were identified, together with biological, social, psychological and environmental factors (Weinberg and Glantz, 1999) that appear to play a role in these associations. In addition, pathways that have been suggested to explain the development of associated mental illness and substance use (Chapter 1) were outlined (Degenhardt et al., 2001).

Further issues, pertinent to co-occurring psychopathology and substance use, with implications for comorbidity treatment and research, were highlighted. These have served to provide a comprehensive overview and understanding of comorbid psychopathology and substance use, as well as to identify areas of knowledge where additional information and research are needed. The following points provide a summary of these issues as outlined in the thesis:

i) Problems associated with the definition and diagnosis of "comorbidity" were discussed. This discussion underscored the differences between dealing with well-established disease entities in other areas of medicine, compared with the less well established, and more diffuse disorders ("behavioural and psychological syndromes that are deviant from some standard normality") in psychiatry (Angold et al., 1999: 58). Reasons provided for examining comorbidity included an attempt to understand the development of neuropsychiatric problems and substance use (Volkow, 2001), and the implications that comorbidity have for treatment, management and the provision of related services (Degenhardt et al., 2001).

ii) Research problems were discussed regarding reference to the term "comorbidity" and the use of differing timeframes, suggesting more specific use of terms to distinguish between concurrent, sequential (or successive), or lifetime comorbidity (Degenhardt et al., 2001).

iii) The distinction was made between comorbidity where mental illness is a risk factor for the development of substance use and related disorders, and the potential for substance use to induce mental illness (Schuckit, 2006), highlighting the issue of temporality and causality in comorbidity.

iv) The limited understanding about the nature of, and pathways to, comorbidity, despite its being considered a common occurrence (Volkow, 2001), was emphasised.

v) Mention was made of the sparse reporting of information regarding research on the treatment of comorbidity (Kaminer et al., 2007), and possible reasons for this were suggested.

vi) The need for more studies on the outcomes of treatment for comorbidity were discussed (Landheim et al., 2006), with particular mention of the need for information on the role of comorbid psychopathology and sociodemographics in outcome following substance use treatment (Compton et al., 2003).

vii) The low research output from developing countries compared with that of developed countries was emphasised (de Graft Aikens et al., 2010). Reference was made to the need to increase available data on neuropsychiatric disorders that will facilitate cross-national comparisons of prevalence rates to guide the allocation of resources and the development of interventions. Particular mention was made of the need for increased rigorous research into chronic diseases in African countries, and the WMH SASH initiative.

viii) The importance of examining comorbid psychopathology and substance use in adolescents and young adults was discussed, with reasons including the evidence for increased prevalence of comorbidity in this developmental stage (Deas, 2010), the need for more information on comorbidity amongst community youth (Langenbach et al., 2010), the potential for longer-term follow-up, and the possibility of improved recall compared with older individuals.

Principal study findings and their contribution to comorbidity knowledge gaps

Overall, all the empirical studies in the thesis have contributed to knowledge of comorbid psychopathology and substance use in the following ways:

i) They have highlighted the notion of comorbidity and its relevance in understanding the development of psychopathology and substance use.

ii) They have contributed to the research output and available data on mental illness and substance use from the African continent, from a sub-Saharan African country, and from a developing country.

iii) They have addressed the issue of limited information available on comorbidity in adolescents and young adults by specifically examining associations between psychopathology and substance use in adolescents and adults aged 30 years and younger.

iv) They have provided data regarding the prevalence of psychopathology, substance use, and comorbidity, they have identified associations between psychopathology and substance use, and they have identified the influence of demographic and/or social factors in these associations and in treatment outcomes (the latter in the follow-up study).

More specifically, the principal findings of the individual studies have contributed the following information (Table 1):

i) With regards to high school students in Cape Town, South Africa,

- Cannabis was significantly associated with all three psychopathologies, namely, PTSD, anxiety and depression. Since this was a cross-sectional study, the causal or temporal roles of either the cannabis use or the psychopathology in the comorbidity are unknown. However, this finding

suggests the need to examine the role of cannabis specifically, and mood and anxiety disorders in particular, as risk factors for comorbidity in school-going adolescents in Cape Town.

- Alcohol use was significantly associated with PTSD and depression, once again suggesting that the specific substance use and specific psychopathology be further examined as risk factors for comorbidity.
- Evidence for the association between grade and specific forms of comorbidity (namely PTSD/alcohol/depression; depression/alcohol/cannabis; anxiety/cannabis; depression/inhalants), suggest that there might be factors related to educational level, or possibly age or developmental stage, that influence the association between specific forms of psychopathology and specific substances of use.
- The role of gender in associations between psychopathology and substance use in school-going adolescents was highlighted by evidence for stronger associations between psychopathology and substance use in females than in males.

Furthermore, though not directly linked to the main study objectives, there were other findings that were consistent with the literature and which locate the problem of comorbidity in a local context:

- On average, female students scored higher than male students on depression, anxiety and PTSD scales. This finding seems to suggest that gender might be associated more with the severity of psychopathology rather than having gender as a risk for specific psychopathology. In general, females have been found to be more likely to have anxiety and mood disorders compared with men (Fernander et al., 2006; Seedat et al.,

2009). As such, the gender differences in the scale scores might reflect the increased risk of young female students for depression, anxiety and PTSD compared with males. The severity of psychopathology was not explored specifically, limiting further comment on the association between psychopathology severity and gender.

- Black students had higher mean psychopathology scores than Coloured or White students, suggesting more severe psychopathology in Black students compared with students of other RCSGs, and a possible link between RCSG and severity of psychopathology. However, this finding is probably best viewed with caution. RCSGs are not biological constructs and might thus have no role in the genetic or physiological predisposition of members from a particular RCSG for psychopathology. In addition, RCSG might have no inherent value as a social construct either in relation to the prevalence of psychopathology in these students (Rockett et al., 2009). Within the South African context, however, use of RCSG might still reflect socioeconomic circumstances, historical injustices and human rights violations as a result of earlier Apartheid policies (Stein et al., 2009). Aspects of these policies might have influenced RCSG differences in psychopathology severity, particularly in the Black community who represent the largest proportion of the South African community, and had the largest proportion of individuals disadvantaged by these policies. The SASH survey of adults found lower risks for mental illness in Whites compared with all other RCSGs (Seedat et al., 2009), further suggesting the possibility of RCSG differences in psychopathology prevalence or severity. However, within the context of the high school student study,

reasons for an association between RCSG and mental illness severity remain speculative as this association was not explored specifically.

- As previously mentioned, associations between psychopathology and substance use appeared to be moderated by grade, and weakly influenced by age and gender. These findings suggest differential associations between psychopathology and substance use, possibly moderated by developmental stage. It is also possible that the so-called gender paradox could be operating in these associations (Monshouwer et al., 2006). Thus, if there was an unequal gender distribution for psychopathology [for example, more internalising disorders in females, more externalising disorders in males (Reinherz et al., 2000; de Graaf et al., 2004)] the group with the lower prevalence rate might have an increased severity of disorder.

ii) With regards to the cross-sectional study of inpatient substance users in treatment for their substance use,

- Inpatient substance users in the Cape Town sample were most likely to be male, Coloured, Muslim, with some high school education, never married, living with immediate family members, and unemployed. These factors reflect the demographic profile of the geographical area of the study sites, and the profile of substance users who seek treatment in the study region (SACENDU, 2009). Non--South African studies have similarly reported inpatient substance users being largely male (Marsden et al. 2000; Langenbach et al., 2010). However, these demographic profiles might also reflect patient preferences for varying treatment modalities offered at the different treatment centres.

- Substance use onset occurred on average by age 14.7 years (SD=2.4). This mean age of onset is consistent with that reported in the SASH community survey (van Heerden et al., 2009) that found substance use had usually been commenced by age 17 years. However, age of substance use onset information is subject to patients' ability to recall this information accurately. Furthermore, first substance use has been reported as associated with availability, social circumstances and environmental influences (Degenhardt, 2010; Mayet et al., 2010), and these factors might have played a role in the age of substance use onset. However, this study did not investigate factors that influence initiation of substance use, so the role of substance use availability, social and environmental circumstances in substance use initiation is unknown for this study sample.
- First substances of use were most likely to be cannabis or crystal methamphetamine. As mentioned earlier, this finding might reflect the social and environmental circumstances of the patients involved (Mayet et al., 2010) and substance use availability (Degenhardt, 2010) since both have been shown to be common substances of use in South Africa (Pluddemann et al., 2010; Peltzer et al., 2010). The significance of first substances of use and their role in subsequent substance use might thus need further exploration.
- Most patients were in treatment for heroin or crystal methamphetamine use. Heroin (Marsden et al., 2000) and crystal methamphetamine (Langenbach et al., 2010) have been reported as common primary substances of use in non-South African studies of substance users in substance use treatment. Primary substance use in substance use inpatients

might reflect the predominant substance use trends at a particular time. However, primary substances of use seem to differ according to the treatment facilities and their locations (Langenbach et al., 2010). Primary substance of use might also reflect the ages of inpatients, with relatively older inpatients generally accounting for a larger proportion of patients with primary use of alcohol (SACENDU, 2009).

- Most patients smoked cigarettes every day. This finding reflects a common trend amongst substance users in treatment for substance use other than nicotine (Langenbach et al., 2010).
- Comorbid current (12-month) non-substance related psychopathology was very common (96.8%) and almost entirely previously undiagnosed (95.8%). The most common comorbid psychopathology diagnoses were anti-social personality disorder, conduct disorder, oppositional defiant disorder and depression. Comparable findings were reported in a similar study conducted in Germany (Langenbach et al., 2010), with a predominance of the conduct, anxiety and mood disorders amongst substance users.

iii) With regards to the follow-up of inpatient substance users,

- Males were more likely than females to complete their inpatient substance use treatment. The findings of Grella (2003) and Knight et al. (2001) seem to suggest that females require more support to engage in, and be retained in substance use treatment. In particular, females seem to require assistance in dealing with family needs, events associated with traumatic experiences (Grella, 2003), incarceration and social relationships (Knight et al., 2001).

- Females were more likely than males to have relapsed by 6 months post-treatment. This result is possibly a consequence of incomplete treatment for substance use, a lack of compliance with substance use treatment, or an indication of the need for continuation of care subsequent to completion of inpatient substance use treatment. However, few gender differences have been found with respect to relapse associated with problematic use of alcohol (Walitzer and Dearing, 2006), although female users of substances other than alcohol seem less likely than males to relapse (Walitzer and Dearing, 2006). These authors found that females were more likely to relapse subsequent to negative life experiences while males were more likely to relapse following positive life experiences, suggesting that the females in the inpatient substance users study for this thesis might have had negative affective experiences that could have influenced their relapse, while the negative experiences of the male inpatients at the time were relatively less likely to encourage their relapse.
- Primary users of crystal methamphetamine were more likely than other substance users to drop out of substance use treatment. The significance of this finding has important implications for service provision particularly since use of crystal methamphetamine amongst substance use treatment seekers has surpassed use of other substances in the Western Cape region of South Africa (SACENDU, 2006).
- The lack of significant associations between psychopathology and treatment outcome in this study was surprising in view of the literature (for example, Compton et al., 2003). This finding might be a result of nearly all study participants (96.8%) having at least one comorbid psychiatric

disorder. In addition, the proportion of substance use patients who had at least one psychiatric disorder in this study far exceeded the proportion that has been found in the South African community (namely 21.3% comorbidity for lifetime disorders and 11.5% comorbidity for 12-months disorders in the SASH survey) as well as exceeding the generally accepted proportion of 70% to 80% comorbidity of substance users in treatment (Kaminer et al., 2007). The high proportion of previously undiagnosed comorbid psychiatric disorder in the inpatient substance users might be a reflection of several factors, for example, a) the severity of their substance use, with increased severity being more likely to be associated with psychiatric problems, and the majority of these patients having been diagnosed with a substance dependent disorder, b) the type of substance use being largely illicit and so-called harder drugs (namely heroin and crystal methamphetamine), c) the possibility that the symptoms of the substance use disorder might have masked the symptoms of psychiatric disorder, leading to treatment being sought for substance use rather than psychiatric disorder, and d) possible ignorance on the part of the patients and their families of the role that psychiatric disorder might play in their problematic substance use, particularly when the substance use is viewed by them as the primary problem or disorder.

iv) With regards to the SASH survey,

- There were significant associations between all the mood disorders and substance use.
- Use of substances was associated with an increased likelihood of anxiety or mood disorders.

These findings have identified associations, and the strengths of these associations, between specific forms of psychopathology (anxiety and mood disorders) and using specific substances of use (namely, tobacco, alcohol, cannabis), in the South African community. For example, significant associations between lifetime PTSD and substance use had odds ratios from 5.2 (with respect to alcohol use) to 8.1 (for cannabis use). Comparative odds ratios for 12-month PTSD were 5.9 and 10.4 for alcohol and cannabis use respectively. Similarly, significant associations between lifetime major depression and substance use had odds ratios that ranged from 1.8 for extra-medical substance use to 3.0 for tobacco use, and 5.6 (for use of opiates), while associations between 12-month major depression and substance use ranged from 1.4 for extra-medical substance use to 3.8 for tobacco use and 10.2 for use of opiates and other substances. These findings demonstrate the potential risk of comorbidity in the presence of substance use or psychopathology. Moreover, these findings identify both associations between specific substances and specific forms of psychopathology, as well as illustrating the strengths of these associations. As such, they can inform the development of treatment interventions, and they can guide targeted provision of services to address the phenomenon of comorbidity.

Thesis strengths and limitations

This thesis has made some significant contributions to the understanding of associated psychopathology and substance use within the South African context.

Firstly, in electing to examine associations between psychopathology and substance use, the research for this thesis has addressed a phenomenon which, though regarded as common, is poorly understood, has many questions that remain unanswered, and where research outcomes have often been unclear or inconclusive. In addition, the introductory and literature review chapters of this thesis have highlighted the issues pertinent to the debates regarding the significance of comorbidity (for example, its role in treatment seeking, substance use treatment outcomes), its challenges (for example, how to define comorbidity, diagnosing comorbidity, treatment of comorbid disorders simultaneously rather than in parallel), and areas where important gaps in knowledge occur (for example, which psychiatric disorders are most commonly associated with which substances of use, what are the risk factors associated with comorbidity, what are the temporal associations between comorbid disorders). The thesis has also foregrounded mental illness and substance use, both of which contribute significantly to South Africa's, Africa's, and the global, burden of chronic disease. Moreover, the empirical studies for the thesis (Chapter 3 to 6) investigated adolescents and young adults, thus addressing groups in which information regarding comorbidity has been lacking. In particular, the thesis has provided information about psychopathology in substance users receiving inpatient substance use treatment in Cape Town, thus examining a group that had previously not been investigated for comorbidity in South Africa.

Secondly, the thesis has made both theoretical and practical contributions to available knowledge about associations between psychopathology and substance use. Theoretically the thesis has contributed to the understanding of comorbidity by highlighting the potential role of factors such as school grade in the association between psychopathology and substance use. The thesis has also contributed information regarding factors (such as gender and specific substances of use) that might play a role in outcomes from treatment for inpatient substance use. Further information has been provided by identifying specific

psychopathology in relation to specific substances of use. For example, the high schools study found significant associations between PTSD and tobacco, alcohol, cannabis and inhalant use, between depression and alcohol or cannabis use, and between anxiety and cannabis use. Some findings in this thesis have corroborated the findings in studies completed in other countries [for example, associations between anxiety or depression and alcohol use (Merikangas et al., 1994; Schmidt, 1995)], highlighting the possibility that comorbid psychopathology and substance use might transcend geographic location. On a practical level, this thesis has contributed to the international database of studies on associated psychopathology and substance use, and, in particular, has increased research output from South Africa with respect to such comorbidity.

Thirdly, a major strength of this thesis lies in its providing information about comorbidity from differing perspectives. The thesis includes two representative studies of community members, namely high school students in Cape Town, and the South African national community, and two studies of inpatient substance users. The thesis thus investigates comorbid psychopathology and substance use in both community and treatment samples.

The approach of using different studies to investigate comorbidity provides an opportunity for different aspects of comorbidity to be addressed and compared. In this thesis these aspects of comorbidity have included identifying factors pertinent to school-going adolescents in the high schools study (for example, school grade) and, in the baseline treatment centres study, factors pertinent to being in treatment (for example, gender, specific comorbid psychopathology). Aspects of comorbidity that can be compared across studies include the occurrence and nature of comorbidity (for example, higher rates of comorbidity in substance users in treatment for substance use than in the high schools and SASH community samples; consistent associations between anxiety/depression and substance use, or treatment outcome across the studies), most common types of substances of use, and the strengths of association

between substances of use and comorbid psychopathology. The different samples could also allow one to generalise to other similar samples, bearing in mind the limitations of sampling in each particular study sample.

By examining both treatment and community samples, the research has simultaneously highlighted areas of both community and clinical research that require further investigation or attention. For example, it would be useful to track the patterns of substance use and psychopathology over time in the high school students and general population (SASH) sample. The data from such research could be used to identify factors that influence comorbidity as well as to inform the development of interventions to decrease the risk of either psychopathology or substance use or comorbidity. Further research could also examine factors that influence treatment initiation and retention in prospective substance use inpatients, and identify factors that influence relapse or re-entry into substance use treatment.

Moreover, secondary analyses of datasets for the high schools study and the SASH study provided the researcher access to datasets that were of a magnitude that exceeded the collection abilities of a single researcher constrained by the cost and time limits of a doctoral thesis.

It is important, however, that the results obtained in the thesis be interpreted with consideration of potential limitations of the thesis as a whole, and the studies completed in particular. The thesis had four major sources of limitation:

Firstly, the literature review, completed in 2008, and subsequent literature searches for references in the articles, were limited to English articles related to empirical, quantitative studies published from 1990 onwards, and these articles were obtained using specific keywords. Thus relevant articles written in other languages, or that used largely qualitative

analyses, were not accessed by the selected keywords, and were published prior to 1990, were excluded.

Secondly, the articles selected for review concentrated on comorbid psychopathology in individuals with substance use and related problems. As such, articles in which individuals with mental illness were examined for comorbid substance use, were regarded as peripheral to the thesis, although recognition of this form of comorbidity was not overlooked. The inpatient studies, by extension, also focussed on individuals who had been identified with substance use problems, and examined these individuals for comorbid psychopathology.

Thirdly, the different studies had some differing demographic variables, substances of use, and psychopathology of interest. This strengthened the overall information obtained from the studies by examining a variety of factors that might be pertinent to comorbidity, as mentioned earlier, but limited potential comparisons between studies. In addition, psychopathology comparisons between the studies could not be done because different assessment instruments were used in the studies. For example, the CIDI and C-DIS IV are diagnostic instruments and, as such, provide diagnoses of psychiatric disorders. In comparison, the high school students used epidemiological scales to identify psychopathology. The scaled scores reflect symptoms and relative severity of psychopathology, but do not provide diagnoses that are comparable to those of the CIDI or DIS. Furthermore, the CIDI and DIS both provide diagnoses based on DSM IV criteria. However, the CIDI has been validated for use cross-culturally (Wittchen et al., 1991), including in South Africa, but has been reported to be time-consuming to administer (Williams et al., 2004). In comparison, validation of the DIS has proven to be more difficult although the instrument has been found to be reliable (mean k=0.69), sensitive (mean sensitivity=75%) and of high specificity (mean specificity=94%) (Robins et al., 1981), and has greater flexibility with respect to the duration of the interview than does the CIDI.

Fourthly, the data for the studies were collected at different times. Thus factors pertinent to the period in time when the data were collected, and which influenced the factors examined in the studies, might have had different effects at these different times, with implications for comparisons across the studies. For example, crystal methamphetamine use increased during the period in which the studies for this thesis were completed (van Heerden et al., 2009). The prevalence of methamphetamine use in the earlier studies [high schools (1997) and SASH (2002-2004)] is likely to under-estimate the prevalence of methamphetamine use in the same communities at the time that the inpatient substance user studies were conducted (namely, 2008 to 2009).

Lastly, the use of self-reports to elicit information about substance use and psychiatric disorder could be a source of limitation in the study. The data obtained relied on the honesty of study participants to provide information truthfully, and accurately, and relied on participants' ability to recall events accurately. However, the information obtained was not verified from sources other than the study participants and the studies did not control for factors such as social desirability bias.

Conclusion and suggestions for further research

This thesis has examined an area of research, namely comorbidity of psychopathology and substance use, an area that has not been subjected to rigorous research attention within the South African context. The findings of this thesis have highlighted the common occurrence of co-occurring psychopathology and substance use, particularly in adolescents and young adults in Cape Town and in South Africa. Such co-occurrence has been associated with increased service utilisation for mental illness, substance use and physical illness (Clark et al., 2009), with cost, intervention, treatment and continued management implications for the

State and for the families of the individuals involved. In addition, knowledge about the nature of associations between psychopathology and substance use and related disorders, remains lacking. For example, the pathways to the development of either the psychopathology and/or the substance use remain unclear and in need of further investigation (Weinberg and Glantz, 1999; Volkow, 2001), particularly relating to possible causal associations between psychopathology and substance use.

More specifically, the empirical studies conducted for this thesis can be used to guide further research, partly by generating new questions based on the research completed, and partly by suggesting ways in which the completed research can be improved upon.

For example, a replication of the high schools survey could examine comorbid psychopathology and substance use in relation to severity of the psychopathology, severity of the substance use, and the role of multiple substances of use in comorbidity. These students could be assessed to examine details regarding the age of onset of disorders relating to psychopathology and substance use. A replication of this study could also (as mentioned previously) provide details about the substances used by current students, compared with the substances used in the original study (1997), thus allowing for the tracking of substance use and associated psychopathology over time. Attempts could be made to verify the sensitive information required, for example, relating to substance use or the occurrence of traumatic events as this might have been subject to a social desirability bias. Furthermore, it would be useful for the high school students to be followed up in a cohort design as this would provide information regarding the antecedents, pre-cursors and possible risk or protective factors of subsequent substance use or psychopathology, and identify mediators of associations, or potential consequences for baseline characteristics (Kleschinsky et al., 2009). To overcome some of the problems encountered with previous attempts at this, the follow up studies will need to minimise attrition. The latter authors (Kleschinsky et al., 2009) have cited monetary

incentives, comprehensive future contact information, frequent field tracking, and searching private and public databases as means of ensuring follow up contact. These techniques might be subject to limitations, including funds, ethical and confidentiality considerations, and the availability of alternative sources of contact, particularly in developing countries where infrastructure might be less-sophisticated than in developed countries. It would thus be important that the follow-up be planned, and be built into the methodology of the studies.

Further research with substance users in inpatient treatment is also needed. A larger and more representative sample of inpatient substance users would have enabled the results to be more generalisable to other inpatient substance users, as well as enabling greater reliable comparisons with representative community studies. As previously mentioned, substance use treatment centres vary in their treatment and/or admission modalities. Further investigations with more representative samples of inpatients might thus better reflect the characteristics of the substance users at these treatment facilities. Studies of comorbid psychopathology and substance use in substance using inpatients could record details regarding the onset of psychopathology, and possibly examine the role of lifetime psychopathology in substance use and its development. The prevalence of tobacco use in this population could be further investigated to examine the role of cigarette use in the development of other substance use, to identify temporal associations between psychopathology and substances of use, and to determine the effects of physical illness associated with tobacco use on psychopathology, other substance use and treatment outcomes. Furthermore, studies of comorbidity in clinical samples could include investigating samples of psychiatric inpatients who use substances, as these could potentially provide comparative information regarding the role of the so-called primary disorder in the development of the so-called secondary disorder .

Similarly, the follow-up study of inpatients would have benefitted from a larger baseline sample size as this would potentially have increased the size of the follow-up sample with

advantages for study power particularly related to sub-group analysis. The value of studies that follow up inpatient substance users, lies in the potential to provide information regarding the efficacy of treatment, and to identify the roles of patient and other factors in treatment outcomes. It would thus be of benefit to pursue further investigations of substance users discharged from inpatient substance use treatment to gauge their progress and identify risks for poor outcomes. Such information could inform treatment policies and interventions to ensure improved outcomes. In a similar vein, follow up of a general population sample, such as the SASH sample, could provide information on the role of comorbidity in mortality, or on the development of either the psychopathology or the substance use in the community over time.

Globally, many studies have engaged, and are currently engaged, in identifying the prevalence of psychopathology, substance use and associations between these. This thesis has contributed to the available data by providing information relating specifically to South Africa and the city of Cape Town. However, more research is required to provide information on the treatment of comorbid psychopathology and substance use (McHugo et al., 2006; Kaminer et al., 2007). Thus, in conclusion, it is sincerely hoped that this thesis will encourage further research into comorbid psychopathology and substance use, with particular emphasis on the ways in which the research findings can be used to develop effective treatment for the individuals affected by such comorbidity.

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Table 1: Summary of thesis studies

	STUDY			
Study characteristics	**High school students**	**Inpatient substance users (baseline)**	**Inpatient substance users (follow-up)**	**SASH**
Chapter in thesis	3	4	5	6
Design	Cross-sectional, random, representative, community sample of high school students	Cross-sectional, consecutive, not representative, treatment sample of inpatient substance users	Cross-sectional follow-up sample of inpatient substance users after discharge from inpatient treatment	Cross-sectional, random, representative, community sample
Sample size	939	95	86	1766
Age	14-24 years	17-30 years (Mean 23.0 years; SD 2.9)	17 to 30 years (Mean 23.0 years; SD 3.0)	18-30 years (Mean 23.6 years; CI 23.4-23.8)

Gender	Male (42.5%) and female	Male (89.5%) and female	Male (88.4%) and female	Male (46.3%) and female
Psychopathology diagnoses	Depression Anxiety Post-traumatic stress disorder	Any current	Any current	Current or lifetime mood and anxiety disorders
Psychopathology instrument(s)	Beck Depression Inventory Zung Self-rating Anxiety Questionnaire Harvard Trauma Questionnaire	Diagnostic Interview Schedule for DSM IV	Diagnostic Interview Schedule for DSM IV	CIDI 3.0
Substance use variables	Ever smoked a whole cigarette Ever had more than a few sips of alcohol Ever smoked cannabis	Any, excluding cigarettes First substance(s) of use Most frequently used substance(s)	First substance(s) of use, excluding cigarettes Most frequently used substance(s), excluding	Ever smoked >100 cigarettes Ever drank alcohol Ever smoked cannabis Ever used medication

	Ever used inhalants		cigarettes	for extra-medical use Ever used hard drugs
Follow up variables	Not applicable	Not applicable	Completed inpatient treatment Relapsed Still/Back in substance use treatment	Not applicable
Substance use instrument	Questionnaire	Diagnostic Interview Schedule for DSM IV Interview Schedule	Interview Schedule	CIDI 3.0
Statistical analyses	Logistic regression using survey design analyses	Logistic regression	Logistic regression	Logistic regression
Evidence found for significant associations between psychopathology and substance use **or treatment outcomes for substance use**	Yes	Yes	Not applicable Yes (marginal)	Yes

Specific statistically significant associations	PTSD and all substances Depression, alcohol and cannabis Anxiety and cannabis	Specific phobia and cannabis as the first substance of use	Primary crystal meth use, and inpatient treatment completion (marginal) Crystal meth as first substance, and relapse (marginal) Current Major Depression and resumption of substance use treatment (marginal)	Increased risk of any mood disorder with substance use